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Coláiste na Tríonóide, Baile Átha Cliath

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**A mixed-methods approach to explore the association  
between age and medication -related problems among  
adults**

A thesis submitted for the degree of

**Doctor of Philosophy**

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By

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# **Abstract**

## **General introduction**

Much attention was focused on the ageing phenomenon and how to improve the quality of life in older people. Medication-related problems (MRPs) can potentially lead to hospital admissions, increased morbidity, mortality, and heightened healthcare costs. Understanding the various risk factors contributing to medication-induced hospitalisations is critical for enhancing patient outcomes in healthcare settings. Older patients have been the primary research focus concerning medication induced-hospital admissions, and most of the associated MRPs have been deemed preventable. Medication-related hospital admissions are a substantial concern in Ireland and worldwide. Research findings on the role of age as a risk factor for these admissions have been varied. The aim of this thesis was to explore the association between age and MRP among adult patients in Ireland and internationally.

## **General method**

This thesis included triangulation between three studies to meet the aim of the thesis. (1) systematic review and meta-analysis, (2) mixed-methods secondary data analysis of the national inpatient experiences survey, (3) mixed-methods content analysis of newspaper articles in Ireland reporting on medication-related harm.

### **(1) Systematic review and meta-analysis**

The literature about the strength of age as a predictor of MRPs and medication-related admission (MRA) is equivocal. Therefore, the aim of this review was to investigate the association between age and MRA to determine if age is statistically associated with MRA, by undertaking systematic review and meta-analysis.

## **Method**

A comprehensive electronic search for relevant studies was undertaken in eight databases. All adult patients aged  $\geq 16$  years were included in this review. The review included all studies that reported hospital admission caused or contributed to by MRAs, including

adverse drug event (ADE), ADR, medication error (ME), and medication non-adherence from the year 2000 that were published in the English language. The Joanna Briggs Institute's (JBI) tool provided by Munn and colleagues from the methodological working group of the Joanna Briggs Institute's "Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data" was used, following necessary modifications, to assess the quality of included studies. Only studies with similar data reporting the proportion of each age category and applying the same categorization to age were pooled and analysed using meta-analysis.

## **Results**

This review identified 48 studies that met the inclusion criteria and were included in the narrative analysis. The total sample size across these included studies was 174,641 patients. There was a meta-analysis generated from this review, comprising 11 studies, aimed to compare the effect size of odds ratios within different age categories within the MRA group. The findings suggest that age is an independent risk factor for MRA in young adults rather than older adults. The quality assessment of the included studies indicated that most studies exhibited moderate quality (n=28). A subset of the remaining studies demonstrated high quality (n=16), while four studies were classified as low quality.

## **Discussion**

This review concludes that younger adults rather than older adults are at an increased risk of MRA. The findings suggest caution against an overemphasis on older age in policy, practice, or research about managing MRA. Future research should explore the independent risk factors contributing to MRA, to inform associated policy and practice. Moreover, it is recommended that further research use a consistent approach to defining age categories. Additionally, when examining the association between age and MRA, adjustments for confounding factors should be considered.

### **(2) Mixed-methods secondary data analysis of the national patient experience survey**

Medication experiences can vary significantly from patient to patient, depending on factors such as the patient-, drug- and organisation-related issues. Substantial attention has been focused on understanding medication management experiences among older patients. Yet, evidence remains scarce regarding the medication experiences of younger adults in a hospital setting. The aim of the study was to describe the medication-related experience of

adults receiving inpatient care in Ireland and to explore the association between age and the submission of free text comments describing negative and positive medication experiences.

## **Method**

This cross-sectional study used secondary data analysis from national patient experiences survey and adopted a sequential explanatory mixed-methods research design. The process involved a comprehensive analysis of both quantitative and qualitative data to enhance understanding of the medication-related experiences of adult inpatients. The quantitative analysis identified the frequency and nature of medication-related experiences and the relationships between demographic or clinical variables and medication-related experience. The free-text responses were qualitatively analysed using thematic analysis to describe the inpatients medication-related experience and to identify targets for improvement.

## **Results**

The results identified that 1577 (4%) out of 39,453 respondents provided comments related to medication., and most (78.4%) of these comments were negative. Younger patients (aged 16 to 64 years) were significantly more likely than older patients ( $\geq 65$  years) to submit a negative comment. An association was also identified between submission of a negative medication experience and overall rating of hospital experience, suggesting that those who experienced a medication-related problem had a poorer hospital experience overall. The qualitative analysis uncovered several themes including: the professional tasks associated with the patient obtaining their medication, the patient's sense of safety and security of medication management, transitional care management, receipt of medication information and patient education, and general care about medication.

## **Discussion**

This secondary analysis identified the challenges faced by adult inpatients with regard to medication during their hospitalisation and at discharge, highlighting the need for better medication processes and communication. Enhancing the quality of prescribing and ensuring that patients receive sufficient information about their medications is crucial.

### **(3) Mixed-methods content analysis of newspapers articles in Ireland reporting on medication-related harm.**

Mass media, including newspapers, provides a popular and reliable source of health information for the general public. Newspapers are important in disseminating health-related news due to their wide readership and easy accessibility. The aim of the study was to describe how MRH, and its association with age, has been reported to the public in Irish newspapers through selected years.

## **Method**

This content analysis study adopted a sequential explanatory mixed-methods approach. The years 2019, 2009, and 1999 were selected to provide an overview of reporting across three decades. A systematic search strategy was employed using the LexisNexis database to search for medical coverage in Irish newspapers. Quantitative content analysis was used to identify the frequency and nature of MRH reporting, and its association with age. Quantitative thematic content analysis was used to summarise the MRH reporting messages available to the Irish public.

## **Results**

This study identified 95 MRH patient cases reported in 78 Irish newspaper articles during the years 2019 (n= 68 cases, 51 articles), 2009 (n=20,20), and 1999 (n=7,7). Non-fatal and non-permanent harm was most frequently (56%) reported. Reports of fatal cases had a similar frequency across younger and older adults. Adults aged 16-64 years were the most frequent subject of the reported MRH cases and the most cited medications were the central nervous system medication, antineoplastic and antiparasitic drugs. The four main themes identified were the professional tasks associated with obtaining medications, patient sense of safety and security of the medication management process, medication information and patient education, and general care about medication.

## **Discussion**

This study identifies an increasing frequency of MRH reporting over-time, about a variety of MRH types and severity, ranging from minor to fatal. The reports provide the public with insights into medication-, patient- and provider-specific issues associated with MRH, and the impacts associated with these. No association between reported MRH and patient age was apparent.

## **General results**

The findings from the two studies undertaken in Ireland (inpatient experience and newspaper coverage of MRH) are consistent with the key finding from our systematic review that there is an absence of an association between age and MRP, including MRA. This suggests that younger people are as likely to experience MRP, including MRA and MRH, as older people and that newspaper reports communicate this to the public. The inpatient experience study found that a lack of communication contributed to medication error, resulting in adverse health outcomes. The newspaper coverage of MRH study found evidence reporting that a lack of information provision during medication prescribing and dispensing disabled patients from supporting their own medication safety.

The triangulated findings from this thesis highlight the need for patients and/or families, regardless of age, to be better involved and heard in their medication management and for future research to better understand the risks for MRA.

## **Conclusion**

The evidence in this thesis supports recommendations to enhance our understanding of risks for medication-related hospital admission and to enhance equitable medication management based on age. Strategies to enhance communication about medication management and to bolster the public's confidence in the safety and security of medication management services should be a priority.

## **Declaration**

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university and it is entirely my own work.

I agree to deposit this thesis in the University's open access institutional repository or allow the Library to do so on my behalf, subject to Irish Copyright Legislation and Trinity College Library conditions of use and acknowledgement.

I consent to the examiner retaining a copy of the thesis beyond the examining period, should they so wish (EU GDPR May 2018).

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**Reema M Munshi**

30/09/2023

## **Dedication**

This dissertation is dedicated with a unique feeling of gratitude and thanks for all the inspiration and support to my lovely mother, **Asia Bahar** and the soul of **Mohammad Munshi** (may God have mercy on him), who was the best Father.

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*“go raibh maith agat”*

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## **List of Awards, Presentations and Publications**

### **Conferences peer reviewed publication:**

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Munshi R, O'Shaughnessy E., Grimes T., Age-related hospitalisation resulting from medication-related problems: A systematic review protocol. 11<sup>th</sup> Medication safety conference, Abu Dhabi, United Arab Emirates, November 2-4, 2018, Poster Presentation, PRESENTED.

## Abbreviations

|            |                                                              |
|------------|--------------------------------------------------------------|
| <b>ADE</b> | <b>Adverse drug event</b>                                    |
| ADR        | Adverse drug reaction                                        |
| ATC        | Anatomical therapeutic chemical classification system        |
| DDD        | Defined daily dose                                           |
| ED         | Emergency department                                         |
| GRAMMS     | The Good Reporting of a Mixed Methods Study                  |
| HIQA       | The Health Information and Quality Authority                 |
| HIQA       | The Health Information and Quality Authority                 |
| HSE        | The Irish Health Service Executive                           |
| MRA        | Medication-related admission                                 |
| MRH        | Medication-related harm                                      |
| MRP        | Medication-related problem                                   |
| NPES       | The Irish National Patient Experience Survey                 |
| OR         | Odds ratio                                                   |
| PIM        | Potentially inappropriate medications                        |
| PIP        | Potentially inappropriate prescribing                        |
| PROMPT     | The Prescribing Optimally in Middle-aged People's Treatments |
| REC        | Research Ethics Committee                                    |
| SD         | Standard deviation                                           |
| TCD        | Trinity College Dublin                                       |
| UK         | The United Kingdom                                           |
| US         | The United States                                            |

# Chapter 1 : Introduction

## 1.1 Medication-related harm

The global consumption of prescribed medications has increased in recent years [1, 2]. This rise can be partly attributed to continuous advancements in the pharmaceutical industry, which have led to the production of a wider variety of drugs [2]. Furthermore, the emergence of new diseases has also increased the demand for medications and contributed to rising healthcare costs [3]. The outcomes of using these medications can vary significantly. Their use might produce the desired therapeutic effects, cause minor adverse effects or, in extreme cases, lead to fatal consequences [2]. Indeed, medications are the most common cause of harm to patients in healthcare systems worldwide [4].

The World Health Organisation's (WHO) third global patient safety challenge, Medication Without Harm, launched in 2017, aimed to decrease the global impact of medication-related harm by 50% over five years to the end of 2022. This recent challenge called on health ministers worldwide to implement national strategies to target four domains of medication safety: (1) the nature of medication products, (2) patient and public engagement, (3) health care professionals and systems and (4) practices of medication. The WHO has also focussed on three priority areas of medication safety that have the most significant impact on patient safety: high-risk situations, polypharmacy and transitions of care [4].

These three priorities intersect in several ways as many patients face combined risks from adverse reactions, polypharmacy and miscommunication. Medical professionals should particularly concentrate on patients at a greater risk of either severe disease or death due to harm associated with medication [4, 5]. These priorities align with this thesis's aim, primarily investigating the most prevalent risks of adverse drug reactions and medication management. Notably, this global patient safety challenge concentrated solely on medication-related harm (MRH), regardless of age. MRH can be defined as "any negative patient outcome or injury related to medication use, irrespective of severity or preventability" [6].

## 1.2 Concepts of MRH

Medication-related problem (MRP) is an umbrella term defined as "An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" [7], and they can occur at any stage of the medication process, such as

prescribing, transcribing, dispensing, monitoring or administration. Most preventable adverse events occur during the prescription (56%) and administration of drugs (34%) [8]. They may include errors such as incorrect dosages or drug interactions, as well as patient non-adherence to medication regimens [9]. The rate of MRPs can vary widely depending on the population studied, the setting, and the specific drugs involved. These variables will be discussed in more detail throughout the introduction.

The extensive use of medications presents a fertile ground for MRPs to occur [10]. An MRP can also be described as a negative outcome due to medication (mis)use and may lead to patient harm [11], either through non-preventable medication adverse effects or by potentially preventable medication errors [9], and/ or failure to achieve treatment goals [11]. A proportion of this harm is severe and could cause or contribute to a patient being hospitalised. A systematic review conducted on hospitalised adult patients found that the prevalence of MRPs ranged from 4.4% to 12.1% of patients [12]. The concept of MRPs, also called drug-related problems, represents all issues that may potentially affect the success of pharmacotherapy, including medication error, adverse drug event (ADE), adverse reactions to medicinal products and adverse drug reaction (ADR) [13, 14]. These concepts overlap between themselves and with MRPs, and each concept has multiple reported definitions. The inconsistency in the terminology and definitions related to medication safety outcomes in the literature leads to challenges in comparing findings across different studies [6].

An ADE is defined as ‘An injury resulting from medication intervention related to a drug’ [15]. The reported prevalence of ADE-related hospitalisations (at the time of admission and those occurring during a hospital stay) varies, for example, 3.2% of hospitalised patients in England, 4.8% in Germany and 5.6% in the United States in a study of hospital administrative datasets [16]. Approximately 15% of hospitalised patients in general internal medicine have been reported to experience ADEs [17]. ADE is a general concept that encompasses harm in the form of an ADR, and error in the form of medication error, which is a preventable ADE [18]. The WHO defines adherence as ‘the extent to which the patient follows medical instructions’ regarding diet, medication and lifestyle changes [19]. Medication non-adherence can negatively affect the health outcomes of patients suffering from short- and long-term conditions [20]. In 2018, a systematic review aimed to estimate how often non-adherence to medication leads to hospital admissions. The study analysed 24 prospective observational studies and found a median prevalence rate of 4.29% of patient

admissions to hospital were as a consequence of medication non-adherence. The main causes of this non-adherence were medication costs and side effects, and cardiovascular medicines were most commonly involved [20].

Medication error has multiple reported definitions, including ‘An error in the stages of the medication process ordering, dispensing, and administering and monitoring the effect causing harm or implying a risk of harming the patient’ [21, 22] and ‘any preventable event that may cause or lead to inappropriate medication or patient harm while the medication is in the control of the healthcare professional, patient or consumer’ [15]. Much attention has been focussed on ADEs and medication errors to reduce the likelihood of harm related to medications. There is an overlap in the description of the errors and the patient harm contributed to by medications. Harm caused by errors has been classified into five degrees: no harm, low harm, moderate harm, severe harm and death [23] (**Table 1-1**).

Table 1-1: Classification of error by the degree of harm caused according to the UK National Patient Safety Agency [23]

| Degree of harm | Definition by National Patient Safety Agency                                                                                                                                   |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| No harm        | Impact prevented: any patient safety incident that had the potential to cause harm but was prevented, resulting in no harm to the person(s) receiving NHS-funded care.         |
| No harm        | Impact not prevented: any patient safety incident that ran to completion, but no harm occurred to the person(s) receiving NHS-funded care.                                     |
| Low harm       | Any patient safety incident that required extra observation or minor treatment and caused minimal harm to the person(s) receiving NHS-funded care.                             |
| Moderate harm  | Any patient safety incident that resulted in a moderate increase in treatment, and which caused significant but not permanent harm to the person(s) receiving NHS-funded care. |
| Severe harm    | Any patient safety incident that resulted in permanent harm to the person(s) receiving NHS-funded care.                                                                        |
| Death          | Any patient safety incident that directly resulted in the death of the person(s) receiving NHS-funded care.                                                                    |

There are multiple definitions of an ADR. In 2001, the European Parliament and Council defined an adverse reaction as ‘a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function’ [24]. In 2010, this was modified to ADR,

defined as ‘noxious and unintended responses to medicinal products not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse and abuse of the medicinal product’, thereby broadening the eligible context [25]. The WHO (1972) defined an ADR as ‘a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function’ [26]. Both the European Parliament and Council’s 2001 definition [24] and the WHO’s 1972 definition [27] focus on therapeutic, prophylactic or diagnostic uses of drugs and are silent regarding harm arising consequent to non-adherence, medication errors or drug interactions. Consistent with the heterogeneity of definitions of adverse (drug) reactions, there is variation in the definitions employed in the literature and consequent variation in the reported prevalence ranges. A retrospective study of adult patients receiving medical care in hospital estimated the frequency of ADR-induced hospital admissions to account for 5.8% of patients [28], **Table 1-2**.

Table 1-2: Overview of key medication-related concepts and definitions.

| Concept                  | Definition                                                                                                                                                                                                                                                                                                                          |
|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MRP                      | “An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes” [7]                                                                                                                                                                                                          |
| ADE                      | “An injury resulting from medication intervention related to a drug” [15]                                                                                                                                                                                                                                                           |
| ADR                      | “noxious and unintended responses to medicinal products not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse and abuse of the medicinal product’, thereby broadening the eligible context” [25] |
| Medication error         | “An error in the stages of the medication process ordering, dispensing, and administering and monitoring the effect causing harm or implying a risk of harming the patient” [21, 22]                                                                                                                                                |
| Medication non-adherence | “the extent to which the patient follows medical instructions’ regarding diet, medication and lifestyle changes” [19]                                                                                                                                                                                                               |

Inconsistencies in the use of terminology and definitions related to medication safety, such as ADEs, ADRs, potential ADEs, medication errors and MRPs, have been reported in previous studies [29, 30]. These inconsistencies have made it difficult to accurately compare and report outcomes across studies [6], as described by the variations in definitions used for

ADRs in **Table 1-3**. A previous systematic review identified multiple definitions for each term, emphasising the need for a standardisation of terminology [30].

Table 1-3: The differences in the definitions of ADRs employed in previous studies.

| Author(s)                  | Year | Definition used                         |
|----------------------------|------|-----------------------------------------|
| Brvar <sup>[28]</sup>      | 2009 | WHO definition for ADR                  |
| Davies <sup>[31]</sup>     | 2009 | Edwards and Aronson definition for ADRs |
| Kongkaew <sup>[32]</sup>   | 2013 | Modified WHO definition for ADRs        |
| Pedrós <sup>[33]</sup>     | 2014 | European Union definition for ADRs      |
| Pirmohamed <sup>[34]</sup> | 2004 | Edwards and Aronson definition for ADRs |

ADR: adverse drug reaction; WHO: The World Health Organisation.

Similarly, different approaches have been used to identify and report MRP in hospitals, including chart reviews [35], computer monitoring [36], incident reports [37], interviews [38], direct care observations [39] and prospective data collection [40]. Each method has its own advantages and disadvantages, and there is no standard method for detecting all types of MRPs. Using incident reporting to track trends over time is questionable, and combining methods such as chart review and computer monitoring could provide a more comprehensive view and valid estimate [41].

### 1.3 MRP-induced hospitalisation in different health care settings

MRPs can manifest across various healthcare contexts, posing risks to patient well-being. These MRPs can lead to hospital admissions, creating a complex challenge for healthcare systems. MRPs can occur during hospitalisation, potentially prolonging a patient's stay, or even at the point of discharge, possibly resulting in readmission shortly after the patient leaves the hospital. A review of observational studies of 22 European studies aimed to estimate the percentage of ADRs across various hospital settings, regardless of the specific definition of ADR used [42]. This included examining the number of patients who experienced ADRs leading to hospital admission, those who developed ADRs during their hospital stays and those who encountered ADRs in outpatient settings. The findings from this review highlight the substantial volume of research conducted on ADRs that result in hospitalisation and those that occur during a hospital stay. The results indicate that the

median percentage of hospital admissions resulting from ADRs was 3.6% (ranging from 0.5% to 12.8%), and 10.1% of ADRs developed during hospitalisation [42]. MRPs that cause or contribute to hospital admissions are discussed more comprehensively in the next Section 1.5.

### **MRP during hospitalisation**

Hospitalisation resulting from MRPs carries associated health and economic burdens for both patients and healthcare systems [43, 44]. MRPs are a relatively common cause of morbidity, hospitalisation [41], mortality (particularly from ADRs) [45] and increased costs [44] and may interfere with the achievement of optimal patient outcomes [46]. A systematic review of retrospective and prospective studies in 2014 reported that 12.1% of adult hospitalisations for those aged  $\geq 18$  years were associated with MRPs [12]. That finding was higher than the prevalence of 3.7% of patients with medication-induced admissions reported in another systematic review in 2007, which included prospective medical record review studies identifying potential medication-induced admissions among patients aged  $\geq 16$  years [47]. In 2020, however, a systematic review and meta-analysis of observational studies on preventable medication harm across medical care settings was undertaken. It found that around 3% of patients are exposed to preventable MRH in medical care, with the highest rate of preventable medication harm, 11%, seen in older patient care. In contrast, it was found that child- or adolescent-based studies reported lower prevalence of preventable harm [48]. This finding underscores that a considerable portion of MRH in the older population is preventable, whereas the proportion of preventable MRH is considerably lower in the younger adult population. Therefore, exploring strategies for addressing non-preventable medication harms in adult (non-older) patients is crucial.

### **MRPs after hospital discharge**

Some studies provide insight into the prevalence of MRPs in patients following hospital discharge, and these MRPs may potentially contribute to readmissions. A systematic review evaluated available evidence on the prevalence and nature of MRH following hospital discharge. It found that for adult patients (excluding the older), ADR affected 15.7% to 20.4% of discharged patients. ADEs prevalence among adult patients (excluding the older)

ranged between 11% and 24%. Meanwhile, ADEs were noted to be within the range of 18.7% to 37% of post-discharge older patients, and ADRs were noted among 27% to 51% of older patients. Indeed, this study reported that a slightly higher range of older people were affected by ADRs and ADEs after hospital discharge [49]. Another retrospective cohort study aimed to assess the risk of hospital admission due to ADRs following discharge, comparing it to admissions unrelated to ADRs in adult patients aged  $\geq 18$  years. The results suggest that patients with a history of ADR-related admissions face a significantly higher risk of experiencing ADR-related admissions again in the short and long term [50].

## 1.4 Risk factors leading to medication-induced hospitalisation

Understanding the various risk factors contributing to medication-induced hospitalisations is critical for enhancing patient outcomes in healthcare settings. There is no doubt that ageing poses challenges to safe medication use, and life expectancy has increased over time. However, evidence reports that MRPs resulting in hospitalisations could be more strongly associated with factors other than age [3, 51]. Still, this thesis will specifically centre on age-related factors to better understand the emphasis on age as a risk factor.

### 1.4.1 Age

Much attention was focussed on ageing and how to improve quality of life for older people. Research, policy and clinical practices emphasised older age groups. For instance, studies have examined MRP [52] and polypharmacy [53, 54] in the context of older cohorts only.

### Tools used in older patients with medication resulting in hospitalisations

Various tools have been developed to detect potentially inappropriate prescribing (PIP) and the quality of prescriptions, as well as to manage clinical outcomes exclusively in older cohorts, such as anticholinergic scales [55, 56], the medication appropriateness index [57, 58] and the Beers criteria [59]. The GerontoNet ADR risk score was validated as a method of identifying patients who are at an increased risk of an ADR. Its validity was confirmed through testing across four geriatric and internal medicine wards in European hospitals [60]. However, when tested on older patients admitted to a university teaching hospital in Ireland,

it was found that the GerontoNet ADR risk score did not reliably predict ADRs in nearly 40% of cases. Because of that, it was reported by the study authors to be [61]. Nevertheless, evidence suggests that the GerontoNet ADR risk score could serve as an effective way to identify older inpatients with complex comorbidities at an elevated risk of experiencing ADRs. This evidence emerges from studies conducted at three academic hospitals in Italy. In these cases, it exhibited good diagnostic accuracy [62].

There are some instruments found to be suitable for detecting medication-induced hospital admissions. The STOPP & START criteria serve as a valuable method for identifying potentially inappropriate medications (PIMs) and potential prescribing omissions in older patients during hospitalisation [63]. Several versions of STOPP & START have been published since the original in 2008 [64] with the second version in 2014, incorporating revisions and additions based on new evidence and expert consensus [63]. A third version has been published in 2023 [65]. In Version 2, the expert panel agreed upon a final list of 114 criteria for STOPP/START, comprising 80 STOPP criteria and 34 START criteria, marking a 31% increase from Version 1 [63]. Version 3 offers an explicit list of the 133 medications that should be discontinued in older adults, marking an increase of 80 medications compared to Version 2. Additionally, Version 3 provides an explicit list of the 57 medications that should be started, reflecting an increase of 23 medications since Version 2 [65].

The STOPP & START version 2008 criteria have been deemed suitable for identifying older individuals who are at risk of preventable medication-related hospital admission, particularly in patients taking two or more PIMs [66]. However, the Beers criteria, another tool developed to detect PIM in older patients did not established a connection between identified PIMs and medication-related admissions [66]. The drug-related hospital admissions (DRA) adjudication guide, another method was developed to detect hospital admissions of older adults resulting from ADRs, and its reliability was satisfactory [67].

Furthermore, several European-funded research projects focus on medication management and the prevention of ADRs in older cohorts only. For example, SENATOR is a software engine for the assessment and optimisation of drug and non-drug therapy in hospitalised older persons with multimorbidity and polypharmacy [68, 69]. Similarly, OPERAM is a project aiming to enhance pharmacological and non-pharmacological treatments among

individuals aged  $\geq 70$  years who have multiple health conditions, with a specific focus on minimising preventable hospital admissions. [70].

On the other hand, in a recent systematic review concentrating on middle-aged adults (aged 45 to 64 years), explicit criteria were identified for defining PIP. This review analysed 22 studies and found that PIP was defined using a total of 15 different criteria. Notably, only one set of criteria, the Prescribing Optimally in Middle-aged People's Treatments (PROMPT) criteria, was specifically designed for middle-aged adults [71], and it is potentially applicable in the primary care prescribing or dispensing stages [72] also applicable to detect PIP at hospital admission [73].

### **Physiology and pharmacokinetics**

Advancing age is characterised by various changes in pharmacokinetics and pharmacodynamics, including age-related renal or hepatic function decline and increasing sensitivity to several drug classes [74]. Pharmacokinetic alterations manifest as a consequence of the natural ageing process, driven by inevitable anatomical and physiological transformations over time. These changes involve the gradual loss of functional units within organs, such as nephrons and neurons, and disruptions in regulatory mechanisms between cells and organs [74]. Consequently, these age-related modifications lower various bodily systems' functionality. The decline in liver mass and reduced liver blood flow associated with ageing lead to a decrease in first-pass metabolism [75, 76]. This reduction results in an increased bioavailability of drugs that typically undergo extensive first-pass metabolism [77]. In healthy older individuals, liver function tests assessing processes like metabolism, elimination of certain substances and other relevant functions do not reveal significant differences between those aged 50-69 and those aged 70-89 [76, 78]. However, age-related declines in renal function, particularly in the glomerular filtration rate, can significantly impact the clearance of various drugs, such as diuretics [79], digoxin [80] and nonsteroidal anti-inflammatory drugs [81]. However, the clinical significance of these reductions in renal excretion depends on the potential toxicity of the specific drug. Additionally, the effect of age on drug sensitivities is influenced by age-related pharmacodynamic changes. For instance, a decline in acetylcholine levels in the ageing brain can lead to a rise in sensitivity to the anticholinergic effects of antipsychotic medications [76].

Despite these age-related physiological changes, clinical trials often exclude older patients or lack adequate evidence and knowledge about how older patients respond to medications [82, 83]. Consequently, assessing the specific effects of ageing in many trials becomes challenging. Even in studies encompassing a wide age range, most do not adequately control for significant clinical variations between participants of different ages, making it difficult to distinguish the independent impact of chronological age [83].

### 1.4.2 Comorbidity

Some studies have recognised comorbidity as a risk factor for patients experiencing MRPs. In a prospective, multicentre study conducted by Leendertse *et al.* [9], comorbidity was identified as a risk factor for preventable medication-related admissions in adult patients, even after adjusting for polypharmacy and medication adherence, OR (95% CI): 8.1 (3.1–21.7) [9]. Another multicentre survey established that comorbidity is a risk factor for patients with severe ADRs that leads to hospital admissions in older patients < 65 years, OR (95% CI): 1.12 (1.05–1.20) [84]. In contrast, in a retrospective case-control study involving adults over 18 years and focussing on fatal ADRs, multivariate correlation analysis revealed that the frequency of severe ADRs was not associated with either comorbidity or age [85].

### 1.4.3 Polypharmacy

It is well known that the consumption of medications is most considerable in older adult patients. In Ireland, it was estimated that from 1997 to 2012, there was an increase in the prevalence of polypharmacy (the use of five or more medications daily) from 17.8% to 60.4% in patients aged  $\geq 65$  years [1]. There has been a definite increase in polypharmacy in recent years, particularly among both middle-aged and older cohorts; it is estimated to have increased from 8.3% to 30.2% for those aged 45-64 years and risen from 17.8% to 60.4% for those aged 65 years [1]. This indicates that polypharmacy and its associated complications are not exclusive to older adults but can affect individuals across the adult spectrum. Another study observed that the number of medications was a stronger risk factor associated with an increased incidence of MRPs than age or gender among patients with polypharmacy [51]. Hence, age does not seem to be an independent risk factor for ADRs [86]. Between 1995 and 2010 in Scotland, the proportion of adults dispensed five drugs or

more per month increased from 11.4% to 20.8% [87]. Meanwhile, the proportion of adults dispensed 10 drugs or more per month increased from 1.7% to 5.8%, (40–49 years 1.7%, 50–59 years 4.1%, 60–69 years 8.7%). The association between age and burden of drug use was strong, and the number of drugs dispensed rose with increasing age [87]. A systematic review in 2008 described the prevalence of hospital admission with ADRs across three age groups (children, adults and the older), drawn from prospective studies that used the WHO definition of ADR [32]. The prevalence of ADR-related admissions was reported as being higher in older patients due to the comorbidity and number of medications used for these people [32].

Although polypharmacy is occasionally linked to old age, this association is not consistently observed [1, 87]. In a retrospective cohort among older veterans, the proportion of all unplanned hospital admissions due to ADRs was 10% in older patients aged 65 years, and polypharmacy was the only significant factor associated with ADRs in older patients when adjusted for independent variables [88]. However, age was not found to be significantly associated with experiencing an ADR [88].

Consequently, PIP is a reliable measure of prescription quality. It refers to using a medication when the potential harms outweigh the benefits [89]. PIP has gained considerable attention in the literature and has been linked to adverse outcomes, including ADEs and medication-related hospitalisations in older patients [89–92]. A repeated cross-sectional study found that the proportion of PIP in older patients ( $\geq 65$  years) increased from 32.6% in 1997 to 37.3% in 2012 in primary care in Ireland [1]. The presence of PIP in older Irish patients ( $\geq 65$  years) is independently linked to hospital admissions [93]. It was found that older individuals aged  $\geq 65$  years who had experienced PIP in accordance with the STOPP & START criteria faced a heightened risk of experiencing preventable medication-related admissions (MRAs) [66].

For example, diabetes is a chronic disease that often co-occurs with other health conditions [94]. Polypharmacy is common in individuals with diabetes, especially those dealing with multiple related conditions. It often leads to the use of medications that may not be suitable [95]. A cross-sectional study examined the occurrence of polypharmacy and PIM use among middle-aged and older individuals with diabetes [95]. It was found that the prevalence of polypharmacy was increased in older and middle-aged individuals from 56.5% of diabetic people in 2012 to 58.2% in 2016 (polypharmacy in 2016 was present in 36.9% of adult

patients aged 45-54 years, 50.3% of older patients aged 55-64 years, and 66.2% of older aged  $\geq 65$  years). While PIM use decreased over time in older individuals, this decline was not observed in middle-aged individuals with diabetes. This suggests that there is a need for efforts to reduce the use of PIMs in populations already dealing with a significant number of medications, particularly in middle age [95].

#### 1.4.4 Medication classes

A considerable portion of older patients experience pain stemming from either acute or chronic illnesses and disruptions. Consequently, healthcare providers often resort to prescribing analgesic medications, encompassing nonsteroidal anti-inflammatory drugs and opioids, or they prescribe antidiabetic drugs, anticoagulant agents and corticosteroids to address this prevalent issue within this demographic [96]. Some studies have found that certain medication classes, such as nonsteroidal anti-inflammatories [28], analgesics, anti-diabetics, antithrombotic, antihypertensives, antipsychotics and anti-neoplastic drugs are most frequently associated with medication-related hospitalisation [2, 97, 98]. A systematic review conducted by Howard *et al.* [99] identified that four specific medication categories (antiplatelets, diuretics, nonsteroidal anti-inflammatories and anticoagulants) accounted for over 50% of preventable MRAs [99].

#### 1.4.5 Health care communication

MRPs lead to patient harm and increase healthcare costs [3]. Applying a mixed-methods approach that involved qualitative analysis, a literature review and expert input, an expert panel identified potential risk factors for MRPs. They found that a topic of importance was communication between healthcare providers and patients' knowledge about their medications [3]. The expert panel rated factors like polypharmacy, renal impairment and dementia as being more crucial in influencing MRPs than age itself [3]. Notably, age was not listed in the final list of most important risk factors.

Howard *et al.* [100] investigated the risk factors associated with preventable MRAs through qualitative interviews involving patients, general practitioners, and community pharmacists. Their interviews identified that the risk factors contributing to preventable MRAs included communication breakdowns and gaps in knowledge at different stages of the medication

process [100]. They did not provide age information for the participating patients, making it unclear whether the participants were adults or older individuals. Therefore, this finding provides valuable insights into understanding medication-related experiences, especially among adult inpatients from the perspective of patients, and the association between age and medication experience, which is the subject of **Chapter 4** of this thesis.

## 1.5 Medication-related hospital admission

Finding the balance between prescription medications' advantages and potential risks is a frequent challenge. This is further complicated by the increasing occurrence of multimorbidity and polypharmacy across all age groups of adults, including older and younger adults [101, 102]. As mentioned previously, MRPs represent an inherent risk associated with prescription medications. They can potentially lead to hospital admissions, increased morbidity and mortality and heightened healthcare costs [9]. Thus, distinguishing between adverse clinical events resulting from an ADR and those due to the natural progression of an underlying disease can be challenging. Therefore, using causality assessment tools is essential in determining the likelihood that a drug is responsible for a suspected ADR [103]. In clinical practice, the most frequently employed and widely accepted causality assessment scales are the probability scales created by the WHO Collaborating Centre for International Drug Monitoring and the Naranjo ADR Probability Scale [104, 105]. According to various studies, the majority of ADR-induced hospital admissions in older adults have been determined to be either probable or possible based on causality assessments [34, 106, 107]. Some studies have reported that around 3.5%–10% of hospital admissions for all adults could be attributed to MRPs [9, 12, 108].

Older patients have been a primary research focus concerning MRAs, and most of these identified MRPs are preventable [109-111]. Various studies conducted between 2009 and 2018 [84, 92, 112-114] have explored the impact of patients' age, polypharmacy and comorbidities on the likelihood of MRAs in older populations, with different cut-offs for old age. These studies shed light on the complex and inconsistent relationship between these variables and MRAs in older adults, (**Table 1-4**).

Table 1-4: The association between age, polypharmacy and comorbidity with MRA in old patients.

| Authors                  | Year | Patients' ages | Test used               | Age as risk factor for MRA                                                 | Polypharmacy as risk factor for MRA | Comorbidity as risk factor for MRA       |
|--------------------------|------|----------------|-------------------------|----------------------------------------------------------------------------|-------------------------------------|------------------------------------------|
| Cabré <sup>[92]</sup>    | 2018 | ≥ 70 years     | Multivariate regression | Non-significant                                                            | <b>Significant</b>                  | Non-significant                          |
| Marcum <sup>[88]</sup>   | 2012 | ≥ 65 years     | Multivariate regression | NA                                                                         | Non-significant                     | Non-significant                          |
| Onder <sup>[84]</sup>    | 2002 | < 65 years     | Multivariate regression | Non-significant                                                            | <b>Significant</b>                  | <b>Significant with severe ADRs only</b> |
| Somers <sup>[114]</sup>  | 2010 | > 65 years     | Bivariate inference     | <b>Significant</b> (patient with MRA slightly <b>younger</b> than non-MRA) | <b>Significant</b>                  | NA                                       |
| Wawruch <sup>[113]</sup> | 2009 | > 65 years     | Multivariate regression | Non-significant                                                            | Non-significant                     | Non-significant                          |

### 1.5.1 The evidence-base of systematic reviews on MRAs

The association between age and MRPs needs to be re-evaluated as advanced age is not consistently identified as a risk factor for MRP-induced hospital admission. A systematic review of prospective observational studies carried out by Mongkhon *et al.* [20] revealed that hospital admissions resulting from medication non-adherence accounted for 29% of all identified MRPs among adult patients. However, this review did not examine the relationship between age and medication non-adherence [115].

Furthermore, Beijer *et al.* [116] found that older patients (≥ 65 years) had a significantly higher mean percentage of ADR-induced hospital admissions compared to non-older patients, suggesting an age association with MRPs [116]. Similarly, Kongkaew *et al.* [32] reported that among older patients, the admission rate for ADRs was notably higher than in younger adults [32]. Mongkhon *et al.* [115] categorised patients into three groups: older, all-age and paediatric. When considering non-adherence-induced hospital admissions, the median prevalence for older patients was 5.1% of hospital admissions (with an interquartile range of 3.8% to 7.6%), while for the all-age population, it was 4.4% of admissions (interquartile range 1.6% to 7.4%). However, it's worth noting that referring to age with the term 'all-age group' may not reflect the adult patient population, as it covers a broader age

spectrum (i.e. including patients in middle age and older patients together). Therefore, a direct comparison between older and younger adult patients was not conducted in this study [115].

In contrast, Oscanoa *et al.* [97] found that ADRs resulting from inappropriate medications were not significantly associated with hospital admission in older patients, highlighting the complexity of this relationship. They defined the older age group as patients aged  $\geq 60$  years [97]. Leendertse *et al.* [117] reported varying prevalence rates of MRA across different age groups (all-age or adults, children and older patients). However, they defined the older age group by the study authors' definition, a cutoff of 65 years or older, which means the cutoff was not constant [117].

None of these systematic reviews has investigated the association between age and MRA or employed robust statistical techniques. The majority have aimed to estimate the prevalence of MRA and have relied on mean or median percentages to determine the prevalence of MRP in older patients, as reported in the included studies. Only a few studies have determined risk factors as reported in the included studies [12, 97] (**Table 1-5**).

Table 1-5: Characteristics of systematic review studies examining MRA.

| Study author                                    | Aim of study                                                                                  | Number of included articles | Meta-analysis undertaken (Yes/No) | Participant age                  | Definition of MRP   | Percent of MRP                                                        | Other comment                                                                                                                                                                                                          |
|-------------------------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------|-----------------------------------|----------------------------------|---------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Al Hamid <i>et al.</i> <sup>[12]</sup> (2014)   | To estimate the prevalence, causes and risk factors of MRPs causing hospitalisation in adults | 45                          | No                                | ≥ 18 years                       | Authors' definition | 4.6% for ADEs, 7% for ADRs and 12.1% for MRPs                         | The common risk factors as reported in the studies were old age and polypharmacy.                                                                                                                                      |
| Beijer <i>et al.</i> <sup>[116]</sup> (2002)    | To determine the percentage of ADR-induced hospital admission                                 | 68                          | No                                | Older (≥ 56 years) and non-older | WHO definition      | 4.9% ± 0.1% of hospitalisation (mean ± confidence interval)           | Per study percentage ADR-induced hospital admission varied from .02% of hospitalisations to 41%. The mean percentage of ADR-induced hospital admission in older patient was four times higher than non-older patients. |
| Dechanont <i>et al.</i> <sup>[118]</sup> (2014) | To estimate the prevalence of drug-drug interaction-induced hospital admissions or visits     | 13                          | Yes                               | All ages                         | NA                  | 1.1% of patients with drug-drug interactions (median) (IQR: 0.4–2.4%) | The prevalence of drug-drug interactions among patients experiencing ADRs at hospital admissions was approximately 2.5 times greater than that observed during hospital visits.                                        |
| Howard <i>et al.</i> <sup>[47]</sup> (2007)     | To determine the percentage, most common drug and underlying causes of preventable MRAs       | 13                          | No                                | ≥16 years                        | Authors' judgement  | 3.7% of patients (median) (Range: 1.4–15.4%)                          | No information was reported about risk factors and age association with MRPs.                                                                                                                                          |
| Kongkaew <i>et al.</i> <sup>[32]</sup> (2008)   | To estimate the prevalence of ADR-induced hospital admissions                                 | 25                          | No                                | All ages (No specification)      | WHO definition      | 5.3% of patients (median) (IQR: 2.7–9.0%)                             | The median prevalence of ADRs varied across different age groups. Among adults, the admission rate for ADRs was                                                                                                        |

| Study author                                     | Aim of study                                                                                                                                                 | Number of included articles | Meta-analysis undertaken (Yes/No) | Participant age                                                           | Definition of MRP      | Percent of MRP                                                                | Other comment                                                                                                                                                                                                                  |
|--------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------------------|---------------------------------------------------------------------------|------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                  |                                                                                                                                                              |                             |                                   | for age categories)                                                       |                        |                                                                               | 6.3% of patients (with IQR of 3.9% to 9.0%), while among older patients it was 10.7% (with IQR of 9.6% to 13.3%).                                                                                                              |
| Leendertse <i>et al.</i> <sup>[117]</sup> (2010) | To explore the relationship between study characteristics (setting, population, outcome, method of data collection and continent) and the prevalence of MRAs | 95                          | No                                | All ages (Older defined by the authors or a cut-off of 65 years or older) | WHO definition         | Range: 0.1% to 54% of admissions                                              | The mean prevalence of MRA with ADE and ADR were found to be higher in the elderly older population than in the all-age or adult populations (for ADRs: 3.60%, 95% CI: 3.39, 3.81 and 1.79%, 95% CI: 1.72, 1.86, respectively. |
| Mongkhon <i>et al.</i> <sup>[115]</sup> (2018)   | To investigate the prevalence of medication non-adherence causing hospital admission                                                                         | 24                          | Yes                               | All ages                                                                  | NA                     | Non-adherence accounted for 4% of all hospital admissions and 29% of all MRPs | The median prevalence of non-adherence-induced hospital admissions was 5.1% of older patients (IQR: 3.8%–7.6%), and for all ages was 4.4% (IQR: 1.6%–7.4%).                                                                    |
| Oscanoa <i>et al.</i> <sup>[97]</sup> (2017)     | To determine the frequency of ADR-induced hospital admission in older patients                                                                               | 42                          | Yes                               | ≥ 60 years                                                                | No specific definition | 8.7% of patients (95% CI: 7.6–9.8%)                                           | ADRs resulting from inappropriate medications were not significantly associated with hospital admission in older patients.<br>The main risk factors were particular medication classes and polypharmacy.                       |

### 1.5.2 The evidence-base for individual studies on MRA

A prospective study conducted by Peyriere *et al.* [119] estimated the prevalence of ADEs leading to hospitalisation across all age groups. This included ADEs that either caused admission, occurred at admission or developed during a hospital stay. The study found that the prevalence of ADE-induced hospitalisation was 9.6% of patients, and around 58% of these ADEs were preventable. When comparing patients with ADEs to those without, it was observed that patients with ADEs had a higher number of medications upon admission ( $5.7 \pm 2.4$  vs  $3.8 \pm 2.9$ ,  $P < 0.01$ ). Patients with ADEs appeared to be older than those without, although this difference did not reach statistical significance (comparing the mean age) [119]. On the other hand, Brvar *et al.* [28] retrospectively estimated ADR-caused hospital admission in adults receiving medical care; they estimated that ADRs caused 5.8% of hospital admissions, and most of these ADRs were preventable. They compared the ages of patients admitted due to ADRs and those without ADRs and identified that the former group was generally older than the latter using multivariate regression analysis ( $P = 0.025$ ) [28].

#### 1.5.2.1 Global association between age and MRA

In the Netherlands in 2020, Lghoul-Oulad Saïd *et al.* [120] published a study that assessed the prevalence of possible MRAs in two age groups: 18-64 years and  $\geq 65$  years. The findings showed that MRAs occurred four times more often in older patients than younger ones. The mean prevalence of MRA was 10.2% of admissions for the older and 2.7% for the younger age groups [120]. Additionally, the potential preventability of MRAs was higher in the older age group. The study did not find any significant change in the prevalence of harm between 2008 and 2013 [120]. This was the first study that compared MRAs between young adults and older patients. However, the sample included people who presented to the emergency department but were not admitted, and this differs from the study populations in other publications, which often included only those admitted to inpatient care [73, 121-123].

In the US, Budnitz *et al.* [98] examined the prevalence of emergency hospitalisations in older Americans (aged 65 and above) from 2007 through 2009. The study found that nearly half of these hospitalisations occurred in adults aged  $\geq 80$  years due to ADEs (48.1% of hospitalisations; 95% CI, 44.6 to 51.6) [98]. No information was provided on the relative volume of admissions due to any cause in each age group.

In Australia, Zhang *et al.* [124] explored trends in ADR-related hospitalisations between 2001 and 2014. The rate of the age-adjusted ADR-related hospitalisations doubled across the study period with an estimated annual increase of 5.8% of residents (95% CI: 5.0%–6.6%). Interestingly, the annual percentage increase in ADR-related hospitalisation in adults aged between 18 and 44 years was 6% of 100,000 residents, while in adults aged 65 to 84 years it was 5.1% [124]. This finding underscores the importance of understanding whether age is itself a risk factor for ADR-related hospitalisation or whether other risk factors are at play. Additionally, an observational prospective study conducted in Italy by Conforti *et al.* [125] reported the frequency of ADR-related admissions among patients aged 65 years and older at 11% of admissions, while 25% of patients had an ADR during their hospital stays. There was no statistically significant difference in age between patients with ADRs compared to those without ADRs [125]. A prospective study by B  nard-Laribi  re *et al.* [108] conducted across public teaching hospitals and general hospitals in France found that the incidence of all patients' hospitalisations related to ADRs was 3.6% of admissions, with 32% of ADR-related hospitalisations being preventable. This incidence increased with age; patients admitted due to ADRs were significantly older than those admitted for other causes. The incidence of ADRs in patients aged 16–64 years was 3.3% of admissions (95% CI: 2.4–4.2), while it was 4.9% (95% CI: 3.8–6.0) in patients aged and  $\geq 65$  years [108].

#### 1.5.2.2 National association between age and MRA in Ireland

In 2012, a cross-sectional study aimed to assess the frequency and preventability of ADR-related hospital admissions in an Irish university hospital. They reported that 8.8% of emergency admissions were ADR-related, and 57.3% of them were potentially preventable. While the article did not provide a detailed breakdown of the findings specifically by age, it did mention that older adults with a median age of 69 years were at a higher risk for ADR-related hospital admissions than non-ADR-related admissions with a median age of 58 years [106].

In 2020, a prospective observational pilot study aimed to determine ADR-related hospitalisation prevalence, severity and preventability in middle-aged patients (45–64 years). The prevalence of ADRs causing or contributing to hospitalisation and preventable ADRs causing or contributing to hospitalisation were 14% and 11% of patients, respectively. The study identified that excessive polypharmacy (defined as ten or more medicines) was

associated with any ADR occurrence in this age group [73]. However, they did not find a statistically significant association between age and ADRs causing or contributing to hospitalisation (adjusted OR (95% CI): 0.96 (0.87–1.07)). These results suggest that middle-aged patients are vulnerable to MRH, but the ADR occurrence in this age group was not associated with age [73].

MRAs are a substantial concern in Ireland and worldwide. Research findings on the role of age as a risk factor for these admissions have varied. While some studies have identified age as a potential risk factor [126, 127], others have not found any significant association [128]. Additionally, certain studies have noted variations in the investigation of MRAs concerning age, especially when utilising univariate analysis [114, 129]. These variations in research outcomes suggest that age alone should not be overestimated as the sole or primary risk factor for MRAs. Therefore, comprehensive analyses should be considered for addressing the association between age and MRAs. These analyses will be discussed in detail in the next chapter and throughout this thesis.

The preceding sections of the introduction, described the intricacies of MRP, specifically focusing on hospital admissions. Additionally, it explored the existing literature and emphasized the critical aspect of age as a potential factor associated with MRAs while noting the equivocal evidence regarding age as a risk factor for admission in previous systematic reviews. The following section will examine patient safety in Ireland, the Irish healthcare system, patient's experience, and challenges in medication management.

## **1.6 Patient safety in Ireland:**

A major challenge to improving healthcare safety is the lack of high-quality information to evaluate performance and identify deficits and risks [130]. Patient safety is a fundamental priority for patients and healthcare organizations in the Republic of Ireland. A recent scoping review provides an overview of the variety of patient safety research being conducted in the Republic of Ireland. This review is intended to guide researchers, healthcare practitioners, and managers to build upon existing research to improve patient safety and the quality of care [131]. It included 31 papers, 24 of which studies were about the measurement and monitoring of safety, and 12 (50%) assessed harms that had happened in the past. However, studies that focussed solely on the safety of a single process, such as medication errors, were not included in this review [131]. The Irish Health Service Executive (HSE) recognises the need for proactive approaches to patient safety, which requires high-quality data to support learning, hazard identification, and implementation of interventions to address these hazards and mitigate their consequences. Effective measurement and monitoring of safety is essential to compare safety performance between healthcare organisations, assess safety intervention impacts, and shift to a proactive safety approach [131, 132]. The research on the measurement and monitoring of safety in the Republic of Ireland is mainly focused on measuring past harm and assessing safety culture, while interventional studies have focused primarily on education and training [131]. Based on these findings, recommendations for future research were made in alignment with relevant aims from the HSE patient safety strategy 2019-2024 to identify specific areas of patient harm to inform safety improvement initiatives [131, 132]. Patient healthcare record reviews are limited in identifying specific areas for improvement, and there is a need for more targeted data to measure and monitor safety [133].

A recent Irish mixed-methods study using data from the Irish National Patient Experience Survey explored the patient experiences of shared decision making in public hospitals [134]. Another questionnaire study reported findings from the Northern Ireland patient experience survey of experiences of care in cancer patients [135]. However, neither of these survey studies addressed any patient medication management experiences.

MRPs in Ireland are common. In 2009, the prevalence of general adverse events (including medication related and non-medication related events) among adult inpatients in Ireland was 12.2% of admissions [136], which increased to 14% in 2015 [137]. Contrastingly, the prevalence of preventable adverse events was 9.1% in 2009 [136] and decreased to 7.4% in 2015 [137]. Adverse events in Ireland are estimated to cost the health service between €91.3 million [138] to €194 million annually [137]. The prevalence of adverse events and preventable adverse events in Ireland's healthcare system is still a concern, with a noticeable increase in adverse events over the years. Although there has been some progress in reducing the occurrence of preventable adverse events [136, 137], the healthcare system needs to address the causes of these events to improve patient safety. On the other hand, the prevalence of ADR-induced inpatient hospitalisation was reported as 8.8% of all patients age in 2014 [106] and 14% of patients aged 45–64 years in 2020 in Ireland [73]. This highlights the need for continued efforts to monitor and improve the quality of care and patient safety in Irish healthcare organisations. Future research should focus on understanding medication management across all adult age demographics to identify areas for improvement. The use of both quantitative and qualitative methods may be necessary to achieve this. Improving medication safety holds particular significance in the Republic of Ireland, as it is a specific HSE patient safety strategy action [132].

## 1.7 Irish healthcare system

In Ireland, the National Care Experience Programme [139], launched in 2017, is a survey administered collaboratively by the Health Information and Quality Authority (HIQA), the HSE and the Department of Health. This programme conducts various surveys to gather feedback on people's experiences with health and social care services. Their goal is to improve the quality of these services. The programme includes annual surveys for inpatient care, maternity care, and nursing home care, and it is developing surveys for maternity bereavement and end-of-life care. The national inpatient experience survey measures

feedback (experience) from people who experienced care in one of 40 public acute hospitals [139].

The national care experience programme funded a research project at the Insight Centre for Data Analytics, NUI Galway, with the support of the HIQA team. This project analysed the qualitative responses (free text) to the 2017 and 2018 national patient experience surveys to enhance the quality of acute healthcare services in Ireland by using advanced analytics techniques to identify factors contributing to positive and negative care experiences and suggestions for improving care [140]. This project addressed the general inpatient experiences and experiences across the different stages of care. This study did not focus on medication-related issues.

HIQA is an independent statutory authority established in 2007 under the Health Act 2007, to enhance Ireland's health and social care services, with responsibility for setting guidelines and standards and regulating and monitoring health and social care services. It plays a role in investigating incidents, conducting national patient safety reviews, and providing guidance on patient safety initiatives to help minimise risks and improve patient outcomes in health and social care services [141].

The HSE is a funded healthcare system that provides all public health and personal social services in hospitals and communities across the Republic of Ireland [142]. The Department of Health is a government department in Ireland governing the quality of health and social services to support and protect the health and well-being of the public, and to achieving the best value from public health system resources [143].

## 1.8 Patient experience

Patient experiences and patient satisfaction are critical measures of healthcare quality as perceived by patients. However, the interchangeable use of such terms can lead to confusion and misunderstanding [144, 145]. Patient experience refers to the broad set of interactions, perceptions and feelings a patient has while navigating the healthcare system. It encompasses many factors, including communication with healthcare providers and the quality of care received. The patient experience is essential to healthcare quality as it directly affects patient satisfaction, adherence to medical advice and health outcomes [144]. In contrast, patient satisfaction is complex and has multiple dimensions, and it is frequently

inadequately defined. At its core, it centres around the subjective experiences of patients, which can vary greatly depending on individual expectations [145]. Understanding the distinction between these concepts is crucial for identifying areas for improvement and providing optimal patient-centred care [146]. Patient-centred care is a specific approach to delivering care that focusses on the needs and preferences of individual patients, while addressing their dignity and respect [146].

Several attempts have been made to explore hospitalised patients' experiences [147-149]. One systematic review of qualitative studies explored patients' experiences in the emergency department, including their perceptions of the emotional impact of the emergency, waiting for the initial assessment, the emergency environment, staff-patient interactions and having their families in the emergency department [147]. However, it did not explore patients' medication-related experiences. Inpatients' (hospitalised) and outpatients' (ambulatory care) hospital care quality at multiple hospitals was surveyed in 2016 and 2018 in China, across six domains: health service efficiency, information guidance, humanistic care, hospital environment, communication with doctors and overall rating [149]. The patients' experiences of treatment were surveyed within the 'communication with doctors' domain using a single, closed-ended question with a score from 1 (strongly disagree) to 5 (strongly agree) [149]. This national survey found that patients reported having overall positive care experiences, and the hospitalisation experience improved over the 2016-2018 period [149]. Webster *et al.* [148] explored patients' hospital stay experiences from admission to discharge by inviting them to describe their experiences and identify any suggestions for improvement in their own words [148]. None of the identified themes addressed medication-related experiences despite capturing the patients' experiences with pain management [148].

Commonly, hospital admission is associated with ADRs and affects patients' mortality and morbidity. A qualitative interview study of 15 patients who were admitted to hospital due to severe ADRs explored the patients' experiences and views on reporting the suspected ADRs and understanding the information they received about their medications [150]. Lorimer *et al.* [150] reported the importance of ensuring patients received and understood all information about their medications (including the nature of reactions and their incidence). Lack of information about a suspected ADR can influence a patient's future perception of medications. They reported that some patients may link these suspected ADR symptoms to their underlying medical conditions [150]. Lorimer *et al.*'s study focussed only on patients'

experiences of ADRs and how they report them. Another study conducted qualitative interviews to develop a conceptual framework of the burden of treatment in patients with chronic disease [151]. It reported some patients' experiences with taking their medications and their confusion regarding a lack of information received about their medications (e.g., the purpose of taking the medication, the time to take it and the type of medication being taken) [151].

## 1.9 Challenges in medication management: insights from patient experience

Patients' medication experiences can be characterised as 'the total of all interactions a patient has with medication throughout their lifetime', encompassing various aspects of their medication journeys [152]. Medication management can be described as a patient-centred approach to ensure the safe, effective and suitable use of medications. It entails a range of services intending to enhance clinical results. These services include conducting medication reviews and health assessments, monitoring treatment plans to ensure their effectiveness and safety, offering education and promoting patient self-management [153]. Managing medications for inpatients is a multifaceted process including prescribing, dispensing, administering and reviewing medications to achieve the best possible therapeutic outcomes [154]. As has been demonstrated, previous research has highlighted several challenges in this process, such as medication errors, ADRs and non-adherence, which can significantly affect patient safety and outcomes. However, this section delves into medication management from the adult patient's perspective. Previous studies have highlighted the association between medication burden or medication experience and adherence to medicines [152, 155, 156]. Mohammed *et al.* [152] performed a qualitative systematic review to understand patients' lived experiences with medicines and explore the influence of medication-related burden on patients' medication therapy and health outcomes in different countries and health settings [152]. The authors highlighted the negative influence of medication-related burden on patient beliefs and behaviours and a potential risk of MRPs that result in non-adherence to medication therapy and poor outcomes [152]. An interview study emphasised the need for improved medication management during hospital discharge, particularly for older individuals, to ensure proper adherence to prescribed medications and prevent the adverse effects of incorrect medication usage [157].

### 1.9.1 Medication experiences in community and primary care

Numerous previous studies have explored the experiences of patients when it comes to medication-related matters, particularly in community or primary care settings. These studies have primarily focussed on understanding older patients' experiences with taking medications, gathering information about medications or addressing issues related to the delivery of repeated prescriptions [158-162]. A qualitative study carried out in a community setting on older patients found that the participants had no concerns about using multiple medications; they felt lucky to have access to these medicines, which they believed were crucial for their well-being. Nonetheless, the main concern was that acceptance of medications relied on them not having adverse effects and questioning if taking multiple medications was beneficial for health. Additionally, their perception of medications depended on their interactions with doctors, particularly trusting competent doctors [158]. In most of these studies, the primary focus was on gaining insights into the experiences of older patients with their medications.

### 1.9.2 Medication experiences during transition care

Problems related to medication management frequently arise during transitional care [163]. Care transitions refer to stages when patients move between different healthcare environments, move between various levels of care within the same setting or shift between various healthcare professionals responsible for their treatment and management. These transitions can include moving from home to a hospital, moving from a hospital to home, transferring between different units within a hospital and transitioning between different hospitals [163].

Particularly for older adults, these transitions can become notably complex and challenging. Delays in the discharge process were a common concern among this demographic. Knight *et al.* [157] found that many of these older patients expressed dissatisfaction with the discharge process, particularly related to perceived delays [157]. These delays were often attributed to the time required for pharmacy preparation and the subsequent wait for medications to be delivered to the ward. Some participants also believed that discharge timing depended on the ward's busyness [157]. A recent systematic review that examined

the experiences and perceptions of older patients regarding medication management communication identified a significant emphasis on understanding the viewpoints of older patients, particularly during the discharge and post-discharge phases. In contrast, there was relatively less exploration of their perspectives during admission, hospitalisation or transitions between different healthcare settings [163]. This review highlights the need to delve deeper into the experiences of older patients during admission and within hospital settings. **Chapter 3** in this PhD thesis seeks to understand the medication management experiences in inpatients during their hospital journeys—from admission to hospitalisation and discharge. This thesis will include all adult patients, including young adults, due to the relative lack of published data regarding their medication experiences in different hospital settings.

### 1.10 Association between age and medication-related experience

The available published research places more emphasis on older patients' medication-related experiences in different healthcare settings, with relatively little investigation of younger adults. For example, a recent systematic review focussed on older patients' experiences regarding medication management during transitions in care and observed that communication breakdowns frequently led to medication discrepancies or adverse events. [163]. This issue was particularly concerning when older individuals transitioned between various care settings. The term 'medication discrepancy' can relate to various issues, including omission of medication, alterations in dosage or route of administration or the addition of medications [164]. Such discrepancies could arise from unintended or intended medication regimen alterations that lack proper documentation or patient comprehension [163]. Additionally, a cross-sectional questionnaire study involving 102 hospitalised patients identified that older patients aged > 65 years faced more challenges in recalling correct medication information (78% compared to 54.3% in younger patients) and were less aware of their own comprehension deficits regarding medication information compared to younger patients. The authors suggest that communication with older patients requires particular attention during the discharge process, however they did not elaborate on any communication strategies [165]. Another study identified that nearly half of older participants aged > 75 years were unaware of their medication change details and the reasons why they occurred during their hospitalisation, and they were highly confused about their

medications [166, 167]. On the other hand, a quantitative study on adults after hospital discharge compared medication adherence in older patients (age > 65 years) to younger adults. It found that older individuals were more adherent to their prescribed medications than younger adults [168].

**Older patient experience with health professionals**

A Swedish study addressing older people's experiences of evaluating their medication treatment found that many of them were willing and able to actively participate in their own medication evaluations. Still, some were unable to participate or were unconcerned with participating. However, older persons sometimes expressed concerns about the lack of comprehensive evaluations of their medications, mainly when they were prescribed by multiple physicians. They felt that there was a lack of cooperation among healthcare providers and were unsure who was responsible for evaluating their treatments. Additionally, they found it difficult to obtain information about their medications' purposes and potential side effects due to time constraints during visits [169]. A qualitative study involving a combination of questionnaires and interviews with older patients aimed to gain insights into their experiences with the discharge planning process. The findings revealed that 71% of older participants reported satisfaction with their overall hospital discharge experiences. Their satisfaction stemmed from active involvement in decision making alongside their caregivers, as well as receiving clear written instructions before their discharge regarding their medications [170]. Swain and Barclay [156] studied older patients' experiences and understanding of medicine and reported that patients need comprehensive written and verbal information about the duration of their medication therapy, indications and suspected side effects to manage their medications. They also need effective communication from doctors and pharmacists about medication choices [156]. Therefore, healthcare providers should recognise that most older patients trust the medication decisions made by doctors and do not believe it is their role to question these decisions [166]. This poses a significant challenge, highlighting the need for healthcare providers to actively engage with patients and inquire about their medications to ensure comprehensive care. It seems evident that active engagement with older patients is necessary. However, there is relatively limited knowledge about younger adults regarding their medication management experiences, their associated needs and whether they require the same level of communication or different healthcare approaches.

**Medication knowledge in older patients**

In an interview-based study that explored medication management in older patients from non-English-speaking backgrounds, it was observed that patients often had limited

knowledge about their medications and any changes made to them. The language barrier played a significant role in this lack of understanding as translated educational materials were not readily available. Additionally, medication changes and variations in brand names contributed to issues with managing medications, like taking a new medication, among older patients in this group after discharge [171]. Older patients acknowledged the information provided by healthcare professionals upon hospital discharge, but the extent to which they found it valuable varied. They highly appreciated the printed list of medications they received from the pharmacist, considering it helpful, informative, well structured and a valuable hospital service [172]. Many individuals aged 75 and older faced challenges regarding the information they received about their prescribed medications upon discharge. This issue stemmed from either a lack of information or an assumption by healthcare professionals that older individuals or their caregivers fully grasped the medication details. Additionally, inadequate explanations about medications at discharge frequently resulted in medication omissions, incorrect dosages and feelings of anxiety and confusion among those aged 75 and older [157]. Again, there is a noticeable gap in knowledge concerning younger patients' understanding of medications, as the focus has predominantly been on older individuals. This underscores the need for future research to address this issue within the younger adult age group.

### **1.11 Impact of communication and education on medication management outcomes**

A quasi-experimental study that used a pre-post design examined the effects of providing older patients with easy-to-read, detailed discharge instructions [173]. A complex intervention to facilitate the transition of older patients from hospital to home, had five core elements: admission form with geriatric cues, facsimile to the primary care provider, interdisciplinary worksheet to identify barriers to discharge, pharmacist–physician collaborative medication reconciliation, and predischARGE planning appointments. A complex intervention has been defined by The original Medical Research Council as “consisting of multiple components acting independently and interdependently, in such a way that made it difficult to identify the ‘active ingredient’” [174]. A larger font size and simple and comprehensible language characterised these instructions, which included clear guidelines on the correct methods, times and reasons for medication usage, as well as the

hospital health professionals' contact information for any questions after discharge. This approach led to a decrease in readmission rates from 22% to 14%. Patients also reported feeling healthier after leaving the hospital and more successful in returning home. This suggests that clear and simple discharge instructions can contribute to improved patient outcomes and transitions from hospital to home [173]. Moreover, a prospective cohort study found that a pharmacist-led programme was highly satisfactory to 98% of hospitalised older patients [175]. This programme, which included medication reviews, reconciliation and counselling upon admission and discharge, was linked with a substantial decrease in inappropriate medication use and MRPs. This pharmacist-led medication review programme represents a significant strategy for augmenting pharmaceutical interventions within geriatric care, particularly concerning prescriptions for patients aged between 45 and 64 years old in hospital settings. While the strategies mentioned above have proven effective, they have predominantly targeted older patient populations, not all adults. There is a pressing need to comprehensively address patient education about medication management across a broader adult age range. Further research is essential to better understand experiences with medication across all age groups rather than focussing solely on older patients.

The previous section explored patients' perspectives of their medication management experiences, shedding light on a crucial aspect often overlooked in the literature, identifying a significant gap in understanding medication experiences during hospital stays. However, the existing body of evidence primarily focusses on the experiences of older adults. In the next section, the spotlight of the thesis shifts to media portrayals—specifically, newspaper reports of instances of medication-related harm (MRH) to understand how the harms were reported to the public and to explore whether any age pattern was evident in the instances reported.

## 1.12 Role of the media in reporting medical issues

There is a growing public interest in medical news, and traditional sources like general practitioners are no longer the sole providers of such information. The media has taken on an expanding role in delivering medical news to the public, dedicating increasing coverage to recent medical developments [176]. Mass media can convey messages to a significant

portion of the population. Newspapers regularly share substantial information about medications and health with the general public [177]. Health promotion messages have been broadcast to the public through mass media with varying degrees of success. Examples include the variable impacts of efforts for smoking cessation [178], improvements in human immunodeficiency viruses testing uptake [179] and enhancements in the utilisation of health services [180]. Despite the variety of health information sources available to the public, such as healthcare professionals, the internet, television and radio, research indicates that newspapers remain an important source for conveying health information [181]. Newspapers play a role in disseminating findings from medical research [182] and persist as a potential source of health-related information for the general public [183]. A longitudinal study investigated the characteristics of medical research that was promoted in press releases by the *Lancet* and the *BMJ* and later covered in newspapers, identifying a few key trends. Newspapers often emphasise findings from observational studies. In particular, negative news related to women's health, reproduction and cancer was most frequently reported [182]. Several studies have explored the various health topics covered in newspapers, including online health information, vaccine programmes and specific medications [184-187]. Section 1.12.1 will focus on studies exploring media coverage of medication issues.

### 1.12.1 Role of newspapers in reporting medication issues

People frequently search for information on beneficial medication products to improve their health and wellness. However, healthcare providers involved in prescribing, advising and providing medication information typically concentrate on the effects of these medications at the cellular and organ levels [188]. This approach often leads to patient prescription information that is detailed and complex. People frequently do not receive the specific information they require, like the effects of medications and how these medications will affect their daily lives. This often leads to patients seeking more information to fill these gaps in understanding [189]. Patients have a variety of sources available to them when seeking information about medications, including online sources. Numerous studies have been carried out on the use of traditional media, such as newspapers or other printed media [183, 186, 190], television [191, 192] and radio [193], for communicating with the public about medications. Catalán-Matamoros and Peñafiel-Saiz's [194] systematic review

revealed that the communication about medications in newspapers typically centres around four main themes: medications, the most common theme, with a particular emphasis on vaccines; advertising, including discussions related to marketing and the promotion of medicines; administration, with content related to providing licences, pharmaceutical funding and crisis communication; and public awareness campaigns, involving public knowledge about medicines or health-related issues. However, the public knowledge about medicines was observed in only one article. It was found that media coverage of medication has demonstrated a positive impact on the general population [194]. For instance, one of the included studies in the systematic review discovered a correlation between the prevalence of risk communication in newspapers and an increase in vaccination rates, underscoring the influential role of media in shaping health decisions [195].

Despite the availability of the media as a source of health or medication information, there is an absence of Irish research that has examined the content of newspaper articles reporting on MRH. Goodfellow *et al.* [183] conducted a content analysis study that explored newspaper reporting of medication adherence and identified it as being infrequent. Notably, this study was the first of its kind to explore medicine adherence reporting by newspapers, with a focus on the UK and the US, while Ireland was not included in the analysis [183]. Prosser and Clayson [196] analysed the nature and frequency of information about prescription medications reported in only two UK newspapers using systematic content analysis [196]. Their findings revealed that medication-related articles predominantly focussed on several aspects, including the benefits and drawbacks of medications, followed by articles addressing medication availability, medical criticism, health issues and their solutions, and the misuse of medicines. Their results suggested that although newspapers frequently convey information about medicines, the content often lacks comprehensive detail and clarity. This limitation hinders readers' ability to thoroughly assess the potential risks and advantages of medications [196].

Moreover, the media can influence the public's decisions on medical choices, including starting or stopping medications. For instance, due to the media's consistent coverage of the adverse effects of statins and other medications, a Danish quantitative study investigated whether a newspaper article in Denmark discussing statin side effects influenced individuals' decisions to discontinue statin use. They reported an increase in statin discontinuation in 2008 following a media event. This effect was particularly notable among individuals prescribed statins for primary prevention and those who had recently started

using statins [197]. This study did not examine the content of newspapers but instead focussed on how patients' decisions are influenced by medical media content. On the other hand, a content analysis study was conducted to examine how statins were portrayed in four UK newspapers. The findings showed that the coverage of statins was more negative than positive, with a ratio of more than 2:1 overall [186]. In Australia, a study using content analysis investigated the reporting of medication errors in newspapers. The findings revealed that Australian newspapers provided limited coverage of medication errors, with most of the coverage centred on broader hospital issues. This suggests there is a clear argument for increasing public awareness and understanding of issues relating to medication safety [190]. A study used content analysis to describe the nature of medical errors reported in Turkish newspapers, particularly those emphasising their severe consequences and the harm caused to patients [198]. It identified that a significant proportion of the medical errors described (40.5%) were reportedly due to negligence on the part of medical staff, with physicians reported to be responsible for these errors in 74.1% of cases. These errors were reported to often cause severe patient harm. The study found that 51.7% of the reported medical errors resulted in patient death, while 25% led to permanent damage or disability [198]. However, none of these articles specified findings related to patient age.

Despite the comprehensive investigation of medical errors in the Turkish media, it is notable that none of the articles analysed in this section explicitly address the relationship between medication harm and patient age. This leaves a gap in understanding whether the instances of harm reported in the media convey any pattern of medication-related harm associated with patient age.

Furthermore, it is also interesting to consider the role of the media in Ireland when reporting MRH. Currently, there is no available data on how MRH cases are presented in Irish newspapers, which could provide valuable insights. Understanding the coverage and reporting style used for MRH incidents in Irish media could contribute to a more comprehensive global picture of how such critical health issues are communicated to the public.

### 1.13 Conclusion

This chapter provided a comprehensive overview of the complexity of MRPs and their contribution to hospitalisation. This exploration was conducted through multiple lenses.

The first lens examined the MRPs that lead to hospital admissions. A review of the identified literature suggests a tendency to overestimate age as a risk factor for such medication-related hospitalisations. Yet, it became evident that there has been a lack of systematic reviews employing robust statistical analyses to verify this correlation substantively. This signifies an area where future research could contribute significantly, and this research gap is addressed in **Chapter 2**.

The second lens explored patient experiences of medication management, particularly focussing on older patients in transitional care. Despite the attention given to this demographic, it was found that evidence is scarce concerning patients' experiences during hospitalisation, irrespective of their age groups. This exposes another potential gap in the literature that invites further investigation and the need to describe patients' perceptions of medication experiences in all adult age groups. This is addressed in **Chapter 3**.

Lastly, the role of the media, specifically newspapers, in reporting MRPs and MRH was examined. It was discerned that descriptions of the harm associated with medication errors are often limited in their scope. Moreover, there is a notable absence of studies describing such reporting in Irish newspapers. This suggests an opportunity for a more in-depth understanding of how this issue is reported in Irish newspapers and whether any pattern of association between MRH and age might be discernible to the Irish public. This is addressed in **Chapter 4**.

In conclusion, this thesis will address the research gaps identified regarding the association between age and MRA, medication management experiences and the nature MRH as reported in newspapers. The next chapter will appraise and describe the methodological approaches used in the literature to explore the relationship between age and MRA.

### 1.14 : Thesis aim and objectives

#### Aim

The overall aim of this PhD thesis is to explore the association between age and MRPs among adult patients in Ireland.

## Objectives

**In order to achieve this aim, the following objectives were pursued:**

- Systematically review the existing published literature to comprehensively identify a possible association between age and MRAs among hospitalised adult patients.
- Examine the findings of a national inpatient experience survey to describe the medication-related experiences of adult inpatients throughout their hospital stays and post-discharge.
- Systematically review Irish newspaper archives to describe how MRH has been reported in Irish newspapers, focussing on understanding the nature of these harms and whether such harms were reported to be related to age.
- Generate recommendations to inform clinical practice, policy makers and future research to improve medication management and ageing.

## 1.15 Thesis Structure

The thesis is organised into six chapters.

**Chapter One** sets the scene by providing the study's background and establishing the context for the research. It explores MRPs as described in the existing literature and from the patients' perspectives regarding their medication management experiences. It then discusses how medication-related issues have been reported in the media, followed by identifying the gaps in current knowledge and suggesting areas for further research as explored throughout this thesis.

**Chapter Two** presents a systematic review and meta-analysis of observational studies, offering a thorough appraisal of the existing literature.

**Chapter Three** introduces a sequential mixed-methods study describing the experiences of adults in Irish hospitals regarding medication management. It investigates the relationship between these experiences and patient age using quantitative analysis. Moreover, it explores

patients' challenges with medication management during their hospital stays through qualitative analysis.

**Chapter Four** presents another sequential mixed-method study, this time examining how medication-related harm was reported in Irish newspapers over the years 2019, 2009 and 1999 and its potential association with different age groups.

**Chapter Five** critically discusses the key findings and their relationship with existing literature. It integrates the study findings with the main theme of the research—age. This chapter also discusses the limitations of the research and concludes with recommendations for clinical practice, policymakers, future research and overall conclusions. A visual overview of the thesis structure is provided in **Figure 1-1**

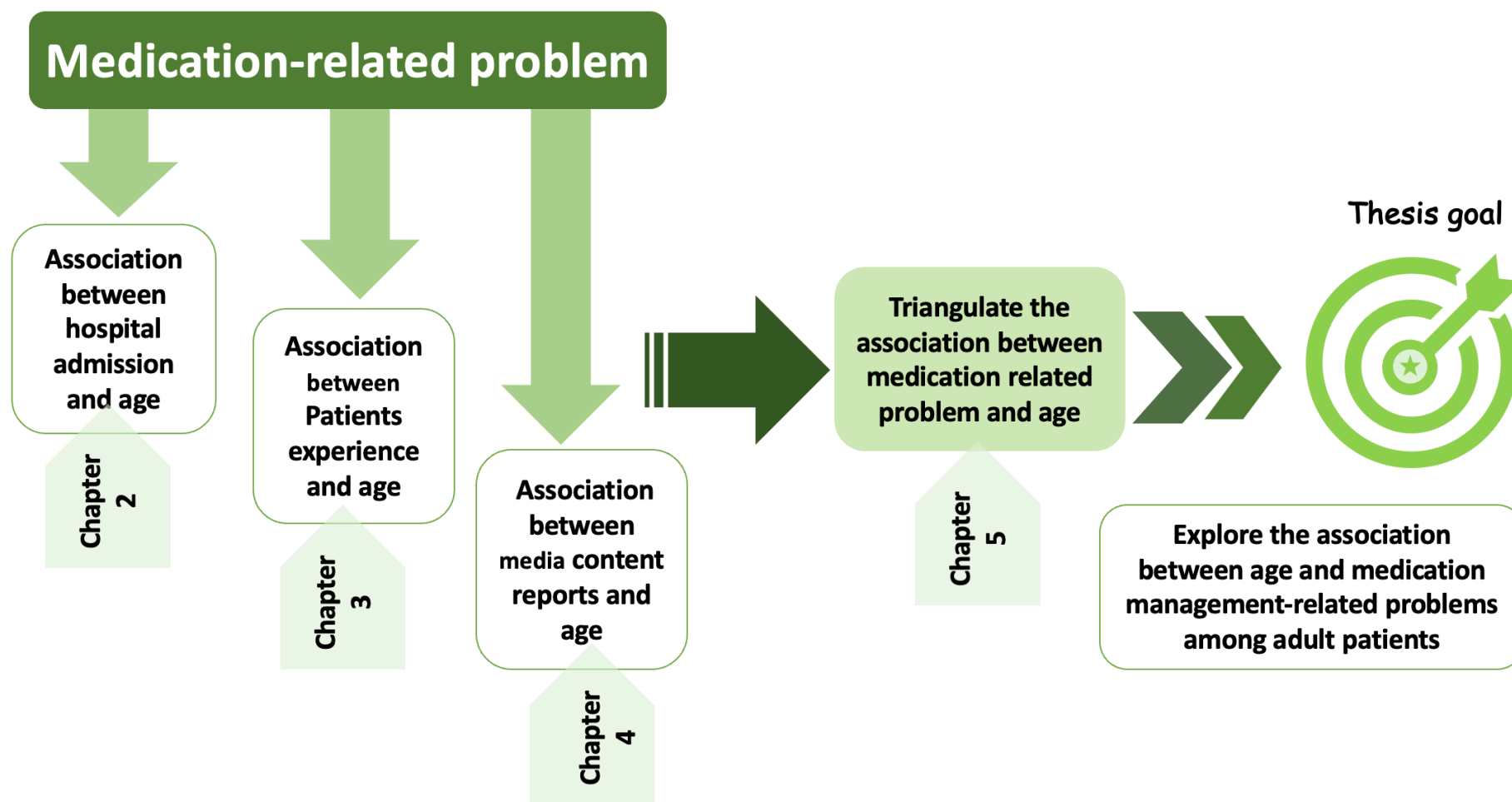


Figure 1-1: Outline of the main thesis structure and chapters.



# **Chapter 2 : Is age a risk factor associated with medication-related hospital admission in adults: A systematic review and meta-analysis**

## 2.1 Introduction

Much attention has been placed on ageing and strategies to improve the quality of life for the older population. Various alterations in pharmacokinetics and pharmacodynamics characterise the advancement of age. This encompasses age-related deterioration in renal and hepatic function and an amplified sensitivity to several pharmacological classes [75]. There is no doubt that ageing poses challenges to safe medication use, and that life expectancy has increased over time. However, evidence suggests that medication-related problems (MRPs) could be more strongly associated with polypharmacy than age [3, 51]. The prevalence of polypharmacy reportedly increased among both middle-aged and older cohorts between 1995 and 2012 [1, 87]. A recent systematic review and meta-analysis on this topic conducted by Hodkinson *et al.*, [48] focussed on preventable medication-related harm in different medical care settings. They found that the overall rate of preventable medication harm was 3%, while it was 9% for all medication harm (including non-preventable harm). This review explored the frequency of medication harm across medical settings and found that it accounts for about half of all preventable harm [48]. This finding demonstrates the seriousness of medication-related harm, which is a frequent event and can lead to severe or potentially life-threatening outcomes. However, the review did not measure any association between medication-related harm and age. It only presented the prevalence rate of preventable medication harm according to age groups (i.e., they categorised the included studies according to age groups) [48].

Hospital admissions caused by MRPs come with significant health and financial burdens, impacting both patients and healthcare systems. Some studies have focussed on describing the frequency of occurrence of drug-related problems in older people exclusively, particularly adverse drug reaction (ADR)-induced hospital admissions. For example, Conforti *et al.*, [125] reported the rate of ADR-related admissions among patients aged 65 years and older as 11% [125]. Notably, the age of patients with ADRs was not statistically different from those without. Oscanoa's 2017 meta-analysis reported the prevalence of hospitalisation resulting from ADRs as 8.7% in a cohort of patients over 60 years old [97]. These two studies investigated older patients only and did not make a direct comparison to younger adults. In 2023, a cross-sectional study investigated the prevalence of ADR-induced hospital admission among patients aged 65 years and older in Ireland [128]. It was found that 10% of older adults' hospital admissions were caused by ADRs, with 71% of ADR-related admissions being preventable. The average age at admission due to ADR was notably lower

than that for non-ADR admissions, as indicated by an adjusted odds ratio (95% CI): 0.96 (0.94, 0.98). However, there was no association between older age and ADR-related admissions [128].

A preliminary search of PubMed, Scopus, PROSPERO and EMBASE found that no systematic reviews since then have considered the association between age and MRPs contributing to hospitalisation. More recent systematic reviews have explored the prevalence of MRP-related hospitalisations [12] and medication non-adherence contributing to hospitalisations [20]. However, they have not focussed on the association between age and MRP hospitalisation, which are the criteria of interest for this review. A meta-analysis was carried out in 2017 on ADR-related hospital admissions among older patients [97]. It was found that polypharmacy was a significant risk factor among older patients, and in most cases the reactions were preventable [97]. In the meantime, polypharmacy can also affect the younger adults [1, 95]. The literature about the strength of age as a predictor of MRPs and medication-related admissions (MRAs) is equivocal, and to the best of our knowledge, no study has systematically reviewed or meta-analysed this topic. There is a need to explore the association between MRP-related admissions and age across both younger and older adult patients. It is therefore essential to understand if age is a risk factor associated with MRAs in order to best guide preventative pharmaceutical care across the adult life span. Therefore, this systematic review attempts to explore the association between age and MRAs.

## 2.2 Review hypothesis

This review was carried out to test the following null hypothesis:

H: Is age a risk factor associated with MRA in adults?

## 2.3 Aim and objectives

This review aims to systematically review and meta-analyse studies that have investigated the association between age and MRA to determine if age is statistically associated with MRA.

**To achieve this aim, the following objectives were addressed:**

- Systematically identify studies that describe the association between age and MRA.
- Appraise the statistical approach employed to examine this association in each included study.
- Critically appraise the quality of each included study.
- Meta-analyse the association between age and MRA, where possible.
- Provide recommendations for future research in this area.

## 2.4 Methods

This review follows the Joanna Briggs Institute (JBI) guidelines for conducting and reporting reviews of risk factors [199]. A systematic review investigating risk factors or aetiology should encompass the following aspects: the group of people being studied (participants), the specific exposure or factor under examination (independent variable, which is age in this review), and the outcome that is being measured (dependent variable, which is MRA in this review). Additionally, this review is prepared according to the Preferred Reporting Items for Systematic Reviews (PRISMA) statement [200]. The registration number in the international prospective register of systematic reviews (PROSPERO) is (CRD42019111598).

### 2.4.1 Eligibility

#### 2.4.1.1 Inclusion criteria

##### Participants

Any study that recruits either the entire adult age span or a defined age group only (for example, aged 65 or older). was included. For studies that included people of all ages, only data for those categorised as adults aged  $\geq 16$  years were considered in this review. There has been debate in the literature regarding the starting age of adulthood; some studies classify adults from the age of 16 [201], while others set it at 18 and above [202]. In this review, the definition of adults included patients aged 16, serving as an average age for the

included patients in these studies within the range of adults aged 18 and above for greater generalizability.

### **Exposure of interest**

Any study that measured aggregate age, regardless of the statistical tests used, was considered. The study must present age details for a patient cohort with MRA and a cohort with another primary reason for admission, henceforth referred to as non-MRA.

### **Outcome**

Any study that reports hospital admission caused by or contributed to MRAs, including adverse drug event (ADE), ADR, medication error, and medication non-adherence, regardless of the definition of MRAs stated in each study.

### **Study design**

Any observational study designs and epidemiological study designs including case series and case-control, retrospective, longitudinal or prospective cohort studies, and cross-sectional studies published in English are eligible for inclusion. An overview of the eligibility criteria (**Figure 2-1**).

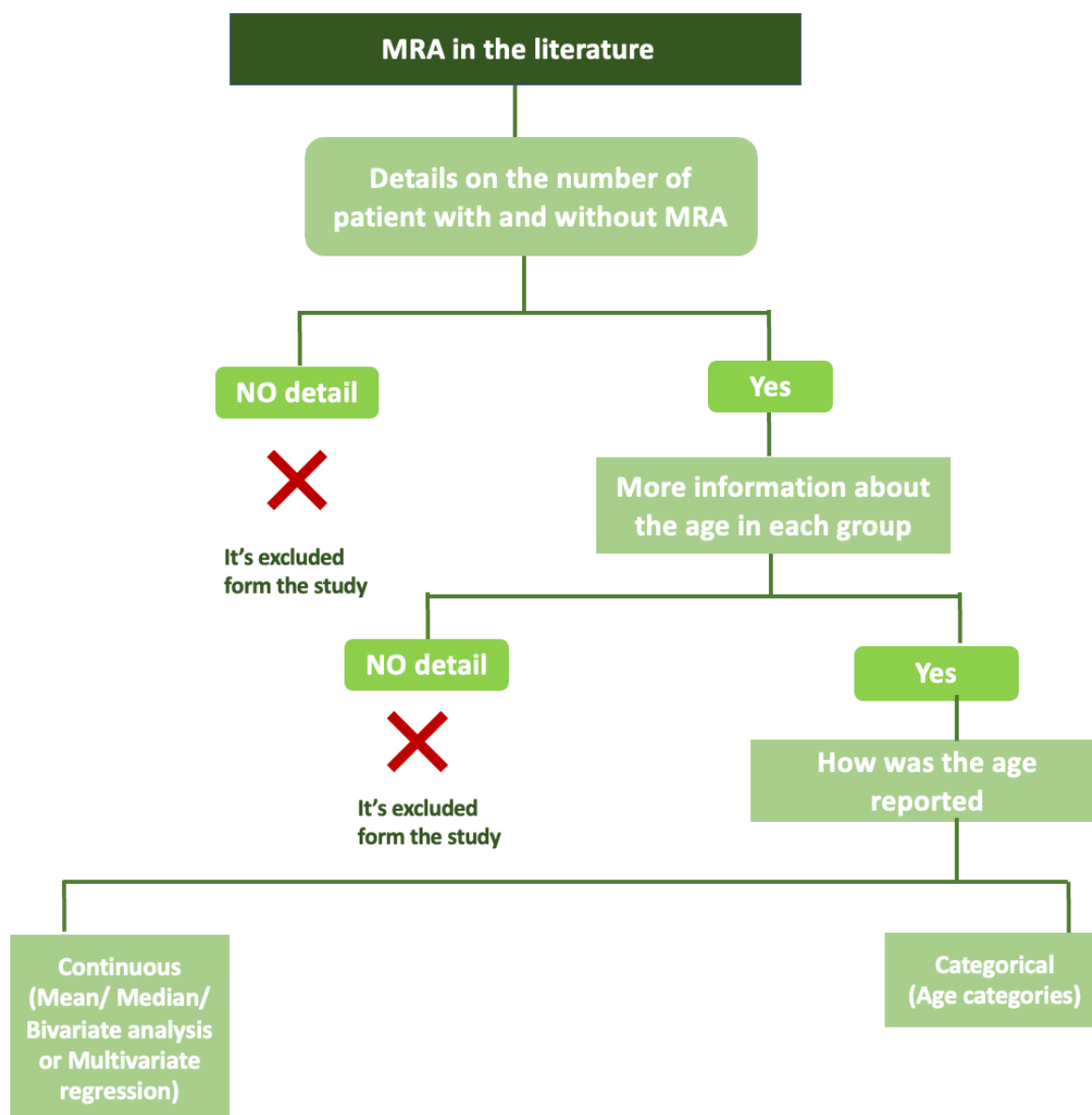


Figure 2-1: Overview of the eligibility criteria.

#### 2.4.1.2 Exclusion criteria

Literature reviews, grey literature, conference proceedings, opinion pieces and commentaries were not included. Studies that were undertaken in cohorts experiencing specific diseases or conditions or using specific medication(s), and also studies focussing exclusively on poisonings or drug abuse or misuse, were further excluded. Studies that only report on emergency department visits that did not lead to hospital admissions were excluded. Studies were excluded if published prior to 2000, or if they were not published in English.

‘To Err is Human: Building a Safer Health System’ is a landmark report published by the Institute of Medicine in the United States in 1999 [203]. The report calls attention to the significant issue of patient safety in healthcare, specifically medical errors. This report is cited because it triggered major changes in worldviews on medication safety. It was expected that in the aftermath of this report there would be greater attention on issues related to MRA. Therefore, this review included articles published since the year 2000, an approach employed by a previous systematic review published in the BMJ [204] .

### 2.4.2 Search strategy

An initial limited search of MEDLINE (Ovid) was undertaken and completed using Medical Subject Heading (MeSH) terms. The search was initiated using the following concepts:

- Medicine-related problems
- Hospitalisation
- Incidence

A similar strategy was undertaken in the databases listed below. The search strategy was adapted to the syntax requirements of each database (use of different treasury of terms). A full search strategy including all synonyms, related terms and Boolean operators (AND and/or OR) was adopted across all databases used (**Appendix I**).

A comprehensive electronic search for relevant studies was undertaken in the following databases:

- MEDLINE (Ovid)
- EMBASE
- Scopus
- Web of Science
- PsycINFO
- CINAHL
- Cochrane Library
- Global Health.

Finally, where required, corresponding authors were contacted for further information that was unpublished in original articles, as well as in cases of missing data. Backward citation chasing was performed by reviewing the bibliography of each included study, and forward citation chasing was performed using Google Scholar. The search was conducted from the inception of the database until September 2023.

### 2.4.3 Study selection

Following the search, full outputs from all the databases were uploaded into EndNote version 9 (Clarivate Analytics, PA, USA) and de-duplicated. Outputs were then imported into Covidence ® to support data management.

The selection of relevant records was carried out independently through primary article screening by two of three reviewers (RM, TG or ENS). The first stage was the title and abstract screening. Articles were divided into three groups: relevant, irrelevant and unsure. Articles deemed by two reviewers to be irrelevant were removed.

In the second stage, the full text articles that were assessed to be potentially eligible (relevant or unsure) were obtained and screened against the inclusion criteria independently by two of four reviewers (RM, TG, ENS or MA). The two independent lists were compared and discussed. Disagreements at each step were resolved with discussion between the two assigned reviewers, or a third reviewer arbitrated if agreement could not be achieved between the two.

### 2.4.4 Data extraction

A data extraction template was designed. Two authors independently extracted data from each included study (RM, TG, ENS or MA). A third reviewer assessed any differences, and these were resolved by discussion until consensus was reached. The data extracted included specific details about the participants, conditions and other characteristics, including the following:

- **Study characteristics:** Authors, unique study identifiers, study years, titles, study periods, sample sizes, geographical locations, study designs, hospital settings, hospital types, number of recruiting centre(s) and eligibility criteria.

- **Participant characteristics:** Demographic data: patients' ages (age categories, number and proportion of patients in different age groups for both MRA and non-MRA), sexes, polypharmacy and comorbidity for both MRA and non-MRA groups.
- **Outcome characteristics:** MRA definition(s) used, type(s) of MRAs, proportion of MRAs, preventability assessments employed and findings, severity assessments employed, and findings and causality assessment methods applied to assess the causality of MRAs' causality of hospital admissions and drugs' causality of MRAs, as well as findings.
- **Analysis characteristics:** Central age for study population and MRA and non-MRA groups, as well as the statistical analytical approach applied in each study.

#### 2.4.5 Assessment of methodology quality

Quality assessment in the context of systematic reviews refers to the procedure used to determine the internal validity and potential biases of studies that satisfy the criteria for inclusion in the review. The JBI approach provides tools for evaluating the quality of various quantitative research designs. These instruments are considered suitable for reviewing studies that explore associations and correlations, with certain adjustments as necessary [199, 205]. Prior to this review, a tool for assessing the quality of prevalence observational systematic reviews was already in existence via JBI [206].

A preliminary search was conducted on previous systematic reviews about MRPs published until 2017 to appraise the quality assessment tools used (**Appendix I**). This appraisal exercise informed the choice of Munn and colleagues from the methodological working group of the Joanna Briggs Institute's "Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data"[205]. It includes ten questions and was adapted with minor modifications to align with the objectives of the current review. The criteria required a clear description of the following: target population, inclusion criteria, sample size, assessment of outcomes and objectives using definitions or tools, MRP categories specified, withdrawal description, outcome measurement, confounding factor identification and analysis and statistical analysis tests. A modification was made to appraise the outcome criteria associated with the comparison of outcomes between the MRA and non-MRA groups (**Table 2-1**).

Table 2-1: Comparison of quality assessment criteria: JBI method versus this review study.

| Criteria            | JBI quality assessment                                                                    | This study quality assessment                                                                     |
|---------------------|-------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Study participant   | Was the sample representative of the target population?                                   | Was the sample representative of the target population?                                           |
|                     | Were study participants recruited in an appropriate way?                                  | Were the criteria for inclusion in the sample clearly defined?                                    |
|                     | Was the sample size adequate?                                                             | Was the sample size adequate?                                                                     |
| Outcome measurement | Were the study subjects and the setting described in detail?                              | For withdrawals, were outcomes described and included in the analyses?                            |
|                     | Was the data analysis conducted with sufficient coverage of the identified sample?        | If comparisons are being made, was there sufficient description of the groups?                    |
|                     | Were objective, standard criteria used for the measurement of the condition?              | Were outcomes assessed using objective criteria?                                                  |
|                     | Was the condition measured reliable?                                                      | Were outcomes measured in a reliable way?                                                         |
|                     | Was there appropriate statistical analysis?                                               | Was there appropriate statistical analysis?                                                       |
| Sub-group analysis  | Are all important confounding factors/subgroups/differences identified and accounted for? | Was the data analysis conducted with sufficient coverage of the confounding factors or subgroups? |
|                     | Were subpopulations identified using objective criteria?                                  | Are confounding factors or subgroups identified and addressed (particularly age)?                 |

Included studies were assessed independently by two of four reviewers (RM, TG, ENS or MA) for methodological quality using a standardised critical appraisal instrument for prevalence data (particularly for systematic review use), specifically the JBI checklist [205, 206]. This checklist includes ten questions to evaluate the internal and external validity of the included studies. Each study was classified into one of three categories depending on the score: low quality (0-4), moderate quality (5-7) and high quality (8-10). Disagreements were resolved through discussion between the two assigned reviewers, or with a third reviewer. All studies were included in the analysis, regardless of quality.

#### 2.4.6 Data synthesis

The extracted data were described in tables and narrative summaries, and they were meta-analysed if possible. The geographic locations of the included studies were classified using World Health Organisation (WHO) country classifications [207]. The proportion of hospital

admissions due to MRA was calculated as the number of patients admitted to hospital due to at least one MRA divided by the total number of eligible patients in each study. The proportion of hospital admissions due to MRA in each age category was calculated as the number of patients with MRAs in the same age category divided by the total number of patients in that age category. The proportion of patients in each age group was calculated as the numerator is the number of patients in each age category who either had MRA or did not have MRA divided by the total number of patients within that particular age group. Therefore, as much as possible, the total sample size represented in the included studies was determined as a total number of patients rather than the total number of ADRs to calculate the number of patients with MRAs and non-MRAs according to age categories. Because of the heterogeneity in the included studies, it was difficult to pool the results due to the overlap in ages across the presented categories. Therefore, age was simplified into three categories, which were used throughout the review: young adults (16-64 years), old adults (65-79 years) and very old adults ( $\geq 80$  years). To pool the estimated mean (the mean of means) in the MRA and non-MRA groups, the following equation was used:

$$\bar{x} = \frac{\bar{x}_1 * n_1 + \bar{x}_2 * n_2 \dots \dots + \bar{x}_{20} * n_{20}}{n_1 + n_2 + \dots \dots \dots n_{20}}$$

A random-effects model was selected to synthesise the data resulting from the heterogeneity between the included studies. Random effects acknowledge that the true effect size may vary between studies due to differences in methodology, populations, or other factors (high level of heterogeneity). While fixed effects assume that all studies share a common true effect size (low level of heterogeneity [208]). Only studies with similar data reporting the proportion of each age category and applying the same categorization to age were pooled and analysed using meta-analysis. Heterogeneity was measured using the  $X^2$  test and the  $I^2$  statistic. A heterogeneity above 50% was considered as substantial heterogeneity, and above 75% was deemed considerable heterogeneity [208]. The effect size was calculated as the mean difference with 95% CI and as odds ratios with 95% CI. All analyses were conducted using Microsoft Excel and Review Manager RevMan 5 (Copenhagen: The Nordic Cochrane Centre, Cochrane).

## 2.5 Results

### 2.5.1 Characteristic of included studies

From all sources, 31967 studies were identified. After removing duplicates, 20581 studies remained. Following title and abstract screening, 20306 were excluded. The remaining 275 studies were deemed eligible for full-text screening. Two and twenty-seven articles were subsequently excluded because they did not report the age profile for both those who experienced and did not experience MRA and/or did not report MRA causality of hospital admission (as distinct from causality of an MRP). In all, 48 studies were included in the systematic review. All included studies were described narratively, while some studies met the criteria for meta-analysis and there was one meta-analysis undertaken, which will be described in Section 2.5.4. A PRISMA flow diagram illustrating the selection of included studies in this review is presented in [209] (**Figure 2-2**).

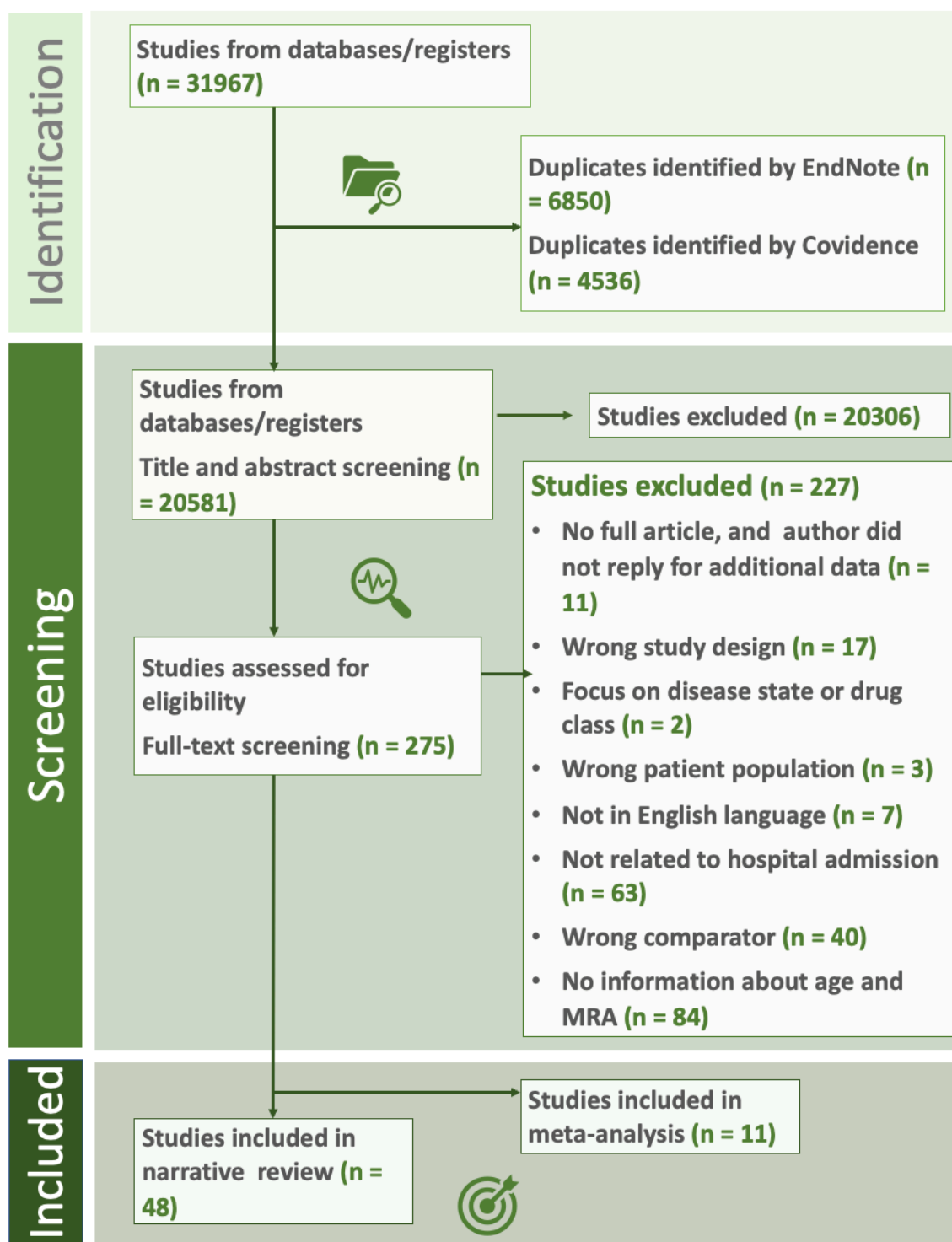


Figure 2-2: Flow diagram of the study selection process.

## 2.5.2 Descriptive characteristics

### 2.5.2.1 Study characteristics

In this review, the total sample size across the 48 eligible studies was 174,641 patients, 10,436 of whom experienced MRAs and 159,792 of whom experienced another primary reason for admission, or non-MRA.

The lowest sample size per study was 100 participants, and the highest was 60,263 participants. The included studies were published between the years 2000 and 2021. Thirty of the studies (63%) were conducted in Europe [33, 34, 73, 84, 92, 106, 107, 113, 114, 122, 126, 128, 201, 210-226] and three (6.3%) were conducted in North America [88, 112, 227], and one in South America [129]. The remainder were undertaken in the African region (n=4) [202, 228-230], the South-east Asia (n=3) [127, 231, 232], the Western Pacific (n=3) [233-235] or the Eastern Mediterranean region (n=1) [236]. However, three studies did not specify the countries in which they were conducted [28, 29, 121]. Out of the 48 included studies, 31 (64.6%) reported cross-sectional designs, 12 reported cohort designs, 3 reported case-control designs and 2 reported pilot designs. All admissions were hospital admissions, and the most common healthcare setting for detecting MRAs was the medical department. In two studies, the population age ranges were 13–91 years and 13–100 years. Lagnaoui *et al.*, [211] included a population age range from 15-94 years [211]. However, Alexopoulou *et al.*, [107] categorised age into three groups: younger than 65, 65–79 and  $\geq 80$ , with population ages ranging from 15–100 years [107]. These four studies were included in the review because the majority of the study population was adults  $\geq 16$  years (an inclusion criterion for this review). A summary of the most critical characteristics of the eligible studies is presented in **Table 2-2**.

Table 2-2: Characteristics of the 48 included studies.

| Author (year)                              | Study design                             | Stage when MRA was assessed/<br>hospital setting               | Sample size | Study population                                                                     | Type of MRA | Number of patients with MRA | Prevalence of MRA %, 95% CI | Number of patients with non-MRA | Definition of MRP |
|--------------------------------------------|------------------------------------------|----------------------------------------------------------------|-------------|--------------------------------------------------------------------------------------|-------------|-----------------------------|-----------------------------|---------------------------------|-------------------|
| Adedapo, A.D., et al.2021 <sup>[230]</sup> | Prospective, cohort study                | HA and DH/departments of internal medicine                     | 1,280       | Adults (range 13–100 years old)                                                      | ADR         | 51                          | 3.9, NA                     | 967**                           | WHO               |
| Ahern et al., 2014 <sup>[106]</sup>        | Prospective, cross-sectional study       | HA/emergency admissions                                        | 856         | Adult patients; the youngest patient admitted with a suspected ADR was 20 years old. | ADR         | 75                          | 8.8, 7.0–10.9               | 781                             | WHO               |
| Alexopoulou et al., 2008 <sup>[107]</sup>  | Prospective study, cross-sectional study | HA/emergency admissions to medical wards                       | 548         | Young adults in the age range 15–100                                                 | ADR         | 70                          | 12.8, NA                    | 478                             | NA                |
| Alvarez et al., 2013 <sup>[129]</sup>      | Prospective, cross-sectional study       | HA/internal medicine ward                                      | 1,045       | Not clear                                                                            | ADR         | 112                         | 10.7, 8.8–12.6              | 933                             | Own definition    |
| Angamo et al., 2017 <sup>[228]</sup>       | Prospective, cross-sectional study       | HA/medical wards                                               | 1,001       | Adults 18 years or older                                                             | ADR         | 103                         | 10.3, NA                    | 898                             | WHO               |
| Asio et al., 2023 <sup>[202]</sup>         | Retrospective, cross-sectional study     | HA/ medical wards                                              | 762         | Adults 18 years or older                                                             | ADR         | 52                          | 8.6, NA                     | 580                             | WHO               |
| Brvar et al., 2009 <sup>[28]</sup>         | Retrospective, cohort study              | HA/medical departments through a medical emergency department) | 520         | Adult patients 18 and older in an age range of 19–94                                 | ADR         | 30                          | 5.8, NA                     | 490                             | WHO               |
| Cabré et al., 2018 <sup>[92]</sup>         | Retrospective, cross-sectional study.    | HA/acute geriatric unit                                        | 3292        | Older patients aged 70 years or older                                                | ADR         | 197                         | 5.9, 5.2–6.8                | 3,095                           | WHO               |

| Author (year)                                   | Study design                         | Stage when MRA was assessed/<br>hospital setting | Sample size | Study population                                             | Type of MRA          | Number of patients with MRA | Prevalence of MRA %, 95% CI | Number of patients with non-MRA | Definition of MRP                      |
|-------------------------------------------------|--------------------------------------|--------------------------------------------------|-------------|--------------------------------------------------------------|----------------------|-----------------------------|-----------------------------|---------------------------------|----------------------------------------|
| Cahir et al., 2023 <sup>[128]</sup>             | Retrospective, cross-sectional study | HA/emergency department                          | 3760        | Older patients aged 65 year and older                        | ADR                  | 361                         | 9.6, NA                     | 437                             | NA                                     |
| Dechanont et al., 2021 <sup>[127]</sup>         | Prospective, cohort study            | HA/internal medicine units                       | 1,776       | Older patients aged 60 year and older                        | Drug-related problem | 56                          | 3.2, NA                     | 1,688                           | The Pharmaceutical Care Network Europe |
| Fattinger et al., 2000 <sup>[218]</sup>         | Retrospective cohort study           | HA and DH/medical inpatient                      | 4,331       | Not clear                                                    | ADR                  | 134                         | 3.3, NA                     | 3,193                           | Not clear                              |
| Giardina et al., 2018 <sup>[219]</sup>          | Prospective, cross-sectional study   | HA and DH/internal medicine                      | 4,802       | Adults (younger than 65 and older than 65)                   | ADR                  | 296                         | 6.2, 5.5–6.8                | 4,370                           | Not clear                              |
| Hopf et al., 2008 <sup>[201]</sup>              | Prospective, pilot study             | HA/emergency department                          | 1,101       | Adults older than 16                                         | ADR                  | 30                          | 2.7, 1.8–3.7                | 29                              | WHO for ADR                            |
| Jolivot et al., 2016 <sup>[217]</sup>           | Prospective, case-control study      | HA/ICU admission                                 | 743         | Adults 18 or older                                           | ADE                  | 173                         | 23.3, NA                    | 570                             | WHO for ADR                            |
| Karuppannan et al., 2013 <sup>[232]</sup>       | Prospective, cross-sectional study   | HA/medical admission units                       | 1,124       | Adults, including those younger than 15, with age categories | ADE                  | 443                         | 39, NA                      | 681                             | WHO for ADR                            |
| Komagamine and Kobayashi, 2019 <sup>[234]</sup> | Retrospective, cross-sectional study | HA/internal medicine ward                        | 1,545       | Adults (interquartile range 66–87, indicating older adults)  | ADR                  | 153                         | 9.9, 8.4–11.4               | 1,392                           | Edwards and Aronson definition         |
| Kongkaew et al., 2013 <sup>[126]</sup>          | Prospective, cohort study            | HA/medical admission units                       | 3,904       | Adults aged 16 years or older, along with other age groups   | ADE                  | 439                         | 11.2, NA                    | 3,291                           | Not clear                              |
| Lagnaoui et al., 2000 <sup>[211]</sup>          | Prospective, cohort study            | HA and DH/internal medicine unit                 | 444         | Adults 15 years old and older; (the range                    | ADR                  | 32                          | 7, NA                       | 328                             | Own definition                         |

| Author (year)                            | Study design                         | Stage when MRA was assessed/<br>hospital setting                                 | Sample size | Study population               | Type of MRA          | Number of patients with MRA | Prevalence of MRA %, 95% CI | Number of patients with non-MRA | Definition of MRP                      |
|------------------------------------------|--------------------------------------|----------------------------------------------------------------------------------|-------------|--------------------------------|----------------------|-----------------------------|-----------------------------|---------------------------------|----------------------------------------|
|                                          |                                      |                                                                                  |             | was from 15–94 years)          |                      |                             |                             |                                 |                                        |
| Laroche et al., 2023 <sup>[226]</sup>    | Prospective, cross-sectional study   | HA/internal medicine ward                                                        | 3648        | All patients                   | ADR                  | 309                         | 8.5,7.6-9.4                 | 3339                            | Own definition                         |
| Lavan et al., 2019 <sup>[222]</sup>      | Prospective, cross-sectional study   | HA/oncology department through emergency, elective and medical oncology day unit | 350         | All patients aged ≥16 years    | ADR                  | 75                          | 21.5, NA                    | 275                             | Edwards and Aronson definition         |
| Lea et al., 2019 <sup>[221]</sup>        | Retrospective, cross-sectional study | HA/internal medicine ward                                                        | 404         | Adults 18 years and older      | Drug-related problem | 155                         | 38, NA                      | 240                             | The Pharmaceutical Care Network Europe |
| Leendertse et al., 2008 <sup>[9]</sup>   | Prospective, case-control study.     | HA/not clear                                                                     | 29,852      | Adult 18 and older             | Drug-related problem | 714                         | 5.6, NA                     | 714                             | WHO for adverse event                  |
| Li et al., 2021 <sup>[235]</sup>         | Retrospective, cross-sectional study | HA/emergency department                                                          | 5521        | Adult 18 and older             | ADR                  | 496                         | 9, NA                       | 5025                            | NA                                     |
| Luttikhuis et al., 2022 <sup>[225]</sup> | Retrospective, cohort study          | HA/emergency department                                                          | 240         | Older patients aged ≥70 year   | Drug-related problem | 73                          | 30.4,NA                     | 167                             | Own definition                         |
| Marcum et al., 2012b <sup>[112]</sup>    | Retrospective, cohort study          | HA/all departments                                                               | 678         | Older patients (age ≥65 years) | Drug-related problem | 40*                         | 5.9, NA                     | 638                             | Not clear (own definition)             |
| Marcum et al., 2012a <sup>[88]</sup>     | Retrospective, cohort study          | HA/ambulatory care setting                                                       | 678         | Older veterans (65 and older)  | ADR                  | 68                          | 10, NA                      | 610                             | NA                                     |

| Author (year)                                | Study design                                      | Stage when MRA was assessed/<br>hospital setting                                 | Sample size | Study population                              | Type of MRA | Number of patients with MRA | Prevalence of MRA %, 95% CI        | Number of patients with non-MRA | Definition of MRP              |
|----------------------------------------------|---------------------------------------------------|----------------------------------------------------------------------------------|-------------|-----------------------------------------------|-------------|-----------------------------|------------------------------------|---------------------------------|--------------------------------|
| Marikova et al., 2021 <sup>[224]</sup>       | Retrospective, cross-sectional study              | HA/ geriatric ward                                                               | 366         | Older patient aged $\geq 78$ year             | ADE         | 43                          | 11.7, NA                           | 323                             | Jonathan R. Nebeker definition |
| McLachlan, 2014 <sup>[233]</sup>             | Prospective, cross-sectional study                | HA/general medicine ward                                                         | 336         | Adults (range 16–92 years old)                | ADE         | 96                          | 28.6, NA                           | 240                             | Jonathan R. Nebeker definition |
| Menéndez-Conde et al., 2011 <sup>[121]</sup> | Prospective, cross-sectional study                | HA/emergency department                                                          | 252         | Adults older than 18 in a range of 21–96      | ADR         | 49                          | 19.4, NA                           | 203                             | NA                             |
| Mjörndal et al., 2002 <sup>[122]</sup>       | Prospective, cross-sectional study                | HA/medicine and cardiology department, including the cardiac intensive care unit | 681         | Adults older than 18 in a range of 19–97      | ADR         | 82                          | 12, NA                             | 587                             | WHO for ADR                    |
| Mouton et al., 2016 <sup>[229]</sup>         | Prospective, cross-sectional survey               | HA/medical wards                                                                 | 1,951       | Adults (interquartile range 34–65)            | ADR         | 162                         | 8.4, 7.2–9.7                       | 1,742                           | Aronson and Ferner for ADR     |
| Ocovska et al., 2022 <sup>[223]</sup>        | Retrospective, cross-sectional study              | HA/emergency department                                                          | 1252        | All adult patients                            | ADR         | 195                         | 15.6, 13.6–17.6                    | 1057                            | Own definition                 |
| Olivier et al., 2002 <sup>[214]</sup>        | Prospective pharmacovigilance, case-control study | HA/medical emergency department                                                  | 671         | Adults (all patients older than 15 years old) | ADR         | 41                          | 6.1 per 100 admissions (4.4–8.3)   | 630                             | WHO for ADR                    |
| Olivier et al., 2009 <sup>[215]</sup>        | Prospective survey, cross-sectional study         | HA/emergency department                                                          | 789         | Older patients (65 or older)                  | ADR         | 66                          | 8.4 per 100 admissions (6.5–10.5). | 723                             | Edwards and Aronson definition |

| Author (year)                                   | Study design                         | Stage when MRA was assessed/<br>hospital setting                                                                     | Sample size | Study population                                                             | Type of MRA          | Number of patients with MRA | Prevalence of MRA %, 95% CI | Number of patients with non-MRA | Definition of MRP              |
|-------------------------------------------------|--------------------------------------|----------------------------------------------------------------------------------------------------------------------|-------------|------------------------------------------------------------------------------|----------------------|-----------------------------|-----------------------------|---------------------------------|--------------------------------|
| Onder et al., 2002 <sup>[84]</sup>              | Retrospective, cross-sectional study | HA/internal medicine wards                                                                                           | 28,411      | Older patients (<65 and >65 years)                                           | ADR                  | 964                         | 3.4, NA                     | 27,447                          | WHO                            |
| Pedrós et al., 2014 <sup>[33]</sup>             | Prospective, cross-sectional study   | HA/not clear                                                                                                         | 4,403       | Adults, categorised as younger than 65 and older than 65                     | ADR                  | 186                         | 4.2, 3.7–4.8                | 4,217                           | European Union                 |
| Pedrós et al., 2016 <sup>[213]</sup>            | Retrospective cross-sectional study  | HA/not clear                                                                                                         | 60,263      | Adults aged 65 years or older                                                | ADR                  | 1,976                       | 3.3, 3.1–3.4                | 58,287                          | European Union                 |
| Pirmohamed et al., 2004 <sup>[34]</sup>         | Prospective, cohort study            | HA/admission through either the accident and emergency department or the acute medical and surgical assessment units | 18,820      | Patients aged > 16 years                                                     | ADR                  | 1,225                       | 6.5, 6.2–6.9                | 17,595                          | Edwards and Aronson definition |
| Pourseyed et al., 2009 <sup>[236]</sup>         | Prospective, cross-sectional         | HA and DH/internal medicine department                                                                               | 400         | (the range was 13–91)                                                        | ADR                  | 7                           | 1.8, NA                     | 353                             | WHO for ADR                    |
| Pouyanne et al., 2000 <sup>[212]</sup>          | Prospective, cross-sectional study   | HA/medical departments                                                                                               | 3,137       | Adults (younger than 15 years old) out of various adult age groups of adults | ADR                  | 100                         | 3.2, 2.4–4.01               | 3,037                           | NA                             |
| Santamaria-Pablos et al., 2009 <sup>[210]</sup> | Prospective, cross-sectional study   | HA/emergency admissions                                                                                              | 163         | Unclear, possibly all patients                                               | Drug-related problem | 53                          | 32.5, 25.8–40.0             | 110                             | Own definition                 |
| Singh et al., 2011 <sup>[231]</sup>             | Prospective, cross-sectional study   | HA/internal medicine department                                                                                      | 3,560       | Not clear                                                                    | Drug-related problem | 118                         | 3.3, NA                     | 3,442                           | WHO for ADR                    |

| Author (year)                              | Study design                             | Stage when MRA was assessed/<br>hospital setting                                            | Sample size | Study population                                     | Type of MRA          | Number of patients with MRA | Prevalence of MRA %, 95% CI | Number of patients with non-MRA | Definition of MRP |
|--------------------------------------------|------------------------------------------|---------------------------------------------------------------------------------------------|-------------|------------------------------------------------------|----------------------|-----------------------------|-----------------------------|---------------------------------|-------------------|
| Smeaton, et al., 2020 <sup>[73]</sup>      | Prospective, pilot study                 | HA/acute medical unit and co-located acute medical assessment unit                          | 100         | Adult 45–64 years old                                | ADR                  | 14                          | 14, NA                      | 79                              | NA                |
| Somers et al., 2010 <sup>[114]</sup>       | Prospective, cross-sectional survey      | HA/geriatric ward through emergency department or after transfer from another hospital ward | 110         | Older patients >65 years                             | Drug-related problem | 23                          | 20.9, NA                    | 87                              | WHO for ADR       |
| van der Hooft et al., 2008 <sup>[29]</sup> | Retrospective, cohort study              | HA/medical wards (internal medicine cardiology surgery paediatrics)                         | 3,515       | Adults (younger than 16) out of different age groups | ADR                  | 115                         | 5.1, 4.3–6.1                | 3,268                           | Own definition    |
| Varallo et al., 2014 <sup>[227]</sup>      | Prospective, cross-sectional pilot study | HA/internal medicine ward                                                                   | 248         | Adults aged 18 years or older                        | ADE                  | 115                         | 46.4, NA                    | 133                             | NA                |
| von Euler et al., 2006 <sup>[220]</sup>    | Retrospective, cohort study              | HA/emergency department to internal medicine ward                                           | 168         | Adults (range 18–89 years old)                       | ADR                  | 18                          | 11, NA                      | 150                             | NA                |
| Wawruch et al., 2009 <sup>[113]</sup>      | Retrospective, cross-sectional study     | HA/department of internal medicine                                                          | 600         | Older patients aged 65 years or older                | ADR                  | 47                          | 7.8, NA                     | 553                             | Not clear         |

Abbreviation: Hospital admission (HA); During hospitalisation (DH), Intensive care unit (ICU); Not available (NA); World health organization (WHO); Adverse drug reaction (ADR); Adverse drug event (ADE); Medication-related admission (MRA).

### **2.5.2.2 Outcome characteristics**

Among the 48 studies that provided definitions for MRP, the majority of these studies applied the WHO definition (**Table 2-2**).

#### **MRP types**

The most common type of MRP identified in this review was ADR in 34 studies [28, 29, 33, 34, 73, 84, 88, 92, 106, 107, 113, 121, 122, 128, 129, 201, 202, 211-215, 218-220, 222, 223, 226, 228-230, 234-236] followed by drug-related problem in eight studies [112, 114, 127, 210, 216, 221, 225, 231], and ADE in six studies [126, 217, 224, 227, 232, 233].

#### **Causality assessment applied**

The assessment of causality between MRP and hospital admission and the causality between reactions and drugs were carried out based on explicit criteria or reviewer judgement. The most common explicit criteria applied to assess the causality of the MRP's causality of the hospital admission were the WHO and Naranjo criteria. The most common explicit criteria applied to assess a drug's causality of MRP was the Naranjo criteria (**Table 2-3**).

Table 2-3: Preventability, severity and drug's causality of MRP and MRP's causality of hospital admission—assessment tools.

| Author (year)                                   | Preventability assessment      | Severity assessment                     | Drug's causality of MRP assessment            | MRP's causality of the hospital admission |
|-------------------------------------------------|--------------------------------|-----------------------------------------|-----------------------------------------------|-------------------------------------------|
| Adedapo, A.D., et al.2021 <sup>[230]</sup>      | Not clear                      | Not clear                               | Own method                                    | Own method                                |
| Ahern et al., 2014 <sup>[106]</sup>             | Hallas criteria                | NA                                      | Naranjo criteria                              | Own method                                |
| Alexopoulou et al., 2008 <sup>[107]</sup>       | Criteria from previous study   | Criteria from previous study            | NA                                            | Naranjo criteria                          |
| Alvarez et al., 2013 <sup>[129]</sup>           | Hallas criteria                | NA                                      | NA                                            | Edwards                                   |
| Angamo et al., 2017 <sup>[228]</sup>            | Schumock and Thornton criteria | NA                                      | Naranjo criteria                              | Own method                                |
| Asio et al., 2023 <sup>[202]</sup>              | Schumock and Thornton criteria | Criteria from previous study            | Naranjo criteria                              | Own method                                |
| Brvar et al., 2009 <sup>[28]</sup>              | Own method                     | NA                                      | WHO                                           | WHO                                       |
| Cabr   et al., 2018 <sup>[92]</sup>             | Hallas criteria                | NA                                      | Naranjo criteria                              | WHO-UMC                                   |
| Cahir et al., 2023 <sup>[128]</sup>             | Hallas criteria                | Hartwig severity scale                  | WHO                                           | Naranjo criteria                          |
| Dechanont et al., 2021 <sup>[127]</sup>         | Hepler Strand criteria         | National Patient Safety Agency criteria | Hallas criteria                               | Hallas criteria                           |
| Fattinger et al., 2000 <sup>[218]</sup>         | NA                             | NA                                      | Karch and Lasagna methods                     | Own method                                |
| Giardina et al., 2018 <sup>[219]</sup>          | Schumock and Thornton criteria | Own method                              | Naranjo criteria                              | Own method                                |
| Hopf et al., 2008 <sup>[201]</sup>              | Hallas criteria                | AN                                      | Naranjo criteria                              | Naranjo criteria                          |
| Jolivot et al., 2016 <sup>[217]</sup>           | Schumock and Thornton criteria | NA                                      | French, Naranjo and Karch and Lasagna methods | Own method                                |
| Karuppannan et al., 2013 <sup>[232]</sup>       | NA                             | NA                                      | Own method                                    | Own method                                |
| Komagamine and Kobayashi, 2019 <sup>[234]</sup> | Hallas criteria                | NA                                      | WHO-UMC criteria                              | Own method                                |
| Kongkaew et al., 2013 <sup>[126]</sup>          | Hepler Strand criteria         | National Patient Safety Agency criteria | NA                                            | Hallas criteria                           |

| Author (year)                                | Preventability assessment                 | Severity assessment          | Drug's causality of MRP assessment     | MRP's causality of the hospital admission |
|----------------------------------------------|-------------------------------------------|------------------------------|----------------------------------------|-------------------------------------------|
| Lagnaoui et al., 2000 <sup>[211]</sup>       | Fatality preventability evaluation method | International definition     | NA                                     | Own method                                |
| Laroche et al., 2023 <sup>[226]</sup>        | Criteria from previous study              | NA                           | The French causality method            | The French causality method               |
| Lavan et al., 2019 <sup>[222]</sup>          | Hallas criteria                           | Hartwig severity scale       | WHO-UMC criteria                       | Own method                                |
| Lea et al., 2019 <sup>[221]</sup>            | NA                                        | NA                           | Not clear                              | Own method                                |
| Leendertse et al., 2008 <sup>[9]</sup>       | Schumock and Thornton criteria            | NA                           | Own method                             | Criteria from previous study by Kramer    |
| Li et al., 2021 <sup>[235]</sup>             | Hallas criteria                           | NA                           | WHO-UMC criteria                       | Own method                                |
| Luttikhuis et al., 2022 <sup>[225]</sup>     | NS                                        | NA                           | Criteria from previous study by Kramer | Criteria from previous study by Kramer    |
| Marcum et al., 2012b <sup>[112]</sup>        | Criteria from previous study              | NA                           | NA                                     | Naranjo criteria                          |
| Marcum et al., 2012a <sup>[88]</sup>         | Own method                                | NA                           | NA                                     | Naranjo criteria                          |
| Marikova et al., 2021 <sup>[224]</sup>       | Schumock and Thornton criteria            | NA                           | WHO-UMC criteria                       | Own method                                |
| McLachlan, 2014 <sup>[233]</sup>             | NA                                        | NA                           | WHO and Naranjo criteria               | Own method                                |
| Menéndez-Conde et al., 2011 <sup>[121]</sup> | Schumock and Thornton criteria            | Schneider scale              | NA                                     | Own method                                |
| Mjörndal et al., 2002 <sup>[122]</sup>       | NA                                        | Own method                   | WHO criteria                           | WHO                                       |
| Mouton et al., 2016 <sup>[229]</sup>         | Schumock and Thornton criteria            | Criteria from previous study | WHO-UMC criteria                       | WHO-UMC                                   |
| Ocovska et al., 2022 <sup>[223]</sup>        | Hallas criteria                           | NA                           | WHO-UMC criteria                       | Own method                                |
| Olivier et al., 2002 <sup>[214]</sup>        | French preventable scale                  | Not clear                    | French causality scale                 | WHO                                       |

| Author (year)                                   | Preventability assessment      | Severity assessment                      | Drug's causality of MRP assessment | MRP's causality of the hospital admission |
|-------------------------------------------------|--------------------------------|------------------------------------------|------------------------------------|-------------------------------------------|
| Olivier et al., 2009 <sup>[215]</sup>           | NA                             | Criteria from previous study             | French causality scale             | WHO                                       |
| Onder et al., 2002 <sup>[84]</sup>              | NA                             | Own method                               | Naranjo criteria                   | Own method                                |
| Pedrós et al., 2014 <sup>[33]</sup>             | NA                             | NA                                       | Spanish pharmacovigilance system   | Own method                                |
| Pedrós et al., 2016 <sup>[213]</sup>            | NA                             | NA                                       | Spanish pharmacovigilance system   | Own method                                |
| Pirmohamed et al., 2004 <sup>[34]</sup>         | Hallas criteria                | NA                                       | NA                                 | Naranjo criteria                          |
| Pourseyed et al., 2009 <sup>[236]</sup>         | Schumock and Thornton criteria | NA                                       | WHO criteria                       | Own method                                |
| Pouyanne et al., 2000 <sup>[212]</sup>          | NA                             | NA                                       | NA                                 | Own method                                |
| Santamaria-Pablos et al., 2009 <sup>[210]</sup> | Criteria from previous study   | US Food and Drug Administration criteria | NA                                 | Own method                                |
| Singh et al., 2011 <sup>[231]</sup>             | Criteria from previous study   | Criteria from previous study             | Not clear                          | Own method                                |
| Smeaton, et al., 2020 <sup>[73]</sup>           | Hallas criteria                | Hartwig severity scale                   | Naranjo criteria                   | Own method                                |
| Somers et al., 2010 <sup>[114]</sup>            | NA                             | NA                                       | Hallas criteria                    | Hallas criteria                           |
| van der Hooft et al., 2008 <sup>[29]</sup>      | Hallas criteria                | Hallas criteria                          | NA                                 | WHO                                       |
| Varallo et al., 2014 <sup>[227]</sup>           | NA                             | NA                                       | Naranjo criteria                   | Own method                                |
| von Euler et al., 2006 <sup>[220]</sup>         | NA                             | NA                                       | WHO criteria                       | Own method                                |
| Wawruch et al., 2009 <sup>[113]</sup>           | NA                             | NA                                       | Own method                         | Own method                                |

Abbreviation: The World Health Organisation-Uppsala Monitoring Centre (WHO-UMC) system; Not available (NA).

### **Preventability assessment applied**

The most common explicit criteria applied to assess preventability were the Hallas criteria (**Table 2-3**). The Hallas criteria assess preventability by categorizing MRP into three main categories: definitely avoidable, possibly avoidable, and unavoidable [237].

### **Severity assessment applied**

The most common explicit criteria applied to assess severity were the Hartwig severity scale and the National Patient Safety Agency criteria (**Table 2-3**). MRP severity was assessed using the Hartwig & Seigel scale, in which severity is graded according to clinical consequence on a scale of one to seven. Mild = Levels 1 and 2; moderate = Levels 3 and 4; severe = Levels 5, 6 and a grade 7 represents a fatal event [238]. The National Patient Safety Agency criteria categorize incidents into five levels of severity: No Harm, indicating no harm occurred; Low Harm, causing minor harm without the need for extra treatment or prolonged hospitalization; Moderate Harm, necessitating additional treatment or prolonged hospital stay without permanent harm; Severe Harm, resulting in significant harm or disability requiring prolonged hospitalization; and Death, indicating the incident led to the patient's death [239].

#### ***2.5.2.3 Analytical approaches applied***

The included studies applied various methods to report aggregate age for both the MRA and non-MRA groups. These methods were: the percentage distribution of age categories (%), central age (Mean or/and Median), whether multivariate regression analysis was conducted, and the p-value of bivariate analysis for each study (**Table 2-4**). These characteristics are essential for understanding the composition of the study samples and the statistical methods employed to assess the association between age and MRA, as will be described in section 2.5.2.6.

Table 2-4: Summary of the methods used to report aggregate age.

| Author (year)                            | % of age categories | Mean | Median | Multivariate regression | P-value of Bivariate analysis |
|------------------------------------------|---------------------|------|--------|-------------------------|-------------------------------|
| Adedapo, 2021 <sup>[230]</sup>           |                     |      |        |                         |                               |
| Ahern, 2014 <sup>[106]</sup>             |                     |      |        |                         |                               |
| Alexopoulou, 2008 <sup>[107]</sup>       |                     |      |        |                         |                               |
| Alvarez, 2013 <sup>[129]</sup>           |                     |      |        |                         |                               |
| Angamo, 2017 <sup>[228]</sup>            |                     |      |        |                         |                               |
| Asio et al., 2023 <sup>[202]</sup>       |                     |      |        |                         |                               |
| Brvar, 2009 <sup>[28]</sup>              |                     |      |        |                         |                               |
| Cabré, 2018 <sup>[92]</sup>              |                     |      |        |                         |                               |
| Cahir et al., 2023 <sup>[128]</sup>      |                     |      |        |                         |                               |
| Dechanont, 2021 <sup>[127]</sup>         |                     |      |        |                         |                               |
| Fattinger, 2000 <sup>[218]</sup>         |                     |      |        |                         |                               |
| Giardina, 2018 <sup>[219]</sup>          |                     |      |        |                         |                               |
| Hopf, 2008 <sup>[201]</sup>              |                     |      |        |                         |                               |
| Jolivot, 2016 <sup>[217]</sup>           |                     |      |        |                         |                               |
| Karuppannan, 2013 <sup>[232]</sup>       |                     |      |        |                         |                               |
| Komagamine, 2019 <sup>[234]</sup>        |                     |      |        |                         |                               |
| Kongkaew, 2013 <sup>[126]</sup>          |                     |      |        |                         |                               |
| Lagnaoui, 2000 <sup>[211]</sup>          |                     |      |        |                         |                               |
| Laroche et al., 2023 <sup>[226]</sup>    |                     |      |        |                         |                               |
| Lavan, 2019 <sup>[222]</sup>             |                     |      |        |                         |                               |
| Lea, 2019 <sup>[221]</sup>               |                     |      |        |                         |                               |
| Leendertse, 2008 <sup>[9]</sup>          |                     |      |        |                         |                               |
| Li et al., 2021 <sup>[235]</sup>         |                     |      |        |                         |                               |
| Luttikhuis et al., 2022 <sup>[225]</sup> |                     |      |        |                         |                               |
| Marcum, 2012a <sup>[88]</sup>            |                     |      |        |                         |                               |
| Marcum, 2012b <sup>[112]</sup>           |                     |      |        |                         |                               |
| Marikova et al., 2021 <sup>[224]</sup>   |                     |      |        |                         |                               |
| McLachlan, 2014 <sup>[233]</sup>         |                     |      |        |                         |                               |
| Menéndez-Conde, 2011 <sup>[121]</sup>    |                     |      |        |                         |                               |
| Mjörndal, 2002 <sup>[122]</sup>          |                     |      |        |                         |                               |
| Mouton, 2016 <sup>[229]</sup>            |                     |      |        |                         |                               |
| Ocovska et al., 2022 <sup>[223]</sup>    |                     |      |        |                         |                               |
| Olivier, 2002 <sup>[214]</sup>           |                     |      |        |                         |                               |
| Olivier, 2009 <sup>[215]</sup>           |                     |      |        |                         |                               |
| Onder, 2002 <sup>[84]</sup>              |                     |      |        |                         |                               |
| Pedrós, 2014 <sup>[33]</sup>             |                     |      |        |                         |                               |
| Pedrós, 2016 <sup>[213]</sup>            |                     |      |        |                         |                               |
| Pirmohamed, 2004 <sup>[34]</sup>         |                     |      |        |                         |                               |
| Pourseyed, 2009 <sup>[236]</sup>         |                     |      |        |                         |                               |
| Pouyanne, 2000 <sup>[212]</sup>          |                     |      |        |                         |                               |
| Santamaria-Pablos, 2009 <sup>[210]</sup> |                     |      |        |                         |                               |
| Singh, 2011 <sup>[231]</sup>             |                     |      |        |                         |                               |
| Smeaton, 2020 <sup>[73]</sup>            |                     |      |        |                         |                               |
| Somers, 2010 <sup>[114]</sup>            |                     |      |        |                         |                               |

|                                     |  |  |  |  |  |
|-------------------------------------|--|--|--|--|--|
| van der Hooft, 2008 <sup>[29]</sup> |  |  |  |  |  |
| Varallo, 2014 <sup>[227]</sup>      |  |  |  |  |  |
| von Euler, 2006 <sup>[220]</sup>    |  |  |  |  |  |
| Wawruch, 2009 <sup>[113]</sup>      |  |  |  |  |  |

#### 2.5.2.4 Prevalence of MRA

The crude prevalence of admitted patients who experienced MRA varied from 1.75% to 46.4% of participants in the included studies. The highest reported prevalence of MRA was in adult patients aged  $\geq 18$  years (46.4%). ADE in young adults aged  $\geq 16$  years was 39%. Drug-related problems in adult patients aged  $\geq 18$  years was 38%. Drug-related problems in adults with unclear age categories was 32.5%. In contrast, the lowest reported prevalence of MRA was observed in young adults aged  $\geq 13$  years (1.75%). The reported proportion in old patients varied from 3.2% to 20.9%, and the most common type of MRA observed was ADR.

#### 2.5.2.5 Age demographics in MRA: the variations

##### Studies presenting age as a categorical variable:

Out of the 48 studies, 12 (25%) were undertaken in old patients, where old age was defined as 65 years or older. Seventeen studies (35%) were performed in adult patients aged  $\geq 18$  years, while 13 studies included both adults and young adults aged  $\geq 16$  years. Six studies did not specify age categories for adult patients (**Table 2-2**). *Marcum et al.*, [112] reported age in categorical groups but did not describe the proportion in each group. These age groups were only used for calculating odds ratios in the regression analysis.

As shown in **Table 2-5**, each study categorised age differently, resulting in heterogeneity between the included studies. The proportion of patients with MRA and those without MRA was calculated using a standard formula for all the included studies. This formula used the number of patients within a specific age category as the numerator and the total number of patients with either MRA or non-MRA as the denominator. However, for **Table 2.5**, we have calculated proportions differently to provide a more specific representation of patient distribution within each age group, as described earlier in Section 2.4. This approach offers a more detailed breakdown of patient proportions within distinct age categories.

Table 2-5: Age profiles for the MRA and non-MRA groups by proportion.

| Author (year)                                   | Total sample size | Age categories | Total number in each age category (%) | Overall number of patients with MRA | Number of patients with MRA by age group | Proportion of patients with MRA by age group (%), 95% CI | Overall number of patients without MRA | Number of patients without MRA by age group | Proportion of patients without MRA by age group (%) |
|-------------------------------------------------|-------------------|----------------|---------------------------------------|-------------------------------------|------------------------------------------|----------------------------------------------------------|----------------------------------------|---------------------------------------------|-----------------------------------------------------|
| Alexopoulou et al., 2008 <sup>[107]</sup>       | 548               | <65            | 192 (35)                              | 70                                  | 18                                       | 9.4, NA                                                  | 478                                    | 174                                         | 90.6                                                |
|                                                 |                   | 65–79          | 212 (38.7)                            |                                     | 32                                       | 15.1, NA                                                 |                                        | 180                                         | 84.9                                                |
|                                                 |                   | ≥80            | 144 (26.3)                            |                                     | 20                                       | 13.9, NA                                                 |                                        | 124                                         | 86.1                                                |
| Dechanont et al., 2021 <sup>[127]</sup>         | 1776****          | 60–69          | 835 (47)                              | 56                                  | 20                                       | 2.4, NA                                                  | 1688                                   | 798                                         | 95.6                                                |
|                                                 |                   | 70–79          | 658 (37)                              |                                     | 31                                       | 4.7, NA                                                  |                                        | 615                                         | 93.5                                                |
|                                                 |                   | ≥80            | 283 (15.9)                            |                                     | 5                                        | 1.8, NA                                                  |                                        | 275                                         | 97.1                                                |
| Giardina et al., 2018 <sup>[219]</sup>          | 4819***           | <65            | 1173 (24.3)                           | 296                                 | 60                                       | 5.1, NA                                                  | 4,370                                  | 1,074                                       | 91.6                                                |
|                                                 |                   | 65–78          | 1364 (28.3)                           |                                     | 89                                       | 6.5, NA                                                  |                                        | 1,228                                       | 90                                                  |
|                                                 |                   | 79–84          | 1112 (23.1)                           |                                     | 71                                       | 6.4, NA                                                  |                                        | 1,010                                       | 90.8                                                |
|                                                 |                   | >84            | 1170 (24.3)                           |                                     | 76                                       | 6.5, NA                                                  |                                        | 1,058                                       | 90.4                                                |
| Karuppannan et al., 2013 <sup>[232]</sup>       | 1124              | <15            | 16                                    | 443                                 | ---                                      | ---                                                      | 681                                    | 16                                          | 100                                                 |
|                                                 |                   | 15–39          | 316 (28.1)                            |                                     | 74                                       | 23.4, NA                                                 |                                        | 242                                         | 76.6                                                |
|                                                 |                   | 40–64          | 552 (49.1)                            |                                     | 252                                      | 45.7, NA                                                 |                                        | 300                                         | 54.3                                                |
|                                                 |                   | ≥65            | 240 (21.4)                            |                                     | 117                                      | 48.8, NA                                                 |                                        | 123                                         | 51.3                                                |
| Komagamine and Kobayashi, 2019 <sup>[234]</sup> | 1545              | <65            | 350 (22.7)                            | 153                                 | 26                                       | 17,NA                                                    | 1392                                   | 324                                         | 23.3                                                |
|                                                 |                   | ≥65            | 1195 (77.3)                           |                                     | 127                                      | 83,NA                                                    |                                        | 1068                                        | 76.7                                                |
| Kongkaew et al., 2013 <sup>[126]</sup>          | 3904              | 16–44          | 693 (17.9)                            | 439                                 | 112                                      | 16.2, NA                                                 | 3291**                                 | 556                                         | 80.2                                                |
|                                                 |                   | 45–64          | 921 (23.8)                            |                                     | 84                                       | 9.1, NA                                                  |                                        | 803                                         | 87.2                                                |
|                                                 |                   | 65–74          | 678 (17.5)                            |                                     | 69                                       | 10.2, NA                                                 |                                        | 580                                         | 85.5                                                |
|                                                 |                   | 75–84          | 911 (23.6)                            |                                     | 115                                      | 12.6, NA                                                 |                                        | 749                                         | 82.2                                                |
|                                                 |                   | ≥ 85           | 663 (17.2)                            |                                     | 59                                       | 8.9, NA                                                  |                                        | 565                                         | 85.2                                                |
| Marcum et al., 2012a <sup>[88]</sup>            | 678               | 65–74          | 273 (40.3)                            | 68                                  | 30                                       | 11, NA                                                   | 610                                    | 243                                         | 89                                                  |
|                                                 |                   | 75–84          | 334 (49.3)                            |                                     | 29                                       | 8.7, NA                                                  |                                        | 305                                         | 91.3                                                |
|                                                 |                   | ≥85            | 71 (10.5)                             |                                     | 9                                        | 12.7, NA                                                 |                                        | 62                                          | 87.3                                                |

| Author (year)                                | Total sample size | Age categories  | Total number in each age category (%) | Overall number of patients with MRA | Number of patients with MRA by age group | Proportion of patients with MRA by age group (%), 95% CI | Overall number of patients without MRA | Number of patients without MRA by age group | Proportion of patients without MRA by age group (%) |
|----------------------------------------------|-------------------|-----------------|---------------------------------------|-------------------------------------|------------------------------------------|----------------------------------------------------------|----------------------------------------|---------------------------------------------|-----------------------------------------------------|
| Menéndez-Conde et al., 2011 <sup>[121]</sup> | 252               | <65             | 79 (31.3)                             | 49                                  | 17                                       | 21.5, NA                                                 | 203                                    | 62                                          | 78.5                                                |
|                                              |                   | >65             | 173 (68.7)                            |                                     | 32                                       | 18.5, NA                                                 |                                        | 141                                         | 81.5%                                               |
| Olivier et al., 2009 <sup>[215]</sup>        | 789               | 65–69           | 97 (12.3)                             | 66                                  | 8                                        | 8.2, NA                                                  | 723                                    | 89                                          | 91.8                                                |
|                                              |                   | 70–74           | 127 (16.1)                            |                                     | 12                                       | 9.4, NA                                                  |                                        | 115                                         | 90.6                                                |
|                                              |                   | 75–79           | 150 (19)                              |                                     | 9                                        | 6, NA                                                    |                                        | 141                                         | 94                                                  |
|                                              |                   | 80–84           | 164 (20.8)                            |                                     | 17                                       | 10.4, NA                                                 |                                        | 147                                         | 89.6                                                |
|                                              |                   | 85–89           | 127 (16.1)                            |                                     | 9                                        | 7.1, NA                                                  |                                        | 118                                         | 92.9                                                |
|                                              |                   | ≥90             | 124 (15.7)                            |                                     | 11                                       | 8.9, NA                                                  |                                        | 113                                         | 91.1                                                |
| Onder et al., 2002 <sup>[84]</sup>           | 28411             | <65             | 8145 (28.7)                           | 964                                 | 279                                      | 3.4, NA                                                  | 27447                                  | 7866                                        | 96.6                                                |
|                                              |                   | 65-79           | 11820 (41.6)                          |                                     | 421                                      | 3.6, NA                                                  |                                        | 11399                                       | 96.4                                                |
|                                              |                   | ≥80             | 8446 (29.7)                           |                                     | 264                                      | 3.1, NA                                                  |                                        | 8182                                        | 96.9                                                |
| Pedrós et al., 2014 <sup>[33]</sup>          | 4403              | <65             | 2031 (46.1)                           | 186                                 | 44                                       | 2.2, NA                                                  | 4,217                                  | 1,987                                       | 97.8                                                |
|                                              |                   | ≥65             | 2372 (53.9)                           |                                     | 142                                      | 6, NA                                                    |                                        | 2,230                                       | 94                                                  |
| Pedrós et al., 2016 <sup>[213]</sup>         | 60263             | 65–74           | 22074 (36.6)                          | 1976                                | 662                                      | 3.0, 2.8–3.2                                             | 58287                                  | 21,412                                      | 97                                                  |
|                                              |                   | 75–84           | 25817 (42.8)                          |                                     | 905                                      | 3.5, 3.3–3.7                                             |                                        | 24,912                                      | 96.5                                                |
|                                              |                   | ≥85             | 12372 (20.5)                          |                                     | 409                                      | 3.3, 3.0–3.6                                             |                                        | 11,963                                      | 96.7                                                |
| Pouyanne et al., 2000 <sup>[212]</sup>       | 3137              | ≤15             | 525                                   | 100                                 | 10                                       | 1.9, 0.91-3.5                                            | 3037                                   | 515                                         | 98.1                                                |
|                                              |                   | 16 to <64       | 1184 (37.7)                           |                                     | 31                                       | 2.6, 1.6-3.7                                             |                                        | 1153                                        | 97.4                                                |
|                                              |                   | ≥65             | 1428 (45.5)                           |                                     | 59                                       | 4.1, 2.7- 5.5                                            |                                        | 1369                                        | 95.9                                                |
| van der Hooft et al., 2008 <sup>[29]</sup>   | 2238*             | younger than 16 | 301                                   | 115                                 | 1                                        | 0.3, 0.1–1.9                                             | 2123                                   | 300                                         |                                                     |

| Author (year)                         | Total sample size | Age categories | Total number in each age category (%) | Overall number of patients with MRA | Number of patients with MRA by age group | Proportion of patients with MRA by age group (%), 95% CI | Overall number of patients without MRA | Number of patients without MRA by age group | Proportion of patients without MRA by age group (%) |
|---------------------------------------|-------------------|----------------|---------------------------------------|-------------------------------------|------------------------------------------|----------------------------------------------------------|----------------------------------------|---------------------------------------------|-----------------------------------------------------|
|                                       |                   | 17–55          | 755 (33.7)                            |                                     | 24                                       | 3.2, 2.1–4.7                                             |                                        | 731                                         | 96.8                                                |
|                                       |                   | 56–75          | 674 (30)                              |                                     | 40                                       | 5.9, 4.4–8                                               |                                        | 634                                         | 94.1                                                |
|                                       |                   | >75            | 508 (22.7)                            |                                     | 50                                       | 9.8, 7.5–12.7                                            |                                        | 458                                         | 90.2                                                |
| Varallo et al., 2014 <sup>[227]</sup> | 248               | 18–59          | 150 (60.5)                            | 115                                 | 66                                       | 44, NA                                                   | 133                                    | 84                                          | 56                                                  |
|                                       |                   | ≥60            | 98 (39.5)                             |                                     | 49                                       | 50, NA                                                   |                                        | 49                                          | 50                                                  |
| Wawruch et al., 2009 <sup>[113]</sup> | 600               | <75 (65–74)    | 245 (40.8)                            | 47                                  | 18                                       | 7.3, NA                                                  | 553                                    | 227                                         | 92.7                                                |
|                                       |                   | ≥75            | 355 (59.2)                            |                                     | 29                                       | 8.2, NA                                                  |                                        | 326                                         | 91.8                                                |

\*This for all acute patients that have age categories and there is planned patients did not included. \*\*Of all 3904 patients, 439 patients had causal ADEs; 144 had noncausal ADEs; 30 had other causal drug-related problems; and 3291 patients had non-DRAs. \*\*\* This number include 17 patients ADRs occurred both before and during the hospital stay (the total =4819). \*\*\*\* this number include 32 patients with medication irrelevant or unevaluated.

**Note: Grey shadow means the patients was excluded from analysis in the review.**

The included studies exhibit inconsistently defined age categories, leading to overlapping age ranges between older and younger adult patient groups across studies. Specifically, some studies including all adult patients utilised age categorisations of <65 years and >65 years [33, 219]. Onder *et al.*, [84] employed the same categorisation of <65 years and >65 years, but specifically for assessing the impact of MRA in older patients. This incongruity in age classification complicates the interpretation of results.

Furthermore, only 16 of the included 48 studies categorised age at all. Of these 16 studies, 12 distinguished between younger adults and older ages. The remaining four studies used unique and different age cut-offs. In contrast, among the 16 studies that categorised adult age, only two distinguished between young adults and middle age (40–65 years). However, these two studies diverged in their definition of an adult: one included all patients aged  $\geq 15$  years, while the other considered only those aged  $\geq 16$  years as adults (**Figure 2-3**).

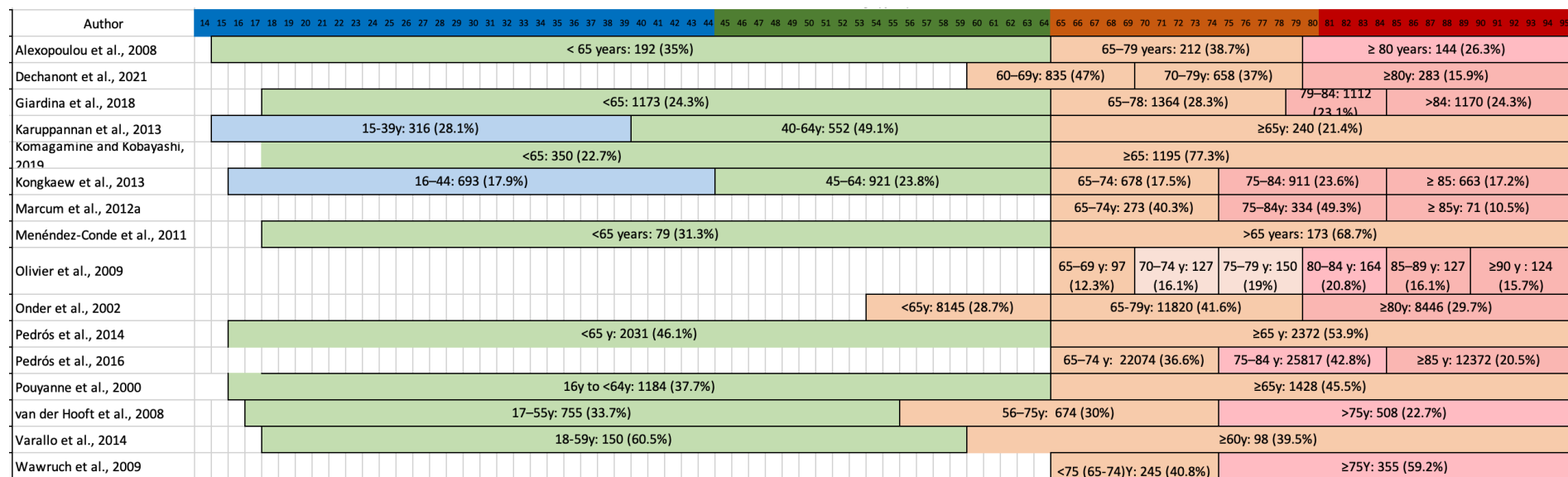


Figure 2-3: Age categories as described in the included studies.

### **Studies presenting age as a continuous variable**

The reporting of aggregate age in the included studies was inconsistent (**Table 2-6**). While some studies reported mean and/or median values for age, others did not. Most studies that reported mean or median age recruited older patients only.

Table 2-6: Age information reported for the exposed MRA and unexposed non-MRA groups by age profile.

| Author (year)                              | Age profile for total study population   |                                     | Age profile                      |                                 |                            |                            |
|--------------------------------------------|------------------------------------------|-------------------------------------|----------------------------------|---------------------------------|----------------------------|----------------------------|
|                                            | Mean of total study population           |                                     | Median of total study population |                                 |                            |                            |
|                                            | Mean, “SD”, range                        |                                     | Median, (IQR), range             |                                 |                            |                            |
|                                            | Mean of total study population           | Median of total study population    | Mean of MRA                      | Mean of non-MRA                 | Median of MRA              | Median of non-MRA          |
|                                            | Mean, “SD”, range                        | Median, (IQR), range                | Mean, “SD”, range                | Mean, “SD”, range               | Median, (IQR), range       | Median, (IQR), range       |
| Adedapo, A.D., et al.2021 <sup>[230]</sup> | 49.3, “18.2”, 13–100                     | NA                                  | NA                               | NA                              | NA                         | NA                         |
| Ahern et al., 2014 <sup>[106]</sup>        | NA                                       | NA                                  | 68.8, “18.0”                     | 44.8, “25.8”                    | Median (95%CI): 73 (69-77) | Median (59%CL): 45 (41-47) |
| Alexopoulou et al., 2008 <sup>[107]</sup>  | Mean (95% CI, range): 65 (64–67, 15–100) | NA                                  | Mean (95%CI): 70.8 (68.9–72.7)   | Mean (95%CI): 64.7 (63.74–65.7) | NA                         | NA                         |
| Alvarez et al., 2013 <sup>[129]</sup>      | NA                                       | NA                                  | 69, SE= 2                        | 68, SE= 1                       | NA                         | NA                         |
| Angamo et al., 2017 <sup>[228]</sup>       | NA                                       | NA                                  | NA                               | NA                              | 40, (28-60)                | 40, (28-55)                |
| Asio et al., 2023 <sup>[202]</sup>         | NA                                       | NA                                  | 37.38 "11.69"                    | 35.65 "15.14"                   | NA                         | NA                         |
| Brvar et al., 2009 <sup>[28]</sup>         | 65.6, 19–94                              | NA                                  | 71.5, 42–89                      | 65.2, 19–94                     | NA                         | NA                         |
| Cabré et al., 2018 <sup>[92]</sup>         | 84.7                                     | NA                                  | 84.9, “6.8”                      | 84.7, “6.5”                     | NA                         | NA                         |
| Cahir et al., 2023 <sup>[128]</sup>        | NA                                       | NA                                  | 79.9 "7.3"                       | 81.6 "7.7"                      | NA                         | NA                         |
| Dechanont et al., 2021 <sup>[127]</sup>    | 71.1, “8.0”                              | NA                                  | NA                               | NA                              | NA                         | NA                         |
| Fattinger et al., 2000 <sup>[218]</sup>    | NA                                       | M: 59, (46- 71);<br>F: 64, (46- 77) | NA                               | NA                              | 60.5, (45- 77)             | 61, (46- 74).              |

|                                                    |                                                                               |                      |                      |                   |                                                                       |                        |
|----------------------------------------------------|-------------------------------------------------------------------------------|----------------------|----------------------|-------------------|-----------------------------------------------------------------------|------------------------|
| Giardina et al., 2018 <sup>[219]</sup>             | NA                                                                            | NA                   | NA                   | NA                | 78, (68–85)                                                           | 78, (65–84)            |
| Hopf et al., 2008 <sup>[201]</sup>                 | NA                                                                            | NA                   | <b>67</b> , 19–91    | <b>62</b> , 19–91 | 71.5, (52.75–81.5)                                                    | 63, (47.5–75)          |
| Jolivot et al., 2016 <sup>[217]</sup>              | NA                                                                            | 65, (51–78)          | NA                   | NA                | Preventable ADE:<br>63, (47– 77)<br>Unpreventable<br>ADE: 65, (55–75) | 65, (50–78)            |
| Karuppannan et al., 2013 <sup>[232]</sup>          | <b>49.7</b> , “17.7”                                                          | NA                   | <b>54.6</b> , “15.8” | NA                | NA                                                                    | NA                     |
| Komagamine and Kobayashi,<br>2019 <sup>[234]</sup> | NA                                                                            | 79, (66–87)          | NA                   | NA                | 83, (71–88)                                                           | 78, (66–87)            |
| Kongkaew et al., 2013                              | <b>65.4</b> , “19.9”                                                          | NA                   | <b>62.4</b> , “21.8” | NA                | NA                                                                    | NA                     |
| Lagnaoui et al., 2000 <sup>[211]</sup>             | <b>59</b> , 15–94                                                             | NA                   | <b>57.5</b>          | <b>59.0</b>       | NA                                                                    |                        |
| Lavan et al., 2019 <sup>[222]</sup>                | NA                                                                            | 65.5, (57–72), 16–90 | NA                   | NA                | 65, (56–70), 16–89                                                    | 66, (57–72), 18–<br>90 |
| Laroche et al., 2023 <sup>[226]</sup>              | 60                                                                            | 68 (43–82)           | <b>69</b>            | <b>59</b>         | 75 (60–86)                                                            | 67 (41–81)             |
| Lea et al., 2019 <sup>[221]</sup>                  | NA                                                                            | 79.4, 23.1–96.4      | NA                   | NA                | 78.4, 32.9–94.9                                                       | 80.3, 23.1–96.4        |
| Leendertse et al., 2008 <sup>[9]</sup>             | All admissions: <b>60</b> ,<br>“18”.<br>Acute admissions:<br><b>62</b> , “19” | NA                   | <b>68</b> , “17”     | <b>67</b> , “16”  | NA                                                                    | NA                     |
| Li et al., 2021 <sup>[235]</sup>                   | NA                                                                            | NA                   | NA                   | NA                | 74 (58–83)                                                            | 55 (35–72)             |
| Luttikhuis et al., 2022 <sup>[225]</sup>           | NA                                                                            | 78 (73–83)           | <b>NA</b>            | NA                | 77 (72–82.5)                                                          | 79 (73–84)             |
| Marcum et al., 2012a <sup>[88]</sup>               | <b>76.4</b>                                                                   | NA                   | NA                   | NA                | NA                                                                    | NA                     |
| Marcum et al., 2012b <sup>[112]</sup>              | <b>76.4</b> , “6.5”                                                           | NA                   | NA                   | NA                | NA                                                                    | NA                     |

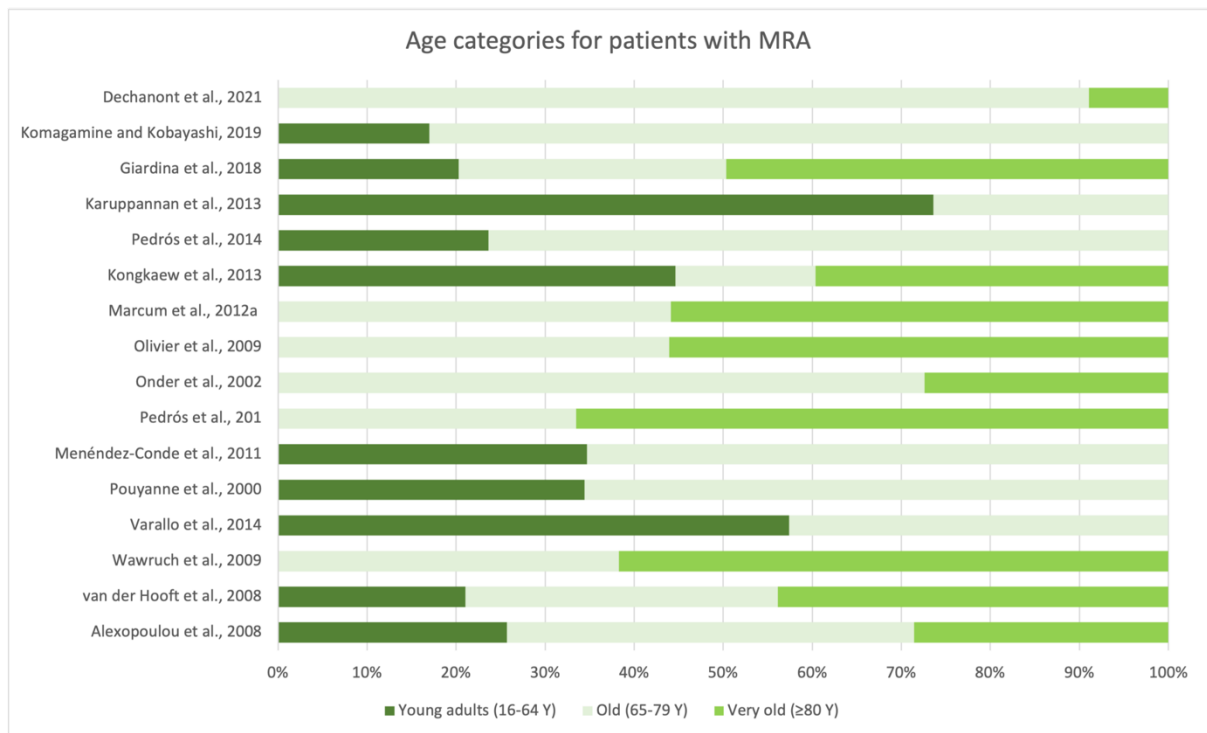
|                                              |                                                                                                         |             |                                                                                                                |                               |                                                |                                                  |
|----------------------------------------------|---------------------------------------------------------------------------------------------------------|-------------|----------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------------------------------|--------------------------------------------------|
| Marikova et al., 2021 <sup>[224]</sup>       | NA                                                                                                      | 86 (82–89)  | NA                                                                                                             | NA                            | 86 (82–89)                                     | 86 (82–89)                                       |
| McLachlan, 2014 <sup>[233]</sup>             | NA                                                                                                      | NA          | <b>65.9</b> , 21–92 of all causing admission<br><b>72.4</b> , 21–92 excluding recreational drugs and overdoses | <b>64.3</b> , 16–91           | NA                                             | NA                                               |
| Menéndez-Conde et al., 2011 <sup>[121]</sup> | <b>68.2</b> , “16.1”, 21–96.                                                                            | NA          | <b>67.8</b> , “17.1”                                                                                           | <b>68.3</b> , “15.9”          | NA                                             | NA                                               |
| Mjörndal et al., 2002 <sup>[122]</sup>       | NA                                                                                                      | NA          | NA                                                                                                             | NA                            | M: 66, 21–92;<br>F76, 21–92;<br>All: 74, 21–92 | M: 71, 19–93;<br>F: 74, 20–97;<br>All: 72, 19–97 |
| Mouton et al., 2016 <sup>[229]</sup>         | NA                                                                                                      | 50, (34–65) | NA                                                                                                             | NA                            | 53, (36–65)                                    | NA                                               |
| Ocovska et al., 2022 <sup>[223]</sup>        | NA                                                                                                      | 71 (58–82)  | NA                                                                                                             | NA                            | 75 (66–84)                                     | 70 (56–81)                                       |
| Olivier et al., 2002 <sup>[214]</sup>        | NA                                                                                                      | NA          | <b>58</b> , “22.2”                                                                                             | <b>55.6</b> , “22.5”          | NA                                             | NA                                               |
| Olivier et al., 2009 <sup>[215]</sup>        | NA                                                                                                      | NA          | <b>80.41</b> , “8.50”, 66–100                                                                                  | <b>80.08</b> , “8.29”, 65–100 | NA                                             | NA                                               |
| Onder et al., 2002 <sup>[84]</sup>           | <b>70</b> , “16”<br><65y: <b>49.4</b> “13.4”, 65–79y: <b>73.1</b> “4.3”, and<br>≥80y: <b>84.9</b> “3.9” | NA          | NA                                                                                                             | NA                            | NA                                             | NA                                               |
| Pedrós et al., 2014 <sup>[33]</sup>          | NA                                                                                                      | NA          | NA                                                                                                             | NA                            | 75, (17.0), 28–97                              | 66, (26.0), 16–102                               |
| Pedrós et al., 2016 <sup>[213]</sup>         | NA                                                                                                      | NA          | NA                                                                                                             | NA                            | NA                                             | NA                                               |
| Pirmohamed et al., 2004 <sup>[34]</sup>      | NA                                                                                                      | NA          | NA                                                                                                             | NA                            | 76, (65–83)                                    | 66, (46–79)                                      |

|                                                 |                               |                    |                                                                  |                      |    |    |
|-------------------------------------------------|-------------------------------|--------------------|------------------------------------------------------------------|----------------------|----|----|
| Pourseyed et al., 2009 <sup>[236]</sup>         | <b>60.41</b> , “16.97”, 13–91 | NA                 | <b>63.14</b> , 44–79                                             | <b>61.22</b> , 13–91 | NA | NA |
| Pouyanne et al., 2000 <sup>[212]</sup>          | NA                            | NA                 | <b>60.5</b>                                                      | <b>52.9</b>          | NA | NA |
| Santamaria-Pablos et al., 2009 <sup>[210]</sup> | <b>64.6</b> , “18.1”          | NA                 | <b>Mean (SD),</b><br>(95%CI): <b>55.9</b><br>(18.2), (48.7-63.1) | NA                   | NA | NA |
| Singh et al., 2011 <sup>[231]</sup>             | <b>49.8</b> , “18.23”         | NA                 | <b>50.5</b> , “17.8”                                             | <b>49.1</b> , “18.6” | NA | NA |
| Smeaton, et al., 2020 <sup>[73]</sup>           | NA                            | 57, (52–61)        | NA                                                               | NA                   | NA | NA |
| Somers et al., 2010 <sup>[114]</sup>            | <b>83.2</b> , “7.5”           | 82.7, 65.5 – 102.5 | <b>80.3</b>                                                      | <b>83.9</b>          | NA | NA |
| van der Hooft et al., 2008 <sup>[29]</sup>      | NA                            | NA                 | NA                                                               | NA                   | NA | NA |
| Varallo et al., 2014 <sup>[227]</sup>           | NA                            | NA                 | NA                                                               | NA                   | NA | NA |
| von Euler et al., 2006 <sup>[220]</sup>         | NA                            | NA                 | <b>72</b> , 29 – 89                                              | <b>65</b> , 18 – 98  | NA | NA |
| Wawruch et al., 2009 <sup>[113]</sup>           | <b>76.6</b> , “6.5”           | NA                 | NA                                                               | NA                   | NA | NA |

#### *2.5.2.6 Association between age and medication-related admission*

In studies where age was reported as a categorical variable, a comparison of the number of patients in different age groups between the MRA and non-MRA groups found variations in the distribution of patients across these age categories. Additionally, there was an overlap in the age groups, and in some studies, the number of older adults experiencing MRA exceeded that of younger patients (**Figure 2-4**). Among young adult groups, 16% of patients experienced MRA. However, there was no variation in the percentages of older and very old patients between the MRA and non-MRA groups (42% older and 42% very old for MRA groups; 46% older and 47% very old for non-MRA groups).

(A)



(B)

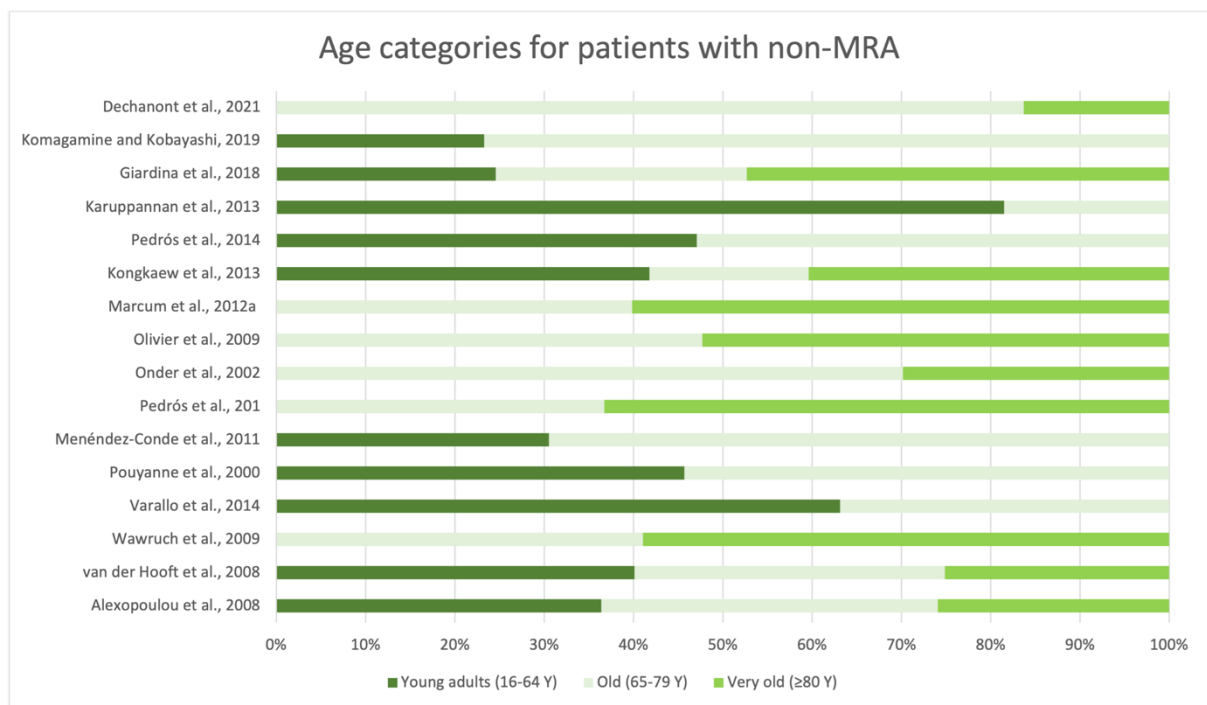


Figure 2-4: Comparing numbers of patients in different age groups between the MRA and the non-MRA groups. (A) for MRA groups and (B) for non-MRA groups.

On the other hand, in the studies that reported age as a continuous variable, it was found that some studies reported a relatively small mean age for patients experiencing MRA, indicating that younger patients were also affected by MRA (**Table 2-6**). The smallest reported mean age in the MRA group was 50.5 years, while in the non-MRA group, it was 44.8 years. Because of the heterogeneity in the included studies and the fact that not all studies reported the mean age, we attempted to calculate the estimated mean only for those studies that provided this data. The pooled estimated mean was calculated for the MRA and non-MRA groups as 63.2 and 57.9 respectively. It was not possible to calculate the confidence interval around the pooled estimated mean because not all of the pooled studies reported the necessary standard deviation to support this calculation, and it was therefore not possible to examine the overlap between these confidence intervals.

The association between age and MRA was explored in several of the included studies using different statistical methods. Bivariate, multivariate or a combination of statistical approaches have been employed to identify this association. The majority of studies used only bivariate statistical tests to identify the association between age and MRA (**Appendix I**). However, despite this limitation, sixteen studies were able to establish a statistically significant difference between the ages of patients admitted due to MRA and those due to non-MRA [33, 34, 92, 106, 107, 114, 126-128, 210, 212, 231-233, 235, 236]. Out of these studies, Somers *et al.*, [114] found that patients admitted for MRP were slightly younger, with a mean age of 80.3 years, compared to those admitted for other reasons, who had a mean age of 83.9 years. The p-value for this association was 0.04, where the statistical test used was not clearly reported [114]. McLachlan *et al.*'s study., [233] identified that the mean age of patients with MRA was similar to those without MRA, with 65.9 years versus 64.3 years ( $p = 0.54$ ). However, when excluding patients with intentional overdose and recreational drug use, the patients with MRA were significantly older with a mean age of 72.4 years (range 21–92 years) ( $p = 0.0007$ ) [233]. However, their bivariate regression analysis using crude odds ratios did not find any significant association between patient age and the MRA group (**Table 2-7**).

Table 2-7: The reported association between MRA and age.

|                                    | Bivariate analysis and regression                                                           |                                                        |         | Multivariate regression                                                    |         |                                                                                                                                                                                                                                                       |                                                                   |
|------------------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------|---------|----------------------------------------------------------------------------|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| Author (year)                      | Test and parameter used for comparing the age between MRA with non-MRA (bivariate analysis) | Crude odds ratio (95% CI) for age association with MRA | P-value | Adjusted odds ratio for age association with MRA (multivariate regression) | P-value | Independent variables assessed in multivariate regression                                                                                                                                                                                             | Comment                                                           |
| Adedapo,2021 <sup>[230]</sup>      | NA                                                                                          | 1.34 (0.73-2.5)                                        | NS      | 1.33 (0.5-3.52)                                                            | NS      | Gender, educational level, average monthly income, alcohol intake, cigarette smoking, fixed-dose combination, duration of hospital stay, number of drugs used a month before admission, number of drugs used on admission, Charlson comorbidity index | No effect                                                         |
| Ahern, 2014 <sup>[106]</sup>       | Student- t test<br>P<0.05                                                                   | NA                                                     | NA      | NA                                                                         | NA      | NA                                                                                                                                                                                                                                                    | NA                                                                |
| Alexopoulou, 2008 <sup>[107]</sup> | Student- t test<br>1. P<0.05                                                                | NA                                                     | NA      | NS                                                                         | NS      | Number of drugs                                                                                                                                                                                                                                       | No effect                                                         |
| Alvarez, 2013 <sup>[129]</sup>     | NS                                                                                          | NA                                                     | NA      | NA                                                                         | NA      | NA                                                                                                                                                                                                                                                    | NA                                                                |
| Angamo, 2017 <sup>[228]</sup>      | NS                                                                                          | NA                                                     | NA      | NA                                                                         | NA      | NA                                                                                                                                                                                                                                                    | NA                                                                |
| Asio et al., 2023 <sup>[202]</sup> | NA                                                                                          | 1.01 (0.99–1.03)                                       | NS      | 1.00 (0.98–1.03)                                                           | NS      | Gender, HIV and antiretroviral therapy, antituberculosis therapy, self-medication, history of drug allergies, comorbidity score and number of drugs                                                                                                   | No effect                                                         |
| Brvar , 2009 <sup>[28]</sup>       | Pearson's correlation was used to correlate age in continuous age variable.                 | NA                                                     | NA      | NA                                                                         | <0.05   | Gender, number of drugs, number of diagnoses, renal failure, liver failure, alcohol abuse, death                                                                                                                                                      | The age of patients admitted due to ADRs was significantly higher |

|                             |                                                                                                                                                                            |                                                                                            |       |                                                                                           |       |                                                                                                                                                                                           |                                                                            |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
|                             | P= not reported                                                                                                                                                            |                                                                                            |       |                                                                                           |       |                                                                                                                                                                                           | compared to patients who were not admitted for ADRs                        |
| Cabré , 2018<br>[92]        | Student- t test for comparing age with ADR and non-ADR and Chi-square test or Fisher's exact test.<br>1. For all ADR causing admission: NS<br><br>2. For >85 years: P<0.05 | "1. For all ADR causing admission: 1 (0.98–1.03)<br><br>2. For >85 years: 0.98 (0.74–1.31) | NS    | NS                                                                                        | NS    | Sex, previous falls, number of drugs pre-admission, sedatives, antidepressants, PIM-Beers list, MNA < 23.5, GFR- MDRD.                                                                    | No effect                                                                  |
| Cahir et al., 2023<br>[128] | NA                                                                                                                                                                         | 0.97 (0.95, 0.99)                                                                          | <0.05 | 0.96 (0.94, 0.98)                                                                         | <0.05 | Gender, functional ability (geriatric syndromes), falls history, comorbidity, polypharmacy, types of medication on admission, and self medication use.                                    | Increasing age was less likely to have an ADR- related hospital admission. |
| Dechanont, 2021<br>[127]    | Chi-square test<br>P = <0.05                                                                                                                                               | NA                                                                                         | NA    | Age "60–69 y" (Reference)<br><br>70–79 y: 1.92 (1.06–3.47)<br><br>≥80 y: 0.68 (0.25–1.86) | <0.05 | Sex, family, number of prescribed medications, hospital dispensed medications, drug store dispensed medications, starting new drugs within 1 week, and starting new drugs within 1 month. | Increasing MRA associated with increasing age                              |
| Fattinger, 2000<br>[218]    | NS                                                                                                                                                                         | NA                                                                                         | NA    | NA                                                                                        | NA    | NA                                                                                                                                                                                        | NA                                                                         |

|                         |                             |                                                |    |                                                                                                                                                                      |       |                                                                                      |                                                                                                                                                |
|-------------------------|-----------------------------|------------------------------------------------|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| Giardina, 2018<br>[219] | NS                          | "Age $\geq$ 85 years:<br>1.08 (0.83–1.42)      | NS | Age $\geq$ 85 years:<br>0.95 (0.72–1.25)                                                                                                                             | NS    | Sex, number of drugs taken, and Charlson comorbidities index score                   | No effect                                                                                                                                      |
| Hopf, 2008 [201]        | NS                          | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Jolivot, 2016<br>[217]  | NS                          | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Karuppannan, 2013 [232] | Chi-square test<br>P<0.05   | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Komagamine, 2019 [234]  | NA                          | "Aged 65 or more years:<br>1.48 (0.95 to 2.30) | NS | "Aged 65 or more years:<br>0.96 (0.60 to 1.54)                                                                                                                       | NS    | Sex, Polypharmacy                                                                    | NA                                                                                                                                             |
| Kongkaew, 2013 [126]    | Chi2 test<br>P <0.05        | NA                                             | NA | (16–44 y is the reference category)<br><br>45–64Y: 0.44 (0.32–0.62)<br><br>65–74Y: 0.47 (0.33–0.67)<br><br>75–84Y: 0.64 (0.46–0.89)<br>85 or older: 0.42 (0.29–0.62) | <0.05 | Length of time since starting new drugs, number of prescription drugs, hospital site | Patients aged 16–44 years compared with patients aged 45 or older, were significantly more likely to be admitted to hospital for a causal ADE. |
| Lagnaoui, 2000 [211]    | NS                          | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Lavan , 2019[222]       | NS                          | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Lea, 2019 [221]         | NS                          | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Leendertse, 2008 [9]    | NA                          | NA                                             | NA | NA                                                                                                                                                                   | NA    | NA                                                                                   | NA                                                                                                                                             |
| Li et al., 2021 [235]   | Mann–Whitney U test, P<0.05 | NS                                             | NS | 1.04 (1.03–1.05)                                                                                                                                                     | <0.05 | Gender, No of medication                                                             | Increasing MRA                                                                                                                                 |

|                                          |                           |                                                                                                       |    |                                                                                          |                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                | associated with increasing age |
|------------------------------------------|---------------------------|-------------------------------------------------------------------------------------------------------|----|------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Luttikhuis et al., 2022 <sup>[225]</sup> | NA                        | 0.98 (0.94–1.03)                                                                                      | NS | 0.96 (0.92–1.01)                                                                         | NS                                                             | Gender, education, nursing home resident or not), geriatric (functional dependency, cognitive impairment and dementia), disease severity (Charlson Comorbidity index, previous hospital admissions, arrival by ambulance) and drug-related (number of medications, polypharmacy)                                                                                                                                                                               | No effect                      |
| Marcum, 2012b <sup>[112]</sup>           | NA                        | Age groups:<br>85+ Y: 1.0 (Reference)<br><br>65–74Y: 0.91 (0.29–2.84)<br><br>75–84Y: 0.84 (0.27–2.60) | NS | NA                                                                                       | NA                                                             | NA                                                                                                                                                                                                                                                                                                                                                                                                                                                             | NA                             |
| Marcum, 2012a <sup>[88]</sup>            | NS                        | NA                                                                                                    | NA | ≥ 85 Y: 1.0 (Reference)<br><br>65–74Y: 0.76 (0.33–1.74)<br><br>75–84 Y: 0.62 (0.27–1.41) | According to age groups:<br><br>65–74 Y: NS<br><br>75–84 Y: NS | <b>Primary independent variable:</b> Polypharmacy<br><b>Control variables adjusted for</b> sex, race, Hispanic, unmarried, Selim physical comorbidity index, Selim psychiatric comorbidity index, non-exempt copayment status, geriatric evaluation and management clinic visit in previous year, number of primary care visits in previous year, emergency department visits in previous year, hospitalisations in previous year, year of hospital admission. | No effect                      |
| Marikova et al., 2021 <sup>[224]</sup>   | Mann–Whitney U test, P NS | NA                                                                                                    | NA | NA                                                                                       | NA                                                             | NA                                                                                                                                                                                                                                                                                                                                                                                                                                                             | NA                             |
| McLachlan, 2014 <sup>[233]</sup>         | Student t-test            | NA                                                                                                    | NA | NA                                                                                       | NA                                                             | NA                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                |

|                            |                                                                                                                                    |                    |                     |                                                                                                                                                    |                         |                                                                                                                                                                 |                                                                                                                                      |
|----------------------------|------------------------------------------------------------------------------------------------------------------------------------|--------------------|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
|                            | <p>P &lt; 0.05 with ADE admissions excluding recreational drugs and overdoses</p> <p>P = NS with all ADE-associated admissions</p> |                    |                     |                                                                                                                                                    |                         |                                                                                                                                                                 | NA                                                                                                                                   |
| Menéndez-Conde, 2011 [121] | NS                                                                                                                                 | NA                 | NA                  | NA                                                                                                                                                 | NA                      | NA                                                                                                                                                              | NA                                                                                                                                   |
| Mjörndal, 2002 [122]       | NS                                                                                                                                 | NA                 | NA                  | NA                                                                                                                                                 | NA                      | NA                                                                                                                                                              | NA                                                                                                                                   |
| Mouton, 2016 [229]         | NA                                                                                                                                 | 1.04 (0.95 – 1.13) | Wald P for Curd= NS | 1.02 (0.91 – 1.14)                                                                                                                                 | Wald P for adjusted= NS | Sex, antituberculosis therapy, antiretroviral therapy and HIV, drug count, and comorbidity score.                                                               | No effect                                                                                                                            |
| Olivier, 2002 [214]        | NS                                                                                                                                 | NA                 | NA                  | NA                                                                                                                                                 | NA                      | NA                                                                                                                                                              | NA                                                                                                                                   |
| Olivier, 2009 [215]        | NS                                                                                                                                 | NA                 | NA                  | NA                                                                                                                                                 | NA                      | NA                                                                                                                                                              | NA                                                                                                                                   |
| Onder, 2002 [84]           | NA                                                                                                                                 | NA                 | NA                  | <p>"1. less than 65: ---<br/>- 65-79Y: 1.05 (0.90–1.23)<br/>80 and more: 0.91 (0.76–1.09)</p> <p>2. (less than 65 vs 65–79Y: 0.98 (0.81–1.20);</p> | NS                      | Sex, drinking and smoking habits, education, Charlson comorbidity index, number of drugs taken at hospital admission, and number of admissions in the last year | <p>No effect</p> <p><b>But age was identified as an independent risk factor associated with only severe ADR-related hospital</b></p> |

|                               |                                      |    |    |                                                        |       |                                                                                                                                      |                                                                                                                                                                                      |
|-------------------------------|--------------------------------------|----|----|--------------------------------------------------------|-------|--------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                               |                                      |    |    | less than 65 vs 80 or more: 0.83 (0.67–1.04)           |       |                                                                                                                                      | <b>admissions,</b> with an odds ratio of 1.50 (95% CI = 1.01–2.23) for patients aged 65–79 years and an odds ratio of 1.53 (95% CI = 1.00–2.33) for patients aged 80 years and above |
| Pedrés, 2014 [33]             | Mann–Whitney and Chi2 test<br>P<0.05 | NA | NA | <65 years: Reference<br><br>≥65 years: 1.59(1.10-2.29) | <0.05 | Number of drugs at admission, length of in-hospital stay, patients requiring stay in special units, length of stay in special units. | Increasing MRA associated with increasing age                                                                                                                                        |
| Pedrés, 2016 [213]            | NA                                   | NA | NA | NA                                                     | NA    | NA                                                                                                                                   | NA                                                                                                                                                                                   |
| Pirmohamed, 2004 [34]         | Mann-Whitney U test<br>P<0.05        | NA | NA | NA                                                     | NA    | NA                                                                                                                                   | NA                                                                                                                                                                                   |
| Pourseyed, 2009 [236]         | Student- t test<br>P<0.05            | NA | NA | NA                                                     | NA    | NA                                                                                                                                   | NA                                                                                                                                                                                   |
| Pouyanne, 2000 [212]          | Poisson distribution<br>P<0.05       | NA | NA | NA                                                     | NA    | NA                                                                                                                                   | NA                                                                                                                                                                                   |
| Santamaria-Pablos, 2009 [210] | Student- t test<br>P<0.05            | NA | NA | 0.981                                                  | NS    | Underlying disease, smoking habit, educational, level comorbidity, complex medication, phytotherapy                                  | No effect                                                                                                                                                                            |
| Singh, 2011 [231]             | P<0.05                               | NA | NA | NA                                                     | NA    | NA                                                                                                                                   | NA                                                                                                                                                                                   |

|                             |                        |                                                                |      |                                                            |    |                                                                                           |           |
|-----------------------------|------------------------|----------------------------------------------------------------|------|------------------------------------------------------------|----|-------------------------------------------------------------------------------------------|-----------|
| Smeaton, 2020<br>[73]       | NA                     | 0.92 (0.82–1.04)                                               | NS   | 0.96 (0.87–1.07)                                           | NS | Sex, CCI score, polypharmacy, potentially inappropriate prescribing                       | No effect |
| Somers, 2010<br>[114]       | Not reported<br>P<0.05 | NA                                                             | NA   | NA                                                         | NA | NA                                                                                        | NA        |
| van der Hooft, 2008<br>[29] | NA                     | NA                                                             | NA   | NA                                                         | NA | NA                                                                                        | NA        |
| Varallo, 2014<br>[227]      | NA                     | "1. Not older:<br>1.00 (0.8-2.1)<br><br>2. Older:<br>1.30 (NA) | (NS) | 1. Not older: 1.00<br>(0.66-1.93)<br><br>2. Older:<br>1.13 | NS | Sex, ethanol consumption, smoking habit, the number of drugs used, and the length of stay | No effect |
| von Euler, 2006<br>[220]    | NA                     | NA                                                             | NA   | NA                                                         | NA | NA                                                                                        | NA        |
| Wawruch, 2009<br>[113]      | NS                     | NA                                                             | NA   | NA                                                         | NA | NA                                                                                        | NA        |

HIV (human immunodeficiency virus); GFR (glomerular filtration rate); MDRD (modification of diet in renal disease); MRA (medication-related admission); MNA (mini nutritional assessment); Not applicable (NA); Not significant P-value (NS); P<0.05 (significant P-value); Odds ratios (OR); PIM (potentially inappropriate medication).

Several studies applied multivariate regression models to explore the relationship between age and MRA, with some studies demonstrating that age was a significant predictor of MRA and others not demonstrating this (**Table 2-7**). Six studies that implemented this technique demonstrated a significant relationship between age and MRA after adjusting for potential independent variables [28, 33, 126-128, 235]. One study found that the likelihood of MRA increased with age but decreased for patients aged 85 years and older [126]. Additionally, it was found that preventable ADR-related hospitalisations were more likely in patients aged 65 years or older compared with non-ADR-related hospitalisations, according to relative risk ratio ( $p = 0.038$ ). Non-preventable ADR-related hospitalisations were more likely to occur in younger adults ( $p < 0.001$ ) [126]. Cahir et al., [128] found that older age was associated with a reduced likelihood of hospital admission related to ADRs [128].

In contrast, Onder et al.,[84] found that age alone cannot be considered a risk factor for ADR-related hospitalisations ( $p$  for linear trend = 0.280). However, patients who experienced severe ADR-related hospitalisations were found to be significantly older than those without severe ADR-related hospitalisations ( $73.1 \pm 12.9$  vs  $69.2 \pm 15.5$ ;  $p = .001$ ). However, when considering only severe ADR-related hospitalisations, age was identified as an independent risk factor associated with ADR-related hospital admissions, with an odds ratios of 1.50 (95% CI = 1.01–2.23) for patients aged 65-79 and an odds ratios of 1.53 (95% CI = 1.00–2.33) for patients aged 80 and older [84]. Consequently, in the current review, age was identified as an independent risk factor for patients with MRA in just four of the 41 studies examined.

### 2.5.3 Study quality assessment

The quality assessment of the included studies indicated that most studies [34, 73, 84, 88, 106, 112-114, 122, 201, 210-212, 214, 217-219, 222-224, 226, 227, 231, 232, 235, 236] exhibited moderate quality ( $n = 26$ ). A subset of the remaining studies [28, 33, 92, 107, 121, 126-129, 202, 215, 216, 221, 225, 228-230, 234] demonstrated high quality ( $n = 18$ ), while four studies [29, 213, 220, 233] were classified as low quality.

#### 2.5.4 Meta-analysis

A meta-analysis was conducted as part of this review, comprising 11 studies, with the aim of comparing the effect sizes of odds ratios within different age categories within the MRA group. **(Figure 2-5)**. There was difference in the odds ratio of MRA for those aged 65 year and over compared with those aged 16 to 64 years using a random effects plot. This random effect plot suggests that younger adults aged 16-64 years were at greater risk for MRA than older adults aged 65 years and older.

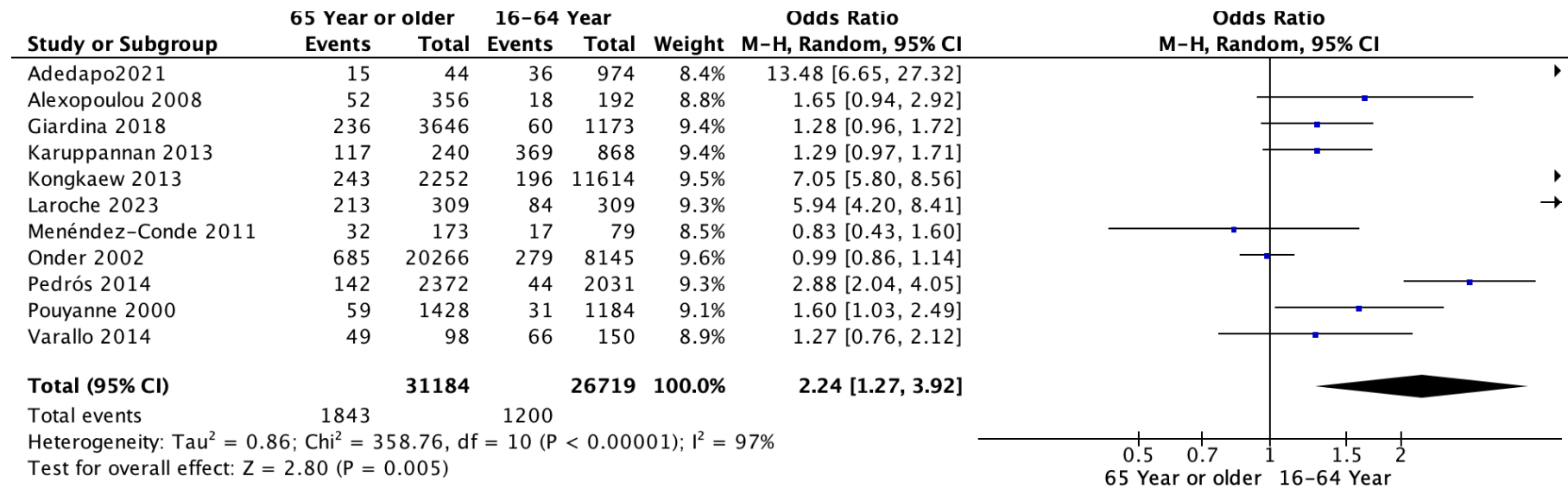


Figure 2-5: Forest plot describing the odds ratio of MRA by age category.

## 2.6 Discussion

### 2.6.1 Key findings

This review identified 48 studies that met the inclusion criteria and were included in the narrative analysis. The total sample size across these included studies was 174,641 patients. There was a meta-analysis generated from this review, comprising 11 studies, aimed to compare the effect size of odds ratios within different age categories within the MRA group. The findings suggest that age is an independent risk factor for MRA in younger adults rather than older adults are at an increased risk of MRA. The quality assessment of the included studies indicated that most studies exhibited moderate quality (n=26). A subset of the remaining studies demonstrated high quality (n=18), while four studies were classified as low quality.

### 2.6.2 Comparison with existing literature

Contrary to the common belief that old age plays a significant role in MRA, primarily due to the complexity of medication regimens and physiological changes in older patients affecting drug metabolism and response [74, 76], our review suggests that age is a statistically significant risk factor for MRA in young adults rather than older patients. This implies that although ageing can introduce changes that might theoretically influence medication-related risks, ageing itself is not a strong risk factor for MRAs. The association between young age and MRA in this review is conflict with the findings of a previous systematic review confirming that age did not seem to be a risk factor for severe ADRs either in the included studies that reported on all adult patients or in those that reported on exclusively older patients aged  $\geq 65$  years only [240]. The risk factors for severe ADR-caused hospitalisations and those that occur during the hospital stay were investigated and reported in the included studies without applying any further statistical analysis. An adverse reaction was defined as a reaction caused by medicinal products, including overdose, misuse, abuse and medication errors, as well as occupational exposure [240]. A meta-analysis conducted by Beijer *et al.*, [116] estimated the percentage of ADR-related hospital admissions and found that the rate was higher in older patients than the non-older cohort. They used the WHO definition for ADR; however, they focussed only on measuring the percentage of ADRs in older and non-older patients [116]. They did not adjust for

confounders. Contrasting with prior reviews, the current systematic review incorporated a more robust meta-analysis to investigate the association between age and MRA regardless of the definition of MRP applied in the included studies.

On the other hand, in 2015, an expert panel of professionals from various hospital settings, including physicians, nurses, and pharmacists, conducted a multidisciplinary triangulation process [3]. They used qualitative analysis and a Delphi technique to reach consensus on the risk factors for MRP among the extremely old [3]. They found that an 80-year-old patient could be in a better health condition than a 60-year-old. Thus, age itself does not constitute such an important risk factor for MRP among hospitalised patients, and they identified other factors such as polypharmacy, dementia and renal impairment, which may be more strongly associated. Their findings did not identify age within the final list of risk factors for MRP. Instead, they sought to identify the patient risk factors for MRPs, irrespective of hospital settings [3].

A more recent cross-sectional study conducted in Ireland and published in 2023 sought to identify the risk factors associated with ADR-related hospital admissions, specifically among older patients aged  $\geq 65$  years [128]. It was identified that older age was not a risk factor for ADR-related hospital admissions. Furthermore, in their adjusted analysis, an increase in age was associated with a lower likelihood of ADR-related hospital admission [128]. The findings of this study are consistent with those of our systematic review and point towards a need for a broader focus beyond age when considering and addressing risk factors for MRAs.

Furthermore, a significant number of the studies included in the current review confirmed an association with age that was based primarily on bivariate analysis [34, 107, 114, 232, 236]. However, the appropriateness of such a method comes into question when considering the complexity of risk factors and their potential interactions. Bivariate analysis, while useful for exploring simple relationships between two variables, falls short when dealing with the multifactorial scenarios that are common in health research. Specifically, it does not account for the potential confounding factors that may distort the true association between age and MRAs. In contrast, a more robust statistical test, such as multivariate regression analysis, is capable of adjusting for these potential confounders [241, 242], providing a more accurate and nuanced understanding of the relationship between age and MRAs. In this review only six studies using multivariate analysis techniques found a significant association between

age and MRAs after adjusting for potential confounding variables [28, 33, 126-128, 235]. Once again, this suggests caution against an overemphasis on older age; and other factors such as gender and MRA preventability may influence the relationship between age and MRA and should be considered in future research.

Previous studies have found that the use of different definitions of MRPs across studies can have a considerable impact on the interpretation and comparison of research findings [6, 30, 243]. MRPs are complex and multifaceted, encompassing various issues related to medication therapy, such as drug interactions, ADRs, medication overdose and recreational drug use. The lack of a consistent definition for medication-related hospital admissions has contributed to the differences in incidence rates reported in various studies [29]. The variability in definitions for medication-related hospital admissions is also a possible reason opposing the assertion of the association between age and MRPs. The definition of MRAs varies between different studies, resulting in a wide range of prevalence rates and difficulty in comparing or pooling data from multiple studies. [30]. For instance, there were significant differences in the characteristics of patients who experienced severe ADRs versus non-severe ADRs when compared with patients who experienced any ADRs versus no ADRs [84]. When the classification of MRP becomes narrower and more specific, such as excluding medication overdose and recreational drug use, the characteristics of the affected patients change. For example, one study reported a significant difference in the experiences of MRA in older patients [233]. This indicates that the relationship between age and MRA may be influenced by the specific types of MRPs considered in a study.

## 2.7 Implication for practice and research

The evidence presented in this review delivers a crucial message to healthcare organisations, researchers and practitioners: old age should not be singularly applied as a risk factor for MRA. Instead, it emphasises the significance of examining all age groups and considering other potential risk factors.

**Practice** –Policy and clinical practices put emphasis on older age groups, and there are various tools and assessments that have been specifically designed with a focus on this demographic and to address the unique medication-related needs of older patients. Efforts should be directed towards developing strategies encompassing a broader spectrum of adult patients, recognising that focussing solely on older patients is insufficient for addressing

MRAs. This involves identifying and adapting tools and how these tools impact MRAs across the adult spectrum. While **Chapter 1** provides a comprehensive overview of tools designed for older patients, extending these efforts across the entire adult population in both research and clinical practice is imperative to ensure more effective MRA prevention strategies.

Examples of tools that have been developed exclusively for older cohorts such as START/STOPP criteria [244], anticholinergic scales [55, 56] and medication appropriateness indexes [57]. The START/STOPP criteria and the medication appropriateness indexes have been employed in studies for the detection of MRPs in inpatients at the time of admission [66, 245]. Another example is the *GerontoNet ADR* score, a prediction tool that has been validated to assess ADRs in hospitalised older patients [60]. A number of European-funded research projects focus on medication management and the prevention of ADRs in older cohorts only, such as SENATOR [68, 69] and OPERAM [70]. In particular, OPERAM is a European multicentre tool, cluster randomised and controlled for optimising the prevention of preventable MRAs in older patients aged  $\geq 70$  years with multimorbidity and polypharmacy [246]. The OPERAM tool was utilised to assess the impact of optimising MRAs in older patients with multimorbidity and polypharmacy [247]. The results indicate a reduction in inappropriate prescribing without any reduction effects on MRA between the intervention and control groups [247]. In contrast, one set of criteria has been developed specifically to explore inappropriate prescribing for middle-aged adults, PROMPT [72, 248], and it has been applied to determine the association between inappropriate prescribing and MRA in this cohort [72].

In line with the existing literature, the tools and screening criteria used to prioritise hospitalised patients who may require pharmaceutical care, including those at risk of MRPs at admission or during hospitalisation, are typically not based on age [249-252]. This aligns with the findings of our review, which suggest that hospital prioritisation should not exclusively depend on old age as it does not emerge as a significant risk factor for MRAs. This highlights the need for a paradigm shift in practice towards the development of screening tools that do not exclusively focus on age or specific age cohorts. Addressing medication-related hospital admissions necessitates a comprehensive strategy. This includes medication reconciliation [253, 254] and identifying and addressing factors that contribute to preventable medication-related hospital admissions [216], which to date have focussed on older patients. The implementation of these high-level practices can encourage healthcare

providers to enhance patient outcomes and reduce the risk of preventable MRPs at admission in older cohorts [255]. Nevertheless, there seems to be a disproportionate emphasis on applying these policies to older age groups. This overemphasis highlights the need for a balanced approach that caters to all adult age demographics.

**Research** –Different age cut-offs may result in different study populations being included or excluded from analyses, which can affect the generalisability of study findings. For example, if one study uses a cut-off of 65 years [114] to define older adults and another study uses a cut-off of 70 years [256], the two studies may include different proportions of the older population, which can affect the prevalence and risk estimates of MRAs in older adults. Additionally, several of the studies included in the current systematic review recruited adult patients aged younger than 64 years old [211, 214, 231, 232], indicating that MRA can affect patients of all ages. However, the lack of consistency in reporting age data makes it difficult to draw definitive conclusions about the relationship between age and MRA.

Furthermore, the necessity for standardised definitions and methodologies to measure and categorise age, particularly in research and clinical practice concerning medication use and hospital admissions, is evident. Such standardisation could bolster the comparability and generalisability of study findings across diverse populations and contexts, thereby facilitating the creation of evidence-based policies and guidelines to enhance medication safety in adults. The specific types of MRPs considered in a study can also significantly influence the identified relationship between age and MRA. Therefore, the nature of an MRP can impact the observed association between age and MRA, underlining the need for the standard selection and definition of MRPs in research studies.

Additionally, it is crucial to comprehend the potential influence of other confounding factors on MRAs without overestimating the role of age. This understanding can help ensure a more accurate interpretation of the factors that contribute to MRA. However, it should be noted that this does not discount the importance of considering age in medication management. It may be that age interacts with other factors to influence the risk of MRA or that the risk associated with age varies depending on the specific medications or medical conditions in question. One study [217] compared the median age between preventable and non-preventable MRA participants, revealing that the median age of those with preventable MRAs was statistically lower than that of individuals with non-preventable MRAs.

Furthermore, another study [122] discovered that there was a difference in age between men and women with MRAs, suggesting the presence of yet other confounding factor. While this review questions the long-held belief that old age is an independent risk factor for MRA, it also highlights the need for further research to comprehensively investigate the other risk factors for MRAs across the entire adult spectrum. Recognising this as a limitation, we identify it as an essential objective for future research.

## 2.8 Strengths and Limitations of the review

The current review has some limitations. First, this review was limited to studies published in English and excluded those that investigated MRA in cohorts using a specific drug or that were affected by a specific disease, which may restrict the breadth of the perspectives and findings considered.

Second, the heterogeneity of the included studies could limit the comparability of study results and make it difficult to draw definitive conclusions about the impact of age as a risk factor for MRA. This limited the number of studies included in the meta-analysis. However, this review minimised the risk of heterogeneity by employing advanced statistical techniques to computationally amalgamate the data from the individual studies, thereby enabling a more robust analysis of the relationship between age and MRA. This included the use of random-effects models to account for the potential heterogeneity between studies. Third, calculating the CI around the pooled estimated mean presented difficulties, and we could not assess the overlap between these CIs. When CIs overlap, it indicates no statistically significant difference between the pooled means. Conversely, non-overlapping CIs suggest a statistically significant difference between the means. Finally, the search strategy was applied up to 2021, but it is important to note that this needs to be updated.

On the other hand, the review also has some strengths. A comprehensive search strategy was employed in eight databases, utilising backward citation tracking for all the systematic reviews and individual studies included. This approach helped ensure a broad and diverse collection of sources. This review followed the JBI quality assessment tool to appraise the quality of the results, and the PRISMA flow diagram illustrated the selection of studies through the various phases of the systematic review. Additionally, we employed multiple contributors to enhance the rigour of the data, and a statistical expert provided advice on the statistical approaches taken and evaluated the statistical results.

### 2.8.1 Limitations of the included studies

Moreover, there were variations in age reporting between the studies investigating MRA in different age groups. Age is a critical variable to consider when investigating MRA since older patients are more vulnerable to these adverse events, and numerous studies have been conducted to explore the impact of age on patient admission [33, 126, 227, 231]. However, our review found inconsistencies in the age categories used across the examined studies, posing a significant challenge when incorporating them into the meta-analysis. Some studies used different age cut-offs to define older adults, such as 60 years, 65 years, or 70 years. Different age cut-offs can affect the interpretation of study findings and may limit the comparability of results across studies. Additionally, it should be noted that this review included two studies with populations ranging from 13 to 91 years, and three studies with populations ranging from 15 to 94 years.

Moreover, the limited availability of data related to age in the studies included, such as the absence of mean ages for the non-MRA groups [126, 210] in some instances, prevented their inclusion in the meta-analysis due to this incomplete information. Moreover, certain studies only offered data on age in the form of regression and odds ratio for age categories [73, 84, 230]. The diversity in age categorisations and presentation across these studies made it difficult to pool these odds ratios, further restricting the volume of data for a comprehensive meta-analysis. To address these limitations and facilitate future studies exploring the association between age and MRA, further research should employ consistent age categories when reporting age-related data, facilitating the aggregation of results in meta-analyses and adopting standardised age reporting methods for both MRA and non-MRA groups.

## 2.9 Conclusion

This review found that age is a risk factor for MRAs in young adults rather than older patients. These findings urge caution against too much emphasis on age alone when addressing MRAs and the need to identify other factors related to hospital admissions. It encourages further research across all adult age groups to enhance the prevention, identification and management of MRAs to enhance care and clinical outcomes for all adults. This chapter serves to clarify how existing literature describes the relationship between age and MRAs. It provides a comprehensive understanding of the role of age as a

risk factor for MRAs, drawing upon a wealth of evidence to present a view of this critical aspect.

### **2.10 In the next chapter**

The subsequent chapter will present the findings of a cross-sectional survey exploring medication management experiences from the patient's viewpoint. It will delve into the relationship between age and these experiences, providing valuable insights into the association between age and medication management.

# **Chapter 3 : Inpatient and post-discharge medication-related experiences in Irish hospitals: a mixed-methods study of adult patients' experiences.**

### 3.1 Background

The medication experience is defined as an individual's subjective experience of taking a medication daily [257]. It is a practice concept that helps healthcare practitioners understand patients' experiences and address their medication-related needs. In addition, it can serve as a guide for practitioners to interpret each patient's unique medication experience [257].

Medication experiences can vary significantly from patient to patient, depending on factors such as the specific drug, dosage, individual health conditions, and the patient's age. A qualitative study investigated the experiences and preferences of frail older patients (aged 68–88 years) regarding the information they received about their cardiovascular medications [161]. Older patients' experiences with medication information fall into "Comfortable with information" and "Insecure with information." Factors such as being provided with detailed answers, use of appropriate language, and proper timing of information (during discharge or a subsequent follow-up visit) were found to make patients feel more comfortable with their medication information [161]. In addition, patients desire straightforward explanations, comprehensive information, and better access to their doctors (which could be compromised due to time constraints or lack of continuity in care) to improve their understanding of medications and feel secure [161]. Another study addressed patients' experiences of medication-related problems and determined that it was influenced by trust and confidence in their healthcare providers, satisfaction with the medication information they received, and the ability to control their medication management [258]. These factors can significantly impact medication adherence and the quality of patient–provider communication [258]. This supports the importance of exploring patients' medication experiences in the Irish healthcare system.

Shoemaker and Ramalho de Oliveira,[257] conducted a meta-synthesis of three different studies to understand the medication experiences and the meaning of medications for adult patients [257]. Their findings revealed that patients become familiar with medications, learn to manage them through personal experience, and become aware of these medications' effects on their bodies. From a patient's perspective, self-managing medications by adjusting doses based on their perceived needs or concerns about dependency is a rational behaviour and helps them preserve control. However, healthcare professionals may label this practice as non-compliance rather than recognising it as a form of exerting control [257]. This study was conducted on adult patients aged 24–74 years old. Another concern that older patients face is the occurrence of medication effects, which were categorised as medication-related

problems from their perspective [259]. Medication side effects are the most common medication-related problem discussed by older adults and clinicians. They often face issues regarding medications' beneficial and adverse effects, including concerns about the medication's effectiveness, current adverse effects, and fear of potential future adverse effects [259]. As described in **Chapter 1**, substantial attention has been focused on understanding medication management experiences among older patients. Yet, evidence remains scarce regarding the medication experiences of younger adults in a hospital setting. This presents a significant gap in our understanding. Therefore, this Chapter seeks to explore the medication management experiences among adults who received inpatient care in Irish hospitals, using the Irish National Patient Experience Survey (NPES).

The NPES is an annual survey of inpatients' experiences of healthcare and is published at the end of each year [260]. The NPES is administered across 40 public hospitals. The survey investigates the general patient's experience across several care settings including: the nursing home, inpatient, maternity, maternity bereavement and the end-of-life and there is a separate survey for each care setting. However, this study will address and analyse general acute care through the inpatient survey to understand the patient's medication-related experiences. The inpatient survey includes 61 questions exploring the patient's experience through their hospital stay. The survey is divided into two sections: (1) 58 structured questions (close-ended-questions) and (2) three free-text questions, (**Appendix II**). It covers several stages of care such as admission to the hospital, care during the stay and at discharge from the hospital. It focusses on several domains such as treatment on the ward, trust in hospital staff, and respect and dignity.

To our knowledge, no previous study has explicitly reported on patients' experiences of medication-related issues from the Irish NPES data. Therefore, we sought to understand and explore Irish adults' experiences with their medication management during their stay in the hospital and post-discharge. Such a study could contribute to improving medication management services and the communication and information exchange between patients, carers and healthcare professionals in Ireland.

### 3.2 Significance of the Study

This study holds significance in exploring adult inpatients' medication-related experiences. The study will contribute to a deeper understanding of the medication management process

throughout hospital stays and post-discharge. The findings will help pinpoint opportunities in which improvements in medication management can be made within hospital inpatient settings from the patient's perspective. Additionally, these findings can be used to inform healthcare policies and practices for better inpatient and post-discharge medication management, ultimately leading to improved patient outcomes and satisfaction. This study could serve as a foundation for further research on medication management experiences and their impact on patient care and outcomes in the future.

### 3.3 Aim and objectives

The aim of this study is to explore adult inpatients' medication-related experiences using a secondary data analysis of the Irish NPES data from 2017, 2018 and 2019. The purpose is to enhance the understanding of patients' perceptions of medication management throughout the hospital stay and post-discharge and to highlight targets for improvement.

**To achieve this aim, the following objectives were set:**

- **Quantitative analysis**
  - Identify medication-related comments from the adult patients' survey responses.
  - Summarise the responses to medication-related questions and the medication-related free-text comments.
  - Explore the relationships between patient demographic characteristics (e.g., age, gender, ethnic background), clinical characteristics, and medication-related experience.
- **Qualitative analysis**
  - Qualitatively analyse the free-text comments to describe the inpatient's medication-related experiences.
  - Identify key challenges faced by adults in managing their medication during hospitalisation and post-discharge.
- **Quantitative and qualitative integration**
  - Integrate the qualitative and quantitative medication management experiences to identify opportunities for improvement.

### 3.4 Methodology

#### 3.4.1 Rational for the choice of research design

Researchers have observed a clear divide between the opposing quantitative and qualitative ideologies. There has always been an emphasis on the differences between quantitative and qualitative approaches rather than on their similarities. Some researchers argue that quantitative and qualitative methodologies stem from fundamentally distinct ontological, epistemological and axiological assumptions about the nature of research. The argument suggests that quantitative research is based on the belief in objective truths and a clear, unambiguous reality. On the other hand, qualitative research assumes a world that is inherently subjective, without a single, undisputed reality [261]. In contrast, the pragmatic approach does not adhere to a single, unified system. Instead, it focusses on identifying and quantifying a research problem. In simple terms, a pragmatic researcher sees the research problem as the key focus and employs various methods to grasp it. This approach often involves using mixed-methods research to obtain results [262]. Creswell [263] in 2014 adopted a definition of mixed-methods research that incorporates its key components: methods, research design and philosophy [263, 264]. In mixed-methods research, the researcher collects and analyses qualitative and quantitative data, integrates the data and their results, organises them into a specific research design and aligns these procedures with theory and philosophy.

This study used a mixed-methods design to answer the research questions and address the objectives. While reviewing the existing literature, it became evident that there were notable gaps in the understanding of medication management experiences during hospital stays across all adult age groups. Although some studies have highlighted this issue, focussing on older patients, very few studies have sought to understand adult medication experiences. There is further a distinct absence of studies exploring the relationship between age and medication experiences in Ireland.

### 3.5 Justification for using an inductive approach

### 3.5.1 Theoretical framework

This section provides an overview of available frameworks to address patient experiences.

- **Patient experiences frameworks**

Peplau's theory of interpersonal relations focusses on a specific aspect of nursing, namely the interpersonal relationship between the nurse and the patient. The phases of the nurse-patient relationship according to Peplau's theory are orientation, working and termination [265]. Another framework that focusses on identifying key parts of the care experience is the Warwick framework. This is a patient experiences framework that focusses on the experiences of patients focussing on certain clinical areas: cardiovascular disease, diabetes and cancer [266]. Additionally, the Institute of Medicine framework, which prioritises patient-centred care, emphasises maintaining patients' dignity and includes domains dealing with patients' values and preferences, physical comfort, expressed needs and emotional support [267]. These frameworks have not been applied to the exploration of medication management issues and therefore were not considered as a good fit with the objectives of this thesis for understanding medication management experiences.

- **Medication management in hospital or elsewhere**

Following a literature review, no theory dealing with medication management issues was identified. The literature that was identified, and the potential advantages and disadvantages of adopting the identified frameworks, are comprehensively described below.

### 3.5.2 Justification for the approach taken in this Chapter from previous literature

The literature was reviewed to identify appropriate analysis techniques for understanding patients' medication management experiences in different healthcare settings, including

inpatient settings [135], emergency departments [147], community dwellings [169] and transitions of care [268-270], using a qualitative approach.

Gadbois *et al.* [269] applied inductive content analysis to understand patients' experiences during the transition from hospital by interviewing patients, hospital staff and nursing facility staff. They identified medication reconciliation problems and the association between the transition from hospital to nursing facilities, as well as medication errors and inaccurate information [269]. Rustad *et al.* [268] explored older patients' experiences during the transition from hospital to healthcare services by qualitatively analysing semi-structured interviews using a content analysis approach [268]. Older patients expressed uncertainty about the information exchanged between hospital and municipal health care staff during the transition process and their misunderstandings of the medication information summaries [268]. The study reported the general experiences of 14 patients aged 80 years and older and described various aspects of the care transition process without focussing on the medication management experience in detail.

Holmqvist *et al.* [169] used semi-structured interviews to describe community-dwelling older persons' (age 75-91 years) experiences of their medication evaluations using an inductive content analysis approach [169]. This study showed the facilitators and challenges for older patients when evaluating their medications.

Brookes and Baker [271] quantitatively and qualitatively analysed the English National Cancer Patient Experience Survey data. The qualitative data were analysed inductively by generating codes from the free-text question responses using a corpus linguistics technique, which is a computerised method helpful in analysing large volumes of patient responses [271]. This study was conducted to explain overall cancer treatment experiences and not medication management experiences specifically [271]. Moreover, Prue *et al.* [135] qualitatively analysed the survey's free-text (open-ended) question responses from the Northern Ireland Cancer Patients Experience Survey using a thematic approach and by categorising responses as either positive or negative. These responses described issues such as the speed of diagnoses and associated treatment and their association with survival rather than in-depth medication management experiences [135].

On the other hand, there were studies that sought to understand medication management, particularly in older patients. Tomlinson *et al.* [272] conducted qualitative semi-structured interviews to explore older patients and their family members' roles in medication

management at discharge using a thematic framework analysis method [272]. Additionally, Moen *et al.* [158] applied qualitative semi-structured interviews to explore older patients' experiences of using multiple medications and their views on their medication routines, with no clear data about their health care settings. They chose a inductive content analysis approach because of the absence of empirical literature and the lack of a theoretical framework regarding the experiences of older multiple medicine users [158].

None of the previous literature follows theoretical or conceptual frameworks to explore patients' experiences in different healthcare settings. However, it demonstrates that using a qualitative inductive thematic approach, which allows for the generation of codes and themes from the data itself [273] to analyse free-text responses, is appropriate (**Table 3-1**). The inductive approach is recommended in cases where there is not enough former knowledge about a phenomenon [274]. Hence, the inductive thematic approach is chosen as it is the most suitable methodology for addressing the research question related to patients' medication management experiences [275].

Table 3-1: Overview of approaches and analyses employed in previous studies addressing medication experiences.

| <b>Authors</b>                          | <b>Aim</b>                                                                                                                                                  | <b>Study design</b>        | <b>Approach</b>                         | <b>Theoretical framework</b> |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|-----------------------------------------|------------------------------|
| Brookes and Baker 2022 <sup>[271]</sup> | Understanding the experiences of patients with different types of cancer who have received treatment for different durations.                               | National experience survey | Inductive thematic technique            | NA                           |
| Gadbois et al., 2019 <sup>[269]</sup>   | Understanding the experiences of patients who transferred from hospitals to skilled nursing facilities by obtaining insights from patients' facility staff. | Semi-structured interviews | Inductive content analysis              | NA                           |
| Holmqvist et al., 2019 <sup>[169]</sup> | Describing older persons' experiences of their medication evaluation in community dwellings.                                                                | Semi-structured interviews | Inductive content analysis              | NA                           |
| Moen et al., 2009 <sup>[58]</sup>       | Exploring older patients' experiences of using multiple medications and their views on their medication routines.                                           | Semi-structured interviews | Inductive conventional content analysis | NA                           |
| Prue et al., 2021 <sup>[135]</sup>      | Understanding cancer care expectance in adults.                                                                                                             | National experience survey | Inductive thematic analysis             | NA                           |
| Rustad et al., 2016 <sup>[268]</sup>    | Exploring older patients' experiences in transition care.                                                                                                   | Semi-structured interviews | Inductive content analysis              | NA                           |
| Tomlinson et al., 2020 <sup>[272]</sup> | Exploring older patients and their families' roles in medication management at discharge.                                                                   | Semi-structured interviews | Inductive thematic framework analysis   | NA                           |

### 3.6 Study design

This cross-sectional study involved secondary analysis of quantitative and qualitative data from NPES. The mixed-methods design was adopted a sequential explanatory design to analyse quantitative and qualitative data and then integrate the findings by using the qualitative data to help explain the quantitative findings [264].

In this design, a researcher first collects and analyses the quantitative (numeric) data. The qualitative (text) data are collected and analysed second in the sequence and help explain, or elaborate on, the quantitative results obtained in the first phase. The second, qualitative, phase builds on the first, quantitative, phase, and the two phases are connected in the intermediate stage in the study [276]. This study employed a quantitative method to investigate the correlation between medication management experiences and age. The study then moved into a qualitative approach to explore patients' perspectives on medication management provide an in-depth understanding of the medication-related experiences of adult inpatients. This exploration, using a qualitative approach, aimed to understand the challenges faced in an inpatient setting, identify opportunities to enhance patients' experiences, and improve the quality of medication management services. Although qualitative and quantitative data are gathered and analysed in separate phases, with the qualitative data often used to elucidate the quantitative findings, the process was completed separately. However, the integration between the quantitative and the qualitative components is important, and this may occur at any stage of the research process, in this study, integration occurred at the analysis stage (**Figure 3-1**).

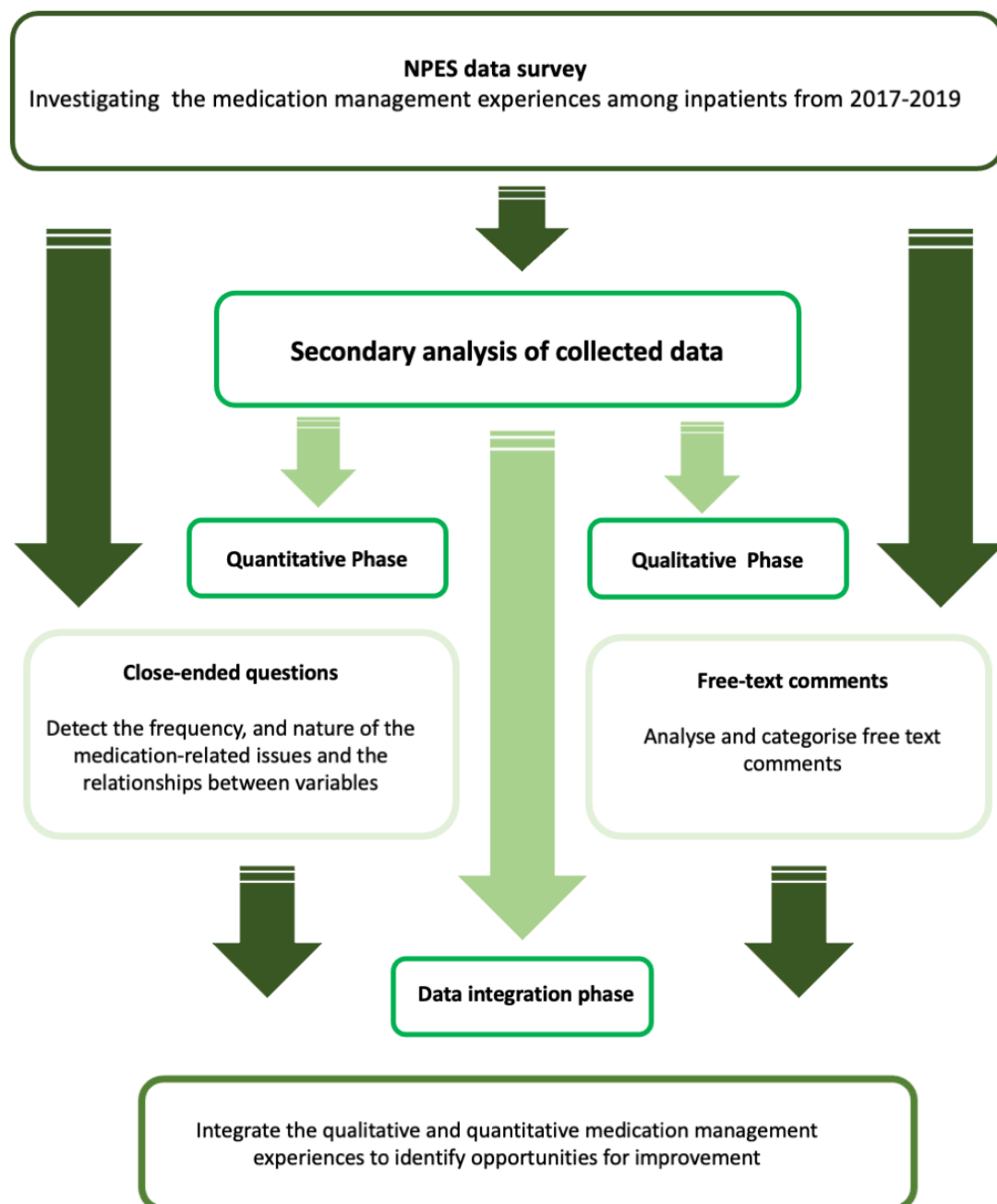


Figure 3-1: Sequential mixed-methods design.

The Good Reporting of a Mixed-Methods Study (GRAMMS) framework was applied to ensure the design and reporting of the study were rigorous [277]. This six-item framework includes (1) justification of using a mixed-methods approach in the research question, (2) design of individual qualitative and quantitative method, (3) methods of individual qualitative and quantitative components, (4) where the integration between methods happened, (5) limitations of one method when the other is present, and (6) insights gained from the completed studies, (**Appendix II**).

## 3.7 Methods

### 3.7.1 Nature of the NPES

#### 3.7.1.1 *The original survey*

The survey containing 58 tick-box questions and three free-text questions invited patients to evaluate various aspects of their hospital stay and provide their overall impression, without specifically focusing on their experiences related to medication management.

**The following areas were included:**

- Admission: Patients were asked about their experiences before being admitted to the hospital. This included questions about waiting times and the overall admission process.
- Care on the ward: Patients were asked to rate their experiences related to the cleanliness of the ward, noise levels, and how responsive the staff were to their needs.
- Examinations, diagnosis, and treatment: This section focused on patients' experiences with healthcare providers. It included questions about communication with the medical staff, involvement in decision-making regarding their healthcare, and the clarity of explanations regarding their diagnosis and treatment.
- Meals: Patients were asked to rate the quality of the food they received during their hospital stay.

- Privacy: This part of the survey assessed whether patients felt they were provided with appropriate privacy during examinations, treatment and discussions about their medical condition.
- Discharge and aftercare: Patients were asked about their experiences when leaving the hospital. This included questions about providing discharge information, follow-up appointments and the availability of support services after leaving the hospital.

### 3.7.1.2 Data access request

To fulfil the purpose of this study of investigating and understanding medication-related experiences, the authors thoroughly reviewed the online version of the questionnaire available on the NPES website [260]. Further details regarding the questionnaire are presented in **Appendix II**. The most relevant survey questions that would contribute to the study aim were proactively selected (**Table 3-2**).

Table 3-2: Relevant questions concerning patient experiences.

| Question number                          | Question text                                                                                                                              |
|------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Close-ended questions</b>             |                                                                                                                                            |
| Q1                                       | Was your most recent hospital stay planned in advance or an emergency?                                                                     |
| Q7                                       | Did you remain in the emergency department for the entire time of your stay?                                                               |
| Q43                                      | Before you left hospital, were you given any written or printed information about what you should or should not do after leaving hospital? |
| Q44                                      | Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand?                         |
| Q45                                      | Did a member of staff tell you about medication side effects to watch for when you went home?                                              |
| Q52                                      | Overall, I had ... experience?                                                                                                             |
| <b>Demographic close-ended questions</b> |                                                                                                                                            |
| Q53                                      | Who was the main person or people who filled in this questionnaire?                                                                        |
| Q55                                      | Do you identify as (gender)?                                                                                                               |
| Q56                                      | What is your month and year of birth?                                                                                                      |
| Q57                                      | What is your ethnic or cultural background?                                                                                                |
| <b>Free-text questions</b>               |                                                                                                                                            |
| Q59                                      | Was there anything particularly good about your hospital care?                                                                             |
| Q60                                      | Was there anything that could be improved?                                                                                                 |
| Q61                                      | Any other comments or suggestions?                                                                                                         |

A request to access the required data was then sought from the data manager, the Health Information and Quality Authority (HIQA), and following approval, the anonymised data were shared in a password-protected Microsoft Excel file to the project supervisor. The authors emphasised the significance of studying medication-related experiences and how the requested data would contribute to advancing knowledge in this field. All details about the research ethical approval are explained in Section 3.7.4.

It is important to note that not all NPES questions were related to medications; only two questions were directly related to medication. The first question (Q44) inquired about whether patients received any explanation regarding the purpose of their medications, while the second question (Q45) focused on whether patients were informed about medication side effects to watch out for upon returning home. Additionally, although one question (Q43) was not directly related to medication, it addressed receiving verbal or written information about post-hospital care instructions in general. This latter question was included in the analysis because it could contain information regarding whether patients received any guidance on their medication usage and management. Furthermore, it is worth noting that the free-text questions were general inquiries in NPES related to inpatient experiences in the hospital. However, these questions were qualitatively analysed after the quantitative analysis was completed.

### ***3.7.1.3 Participants of the NPES***

All patients aged 16 and over who spent 24 hours or more in one of the 40 public hospitals, were residents in Ireland, and were discharged within a defined time period (discharge during May in each survey year) were eligible to be included.

#### **Survey distribution and data collection:**

The eligible participants received the survey by post within two months of their hospital discharge. This survey invited participants to share their hospital journey experience and provided suggestions for care improvements they believe are necessary. Participants were given the option to complete the survey online using a smartphone, laptop or tablet or by returning a paper-based survey by post, and patients were allowed to fill out the survey on their own or with the help of another person. If they needed someone to fill out the survey

on their behalf, that person should have ensured that the answer reflected the patient's experience.

### 3.7.2 Data extraction and management

#### 3.7.2.1 Data extraction

The requested dataset of the NPES questionnaire was extracted and prepared by the HIQA. Although the survey was conducted anonymously, it included information about the hospitals in which individuals received care, as well as other potentially identifying details. Therefore, the data were anonymised and de-identified by the HIQA to protect patient and organisational privacy prior to data transfer in the Excel format. All details regarding diagnosis, medical conditions and medications were redacted. Each calendar year was supplied in a separate sheet in the Excel file, which contained both qualitative and quantitative data. Additionally, a book of codes was provided to aid in understanding the data.

The data were collected by HIQA, and some of these data were manipulated by HIQA prior to extraction and transfer to TCD. These altered data include age and the omission of text that named any medication name and diagnosis, **Table 3-3**.

Table 3-3: HIQA data collection and presentation of some details.

| HIQA collection of data                                           | HIQA presentation of extracted data                                                                                                     |
|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Age was collected as month and year of birth                      | Age was categorised into the following age brackets:<br>16-35 years<br>36-50 years<br>51-65 years<br>66-80 years<br>81 years and older. |
| Free-text answers were filled out by patients or their relatives. | data details about medication names and diagnosis were redacted from the free-text data.                                                |

#### 3.7.2.2 Data management

##### Quantification of text data

Initially, free-text responses were quantified through the identification of medication-related responses via keyword searches. Subsequently, the free-text responses were quantified into numerical representations, facilitating quantitative analysis without necessitating in-depth reading or analysis of the text. The quantitative phase, focusing on medication-related responses to open questions, was completed first. Further detail is presented below in section 3.7.3.

### **Phase 1: Quantitative data management**

#### **Quantitative data were divided into two types:**

- **Original variables:** These variables were collected in their raw form without undergoing any alteration or transformation. These variables included data obtained from closed questions. They provided direct information about the characteristics and experiences of the patients and were analysed in their raw form without modification.
- **Manipulated variables:** These variables were derived from the original variables through certain categorisations. They were created to provide a deeper understanding or to facilitate analysis. This involved converting free-text responses into quantitative variables and creating meaningful categories for further analysis.

### **Management of the free-text questions**

The primary variable in this section is "medication-related experiences" which identified whether the response reported anything to do with medications or not. A comprehensive list of words and synonyms related to medication was generated. The search function (Control + F) was used to identify and tag comment containing these words, (**Appendix II**). The filter function was then applied to facilitate a more detailed review of the tagged cells. This intensive review enabled the identification of medication-related comments.

Those responses that were medication-related were then further categorised as described below. The process of creating categorical variables from the free-text questions involved the reading and interpretation of the free-text responses by the PhD student. These medication-related comments were then further transformed into new variables as described

in **Table 3-4** and **Table 3-5**. The classification of comments as negative or positive was based on patient responses regarding their experience with the medication management process. Positive comments were identified when patients expressed experience, such as medication being provided on time or appreciation for being referred to a clinic for follow-up regarding new medication post-discharge. Conversely, negative comments arose from concerns or issues experienced by patients, such as receiving an additional tablet without any explanation or discussion. These categorical variables were extracted from the free-text questions to capture relevant information and enable more insights into the medication-related experiences, were then utilised in the quantitative analysis. Variables that were not included in the transformed categories were treated as missing data and were not subjected to transformation.

The data transformation process was verified to ensure that it did not result in any data loss or corruption, meaning there were no missing values or inconsistencies introduced during the transformation. Following that, cross-validation was conducted to compare the transformed data with the original data using cross-tabulations. This validation process aimed to confirm that the new categories aligned with the intended changes.

Table 3-4: Categorical variables derived from free-text questions (questions 59, 60, and 61).

| Variables                                                         | Categories                                                                                                                                                                                 | Transformed categories                                                                                                                       |
|-------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Medication-related experiences                                    | <ul style="list-style-type: none"> <li>Medication-related,</li> <li>Non-medication related</li> </ul>                                                                                      | NA                                                                                                                                           |
| Nature of medication experience from the respondent's perspective | <ul style="list-style-type: none"> <li>Positive</li> <li>Negative</li> <li>Neutral</li> <li>Cannot categorise</li> </ul>                                                                   | <ul style="list-style-type: none"> <li>Negative medication experience responses</li> <li>Positive medication experience responses</li> </ul> |
| Stage of care                                                     | <ul style="list-style-type: none"> <li>At admission</li> <li>In the ward</li> <li>At discharge</li> <li>After discharge</li> <li>Not clear</li> </ul>                                      | NA                                                                                                                                           |
| Stage of medication management                                    | <ul style="list-style-type: none"> <li>Administration</li> <li>dispensing</li> <li>Prescribing</li> <li>Monitoring</li> <li>Medication discussion (with patient)</li> <li>Other</li> </ul> | NA                                                                                                                                           |

Table 3-5: Re-coding and transforming the variables.

| Variables                                             | Original HIQA categories                                                                                                                                                      | Transformed categories                                                                                    |
|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Explanation provided of the purpose of the medication | <ul style="list-style-type: none"> <li>Yes, completely</li> <li>Yes, to some extent</li> <li>No</li> <li>I did not need an explanation</li> <li>I had no medicines</li> </ul> | <ul style="list-style-type: none"> <li>Yes</li> <li>No</li> <li>I did not need any explanation</li> </ul> |
| Monitoring for medication side effect                 | <ul style="list-style-type: none"> <li>Yes, completely</li> <li>Yes, to some extent</li> <li>No, I did not need an explanation</li> </ul>                                     |                                                                                                           |

### Management of closed-ended questions

The variables from the closed-ended questions were already processed and categorised by the HIQA beforehand. Coding of these variables was carried out by the HIQA as part of their data management process, ensuring that the data were organised and ready for analysis.

In the Excel sheet, it was detected that some of the original variables in this study consisted of scales that were inconsistent across the different years. For example, the method for rating the overall hospital experience varied across different years. For 2017–2018, the rating scale ranged from 1–11, whereas in 2019, a different scale ranging from 0–10 was adopted.

After that, the datasets from each calendar year were merged into a single dataset using the SPSS Import Data function. It was necessary to ensure consistency by aligning the scales used for these variables. This was fixed using the Transform > recorded into different variables function in SPSS and was done to facilitate accurate comparisons and meaningful analysis across the study years. To ensure accuracy, these values were cross-verified against the original data source, and the necessary corrections were, as demonstrated in **Table 3-6**. In addition, the supervisor verified the accuracy of a proportion of the manipulated data.

Table 3-6: Alignment of original variable scales for cross-year comparison.

| Variables                                       | 2017                                                                                                                                                                                                                                             | 2018                                                                                                                                                                                                                                             | 2019                                                                                                                                                                                                            | The modification                                                                                                                                                                                                                                                            |
|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Overall rate of hospital experience             | Rate from 1–11                                                                                                                                                                                                                                   | Rate from 1–11                                                                                                                                                                                                                                   | Rate from 0–10                                                                                                                                                                                                  | Re-code the rating scale of 2019 to 1–11                                                                                                                                                                                                                                    |
| Gender                                          | Male, female                                                                                                                                                                                                                                     | Male, female, other                                                                                                                                                                                                                              | Male, female                                                                                                                                                                                                    | The “other” option in 2018 was excluded from the study due to its small sample size                                                                                                                                                                                         |
| The main person who filled in the questionnaire | <ul style="list-style-type: none"> <li>the patient</li> <li>a friend or relative of patient</li> <li>both patient and friend/relative together</li> <li>the patient with the help of someone</li> </ul>                                          | <ul style="list-style-type: none"> <li>the patient</li> <li>a friend or relative of patient</li> <li>both patient and friend/relative together</li> <li>the patient with the help of someone</li> </ul>                                          | <ul style="list-style-type: none"> <li>the patient</li> <li>the patient with the help of someone</li> <li>a person acting on the patient's behalf</li> </ul>                                                    | <p>The scale “a friend or relative of patient” in 2017 and 2018 was considered the same as “a person acting on the patient's behalf” in 2019</p> <p>“Both patient and friend/relative together” in 2017 and 2018 was merged with “the patient with the help of someone”</p> |
| Ethnicity                                       | 2) White Irish<br>3) Irish traveller<br>4) Any other White background<br>6) Black, African<br>7) Any other Black background<br>9) Asian, Chinese<br>10) Any other Asian background<br>11) Other ethnic background<br>12) Other ethnic background | 2) White Irish<br>3) Irish traveller<br>4) Any other White background<br>6) Black, African<br>7) Any other Black background<br>9) Asian, Chinese<br>10) Any other Asian background<br>11) Other ethnic background<br>12) Other ethnic background | 1) White Irish<br>2) Irish traveller<br>3) Any other White background<br>4) Black, African<br>5) Any other Black background<br>6) Asian, Chinese<br>7) Any other Asian background<br>8) Other ethnic background | <p>The numbers were re-coded in 2019 to match the numbers in 2017 and 2018</p> <p>Category (11) in both 2017 and 2018 was deleted because no response used this code</p>                                                                                                    |
| Reason for admission                            | Not recorded                                                                                                                                                                                                                                     | The category label 8 indicated adverse                                                                                                                                                                                                           | The category label 6 indicated adverse reaction                                                                                                                                                                 | For 2017, this was reported                                                                                                                                                                                                                                                 |

| Variables | 2017 | 2018                               | 2019                      | The modification                                                                                           |
|-----------|------|------------------------------------|---------------------------|------------------------------------------------------------------------------------------------------------|
|           |      | reaction as a reason for admission | as a reason for admission | as missing value<br><br>For years 2018 and 2019, was merged into two categories: adverse reaction or other |

## **Phase 2: Qualitative data management:**

### **The following steps were undertaken:**

- **Coding Frame Development:** Two authors read a randomly selected 10% sample of the free-text responses. Through inductive coding, they identified and categorised key themes and patterns in the narrative descriptions of medication-related experiences. This process assisted in developing a coding frame that ensured consistency in the analysis.
- **Consensus Building:** The two authors collaborated to reach a consensus on the coding frame by discussing and resolving any differences in their coding. This step helped enhance the reliability and validity of the analysis.
- **Full Report Coding:** The remaining free-text reports were coded by the PhD student using the established coding frame. This involved systematically applying the identified themes and categories to the narrative descriptions.
- **Uncertain Cases:** Any uncertain or ambiguous cases encountered during the coding process were identified by the PhD student. These cases were then returned to the research team for further review and discussion to ensure accurate and reliable analysis.

### **Numerous measures were employed to ensure the security of the following:**

- **Data Storage and Organisation:** The data were securely stored in a structured format, specifically Excel spreadsheets and SPSS statistical sheets. These files were password-protected to ensure the security of the data.
- **Data Backup and Security:** Regular data backups were performed to prevent any potential loss or damage to the dataset. Three copies of the data were created and stored in different locations to enhance data safety. The copies were kept in the C: drive on the author's laptops. Additionally, an encrypted copy was saved in a shared folder in MS OneDrive, adding an extra layer of security to protect the data from unauthorised access. This encryption measure was implemented to safeguard the data and prevent unauthorised access. Furthermore, a log of all processing steps was diligently recorded.

### 3.7.3 Data analysis

#### *3.7.3.1 Phase 1: Quantitative analysis*

This phase involved collecting data on direct medication-related experiences by quantitatively analysing responses to closed-ended questions and by applying “quantitative content analysis” to the responses to free-text questions. Additionally, the descriptive analysis of the important variables for understanding and exploring the medication-related experiences was included.

The main closed-ended question and free-text questions that were used in this phase and the main statistical analysis plan are presented in **(Table 3-7)**.

Table 3-7: The main questions used in the phase 1 quantitative data with the main statistical plan.

| Question number                    | Question text                                                                                                                              | Variable short name                          | Analysis plan                                                                                                 | Statistical test                                                                                                                                                      |
|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|---------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Close-ended questions              |                                                                                                                                            |                                              |                                                                                                               |                                                                                                                                                                       |
| Q1                                 | Was your most recent hospital stay planned in advance or an emergency?                                                                     | Emergency admission and stay                 | Explore the association between medication-related experience and <b>type of care (emergency or planned)</b>  | 1. The data were summarised, and the frequency was determined using univariate analysis.<br>2. Chi-square test ( $\chi^2$ ) was applied to determine the association. |
| Q7                                 | Did you remain in the emergency department for the entire time of your stay?                                                               |                                              |                                                                                                               |                                                                                                                                                                       |
| Q43                                | Before you left hospital, were you given any written or printed information about what you should or should not do after leaving hospital? | Given written information                    | Identify the association between the medication-related experience and <b>the general hospital experience</b> |                                                                                                                                                                       |
| Q44                                | Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand?                         | Explain the purpose of the medication        |                                                                                                               |                                                                                                                                                                       |
| Q45                                | Did a member of staff tell you about medication side effects to watch for when you went home?                                              | Monitoring medication side effects           |                                                                                                               |                                                                                                                                                                       |
| Q54                                | The main reason for your most recent stay in hospital                                                                                      | Admitted for adverse reaction management     |                                                                                                               |                                                                                                                                                                       |
| Q52                                | Overall, I had ... experience?                                                                                                             | Overall rating of hospital experience        |                                                                                                               |                                                                                                                                                                       |
| Demographic closed-ended questions |                                                                                                                                            |                                              |                                                                                                               |                                                                                                                                                                       |
| Q53                                | Who was the main person or people who filled in this questionnaire?                                                                        | The main person completing the questionnaire | <b>Demographic variables</b> to identify and describe any association with medication related experience.     | 1. The data were summarised, and the frequency was described using univariate analysis.                                                                               |
| Q55                                | Do you identify as (gender)?                                                                                                               | Gender                                       |                                                                                                               |                                                                                                                                                                       |
| Q56                                | What is your month and year of birth? (Age groups)                                                                                         | Age groups                                   |                                                                                                               |                                                                                                                                                                       |

| Question number            | Question text                                                  | Variable short name                                                                                                                                                                                                                                   | Analysis plan                                                                              | Statistical test                                                                    |
|----------------------------|----------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Q57                        | What is your ethnic or cultural background?                    | Ethnicity                                                                                                                                                                                                                                             |                                                                                            | 2. ( $\chi^2$ ) was applied to determine the association.                           |
| <b>Free-text questions</b> |                                                                |                                                                                                                                                                                                                                                       |                                                                                            |                                                                                     |
| Q59                        | Was there anything particularly good about your hospital care? | Comments interrogated and categorised as the following: <ul style="list-style-type: none"> <li>• Medication-related comments</li> <li>• Nature of medication experience</li> <li>• Stage of medication experience</li> <li>• Stage of care</li> </ul> | Quantitative content analysis applied to transform the comments into categorical variables | The data were summarised, and the frequency was analysed using univariate analysis. |
| Q60                        | Was there anything that could be improved?                     |                                                                                                                                                                                                                                                       |                                                                                            |                                                                                     |
| Q61                        | Any other comments or suggestions?                             |                                                                                                                                                                                                                                                       |                                                                                            |                                                                                     |
|                            |                                                                | Comments interrogated and categorised as the following: <ul style="list-style-type: none"> <li>• Positive comment</li> <li>• Negative comment</li> <li>• Neutral comment</li> </ul>                                                                   |                                                                                            | Bivariate analysis using ( $\chi^2$ )                                               |

Initially, a univariate descriptive analysis was conducted to describe the frequency and percentage of demographic characteristics and response categories within each study year.

Next, a bivariate analysis was performed to explore the relationships between medication-related experiences and demographic and general hospital characteristics, as described below and in **Table 3-8**.

Table 3-8: Analysis of medication-related experiences and associated characteristics.

| Dependent variables (categories)                                            | Independent variables            |                                                                                                                                                                                                                                               | Statistical tests                     |
|-----------------------------------------------------------------------------|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| Medication-related experience<br><br>(Positive or other, Negative or other) | Demographic characteristics      | <ul style="list-style-type: none"> <li>• Age</li> <li>• Gender</li> <li>• Ethnicity</li> <li>• The main person completing the questionnaire</li> </ul>                                                                                        | Bivariate analysis using ( $\chi^2$ ) |
|                                                                             | General hospital characteristics | <ul style="list-style-type: none"> <li>• Emergency admission and stay</li> <li>• Provision of written information</li> <li>• Explanation provided regarding the purpose of medication</li> <li>• Monitoring medication side effect</li> </ul> | Bivariate analysis using ( $\chi^2$ ) |
| Binomial medication experience (negative or other)                          | Demographic characteristics      | <ul style="list-style-type: none"> <li>• Age</li> <li>• Gender</li> <li>• Ethnicity</li> <li>• The main person completing the questionnaire</li> </ul>                                                                                        | Bivariate analysis using ( $\chi^2$ ) |
|                                                                             | General hospital characteristics | <ul style="list-style-type: none"> <li>• Emergency admission and stay</li> <li>• Provision of written information</li> </ul>                                                                                                                  | Bivariate analysis using ( $\chi^2$ ) |

| Dependent variables<br>(categories) | Independent variables |                                                                                                                                                       | Statistical tests  |
|-------------------------------------|-----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
|                                     |                       | <ul style="list-style-type: none"> <li>Explanation provided regarding the purpose of medication</li> <li>Monitoring medication side effect</li> </ul> |                    |
|                                     |                       | Overall hospital rating                                                                                                                               | Independent t-test |

To examine the relationship between medication-related experiences and categorical demographic variables, a chi-square test was performed. This assessed the association between medication-related experiences and demographic characteristics including gender (male, female), age group (16–35 years, 36–50 years, 51–65 years, 66–80 years, 81 and older), ethnicity (White Irish and other ethnic background) and by whom the questionnaire was completed (patient self, patient with the help of someone, or a person acting on the patient's behalf).

Similarly, the association between medication-related experiences and general hospital characteristics was examined using chi-square test. The independent variables included type of admission (emergency, planned, or other), emergency department (ED) stay (remained in ED for entire stay or transferred to hospital ward), provision of written information (yes, no, or I did not want or need any written or printed information), explanation provided of the purpose of the medication and about the monitoring for medication side effect (yes, no, or I did not need any explanation) and overall rating of hospital experiences (rated from 1 to 11, where 1 indicated very poor and 11 indicated very good).

The statistical significance was set at  $p < 0.05$ . Detailed information about the dependent and independent variables can be found in the corresponding **Table 3-8**.

Finally, a multinomial regression analysis was conducted to examine the variables most strongly associated with a respondent reporting a negative or positive medication-related experience. Any independent variables that showed a significance level of  $p < 0.01$  in the bivariate analysis were entered into the regression model. The regression analysis, a robust statistical method, was used to examine the correlation between the dependent variable and

independent variables. The regression analysis was conducted using JASP (Version 0.14) software. [278]. The statistical significance of the regression model was determined by examining the 95% CI of the odds ratio. A 95% CI falling below or above 1 indicates statistical significance, while a 95% CI that crosses 1 indicates non-significance.

### 3.7.3.2 Phase 2 thematic qualitative analysis

This phase included the qualitative analysis and categorisation of free-text responses to describe and summarise the information about medication management. The details regarding the free-text questions utilised in this phase in **Table 3-9**. This process applied inductive “thematic qualitative analysis” to identify recurring themes and patterns within the responses. The aim was to gain a comprehensive understanding of the various aspects of medication management expressed by the participants.

Table 3-9: Free-text questions used in the qualitative phase.

| Question number | Question text                                                  | Analysis plan                |
|-----------------|----------------------------------------------------------------|------------------------------|
| Q59             | Was there anything particularly good about your hospital care? | Employ the thematic analysis |
| Q60             | Was there anything that could be improved?                     |                              |
| Q61             | Any other comments or suggestions?                             |                              |

Thematic framework analysis was used to organise and interpret the qualitative data, following the inductive approach. The six stages of the framework analysis were followed: data familiarisation, code generation, developing an initial thematic framework, applying the thematic framework, reviewing data extracts, and data interpretation [279, 280].

- **Familiarisation with the data:** The researcher read and re-reads the free-text questions to gain a deep understanding of and become fully immersed in the data. This process allowed the researcher to become intimately acquainted with the participants' experiences and insights regarding medication-related experiences. Additionally, any data that did not fit well

into the assigned categories were grouped as "can't be categorised" and were not included in the subsequent steps of the analysis.

- **Code generation:** A stage in which the researcher carefully reviewed the free-text questions and identified meaningful concepts and sub-themes within the data. These concepts were then assigned specific codes that represent the essence of each idea or topic, corresponding to the purpose of the study. For example, sub-themes such as “efficacy of medication”, “medication time”, “medication causing problem”, “waiting for medication/delay in medication management”, and “patient education/ health care communication”.
- **Developing an initial thematic framework:** After coding the first few comments, the researcher identified and clustered codes into initial sub-themes and determines whether they accurately reflect the data. These sub-themes such as "prescription not given to the patient at discharge/or delayed", "medication error at discharge or at admission", and "communication between hospital and primary care (timing or content)". These sub-themes were further grouped together and defined as "care transition".
- **Applying the thematic framework:** In this stage, the remaining comments were indexed using the existing themes and sub-themes. The constant comparison method and memo-writing process were employed during this stage. If new themes emerge, the old ones were reviewed and renamed to reflect the emergence of these new themes. This process continues until no new themes are generated.
- **Reviewing data extracts and developing framework matrix:** The consistency of the data extracts was evaluated to confirm their alignment with the designated themes and sub-themes. This assessment helped in identifying the need to refine the labels, if necessary. After coding all the data, the themes and sub-themes were reviewed to check for duplicates and overlap, and if needed, the number of sub-themes/categories was reduced. A spreadsheet was used from the beginning to generate a matrix, and the data was charted into a framework matrix.
- **Data interpretation:** The researcher developed interpretations based on patterns and themes to understand the data. These interpretations aimed to

provide meaningful insights and understanding of the phenomenon of medication management experiences. The findings were presented in a clear and concise manner using appropriate quotations or examples from the data to support the interpretations.

### 3.7.4 Ethical approval

The study was approved by the School of Pharmacy and Pharmaceutical Sciences Research Ethics Committee (REC), Ref.2021-12-01. The Data Access Request Form was accepted from the National Care Experience Programme (**Appendix II**). It is essential to highlight that the data requested for this study was initially obtained in 2019. However, the COVID-19 pandemic significantly affected the research activities, resulting in delays in accessing and working with the data. These restrictions included the return of the PhD student to her home country during the pandemic (2020–2021), which presented logistical challenges in accessing the data outside of Ireland. The supervisor was the project principal investigator and drafted the ethics application, and the PhD student was a researcher who led all data management, reviewed the ethics application, and contributed to editing and finalising the form.

## 3.8 Results

The survey included a total population of 39,453 responses across three years. The proportion of respondents who provided at least one free-text medication-related comment was 4% (n=1577). The overall proportion of medication-related comments was relatively consistent across the years (**Table 3-10**).

Table 3-10: Frequency of medication-related comments across the three years.

| Survey year | Medication-related comment, n (%) | Non-medication-related comment, n (%) | Total | Response rate (%) |
|-------------|-----------------------------------|---------------------------------------|-------|-------------------|
| 2017        | 585 (4.3%)                        | 13121 (95.7%)                         | 13706 | 51                |
| 2018        | 496 (3.7%)                        | 12908 (96.3%)                         | 13404 | 50                |
| 2019        | 498 (4%)                          | 11845 (96%)                           | 12343 | 46                |
| Total       | 1577 (4%)                         | 37874 (96%)                           | 39453 | NA                |

### 3.8.1 Demographic characteristics of the study population:

The majority of respondents were White Irish (88.8%), with only a small proportion (8.5%) belonging to minor ethnic groups (**Table 3-11**). The study population had a diverse age distribution, with the largest group being the 66 to 80 years old age group (35.4%). The gender distribution was nearly balanced, with a slightly higher proportion of female patients (50.7%). The majority of patients were admitted to the hospital as emergency cases (65.7%), and most patients were transferred to a hospital ward (64.7%) following their emergency department stay.

Table 3-11: Respondents' demographic and clinical characteristics.

| Characteristic                                           | Number (%)    |
|----------------------------------------------------------|---------------|
| Ethnicity                                                |               |
| • White Irish                                            | 35035 (88.8%) |
| • Other ethnic background                                | 3350 (8.5%)   |
| • Missing value                                          | 1068 (2.7%)   |
| Age groups                                               |               |
| • 16 to 35 years                                         | 3144 (8%)     |
| • 36 to 50 years                                         | 5232 (13.3%)  |
| • 51 to 65 years                                         | 10039 (25.4%) |
| • 66 to 80 years                                         | 13952 (35.4%) |
| • 81 years and older                                     | 6395 (16.2%)  |
| • Missing value                                          | 691 (1.8%)    |
| Gender                                                   |               |
| • Male                                                   | 19427 (49.2)  |
| • Female                                                 | 20018 (50.7%) |
| • Other                                                  | 8 (0%)        |
| Admission type                                           |               |
| • Emergency or urgent                                    | 25912 (65.7%) |
| • Planned or waiting list                                | 8955 (22.7%)  |
| • Something else                                         | 1908 (4.8%)   |
| • Missing value                                          | 2678 (6.8%)   |
| Remained in the emergency department for the entire stay |               |
| • Yes                                                    | 747 (1.9%)    |
| • No (transferred to hospital ward)                      | 25510 (64.7%) |
| • Missing value                                          | 13196 (33.4%) |

### 3.8.2 Medication-related experiences

### *3.8.2.1 Summary of the responses to the medication-related questions in the survey*

Within the questionnaire, two specific questions were related to medication and one question indirectly related to medications. There were no observed differences in the responses to these medication-related questions for all individuals who responded to the questionnaires across the three years (**Table 3-12**). A considerable proportion of respondents (46.4% in 2017, 44.3% in 2018, and 30% in 2019) reported not receiving adequate written or printed information. Approximately one-third of respondents each year indicated that they did not receive an explanation as to the purpose of the medicines to take at home (9.3% in 2017, 9% in 2018, and 8.8% in 2019). Regarding receiving an explanation about monitoring for medication side effects, similar proportions of participants reported that they did not receive this support (31.7% in 2017, 30.1% in 2018, and 29.5% in 2019). However, the variable (Reason for admission: adverse reaction) was more frequently represented in non-medication comments compared to medication comments, with only 17 instances in the latter category (small number). For that reason, the variable (Reason for admission: adverse reaction) was removed from the analysis of medication-related comment.

Table 3-12: Summary of responses to direct and indirect medication-related directly and indirectly questions across the three years.

|                                                                                                                          | 2017, n (%) | 2018, n (%) | 2019, n (%) | Total across the three years |
|--------------------------------------------------------------------------------------------------------------------------|-------------|-------------|-------------|------------------------------|
| Q43 Were you given any written or printed information about what you should or should not do after leaving the hospital? |             |             |             |                              |
| • Yes                                                                                                                    | 6857 (53.6) | 6949 (55.7) | 5944 (51.1) | 19750 (53.5)                 |
| • No                                                                                                                     | 5929 (46.4) | 5525 (44.3) | 3490 (30)   | 14944 (40.5)                 |
| • I did not want or need any written or printed information                                                              | N/A         | N/A         | 2190 (18.)  | 2190 (5.9)                   |
| • Total number of responses                                                                                              | 12786       | 12474       | 11624       | 36884                        |
| • Item response rate (%)                                                                                                 | 93.3        | 93.1        | 94.2        | 93.4                         |
| Q44 Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand?   |             |             |             |                              |
| • Yes                                                                                                                    | 9349 (72.2) | 9232 (73.2) | 8521 (73.1) | 27102 (72.8)                 |
| • No                                                                                                                     | 1206 (9.3)  | 1129 (9)    | 1025 (8.8)  | 3360 (9)                     |
| • Did not need explanation                                                                                               | 2385 (18.4) | 2250 (17.8) | 2109 (18.1) | 6744 (18.1)                  |
| • Total number of responses                                                                                              | 12940       | 12611       | 11655       | 37206                        |
| • Item response rate (%)                                                                                                 | 94.4        | 94.1        | 94.4        | 94.3                         |
| Q45 Did a member of staff tell you about medication side effects to watch for when you went home?                        |             |             |             |                              |
| • Yes                                                                                                                    | 5655 (48.1) | 5579 (48.8) | 5230 (49.4) | 16464 (48.7)                 |
| • No                                                                                                                     | 3724 (31.7) | 3442 (30.1) | 3125 (29.5) | 10291 (30.5)                 |
| • I did not need explanation                                                                                             | 2375 (20.2) | 2417 (21.1) | 2242 (21.2) | 7034 (20.8)                  |
| • Total number of responses                                                                                              | 11754       | 11438       | 10597       | 33789                        |
| • Item response rate (%)                                                                                                 | 85.8        | 85.3        | 85.9        | 85.6                         |

### *Nature of medication-related free-text comments*

Across the three years, the "in-ward" setting emerged as the most common stage of care about which patients submitted their comments describing a medication-related experience (**Table 3-13**). This stage consistently received more patient comments about medications compared to other stages. The "at discharge" stage was also notable, with a significant proportion of patients submitting their medication experiences. For question number 60, which asked about areas for improvement in the patient hospital journey, a notable proportion of participants provided feedback related to medication experiences and suggested areas for improvement across the three years than for other questions. However, the percentage of total participants providing such feedback decreased over the years.

Table 3-13: Frequency of medication-related comments reported by stage of care over three years.

| Stage of care                                                      | 2017, (n%) | 2018, (n%) | 2019, (n%) | Total across the three years |
|--------------------------------------------------------------------|------------|------------|------------|------------------------------|
| Q59 Was there anything particularly good about your hospital care? |            |            |            |                              |
| At admission                                                       | 5 (8.3)    | 8 (13.6)   | 7 (9.2)    | 20 (10.3)                    |
| In ward                                                            | 43 (71.7)  | 32 (54.2)  | 46 (60.5)  | 121 (62.1)                   |
| At discharge                                                       | 7 (11.7)   | 3 (5.1)    | 3 (3.9)    | 13 (6.7)                     |
| After discharge                                                    | NA         | NA         | NA         |                              |
| Not clear                                                          | 5 (8.3)    | 16 (27.1)  | 20 (26.3)  | 41 (21)                      |
| Total                                                              | 60         | 59         | 76         | 195                          |
| Item response rate (%)                                             | 0.4        | 0.4        | 0.6        | 0.5                          |
| Q60 Was there anything that could be improved?                     |            |            |            |                              |
| At admission                                                       | 27 (9.2)   | 24 (8.6)   | 26 (10)    | 77 (9.2)                     |
| In ward                                                            | 162 (55.5) | 144 (51.8) | 126 (48.5) | 432 (52)                     |
| At discharge                                                       | 64 (21.9)  | 75 (27)    | 69 (26.5)  | 208 (25.1)                   |
| After discharge                                                    | 8 (2.7)    | 7 (2.5)    | 5 (1.9)    | 20 (2.4)                     |
| Not clear                                                          | 31 (10.6)  | 28 (10.1)  | 34 (13.1)  | 93 (11.2)                    |
| Total                                                              | 292        | 278        | 260        | 830                          |
| Item response rate (%)                                             | 2.1        | 2.1        | 2.1        | 2.1                          |
| Q61 Any other comments or suggestions?                             |            |            |            |                              |
| At admission                                                       | 15 (7.9)   | 13 (8.4)   | 15 (8.8)   | 43 (8.4)                     |
| In ward                                                            | 81 (42.9)  | 63 (40.9)  | 80 (47.1)  | 224 (43.7)                   |
| At discharge                                                       | 58 (30.7)  | 45 (29.2)  | 56 (32.9)  | 159 (31)                     |
| After discharge                                                    | 5 (2.6)    | 4 (2.6)    | 5 (2.9)    | 14 (2.7)                     |
| Not clear                                                          | 30 (15.9)  | 29 (18.8)  | 14 (8.2)   | 73 (14.2)                    |
| Total                                                              | 189        | 154        | 170        | 513                          |
| Item response rate (%)                                             | 1.4        | 1.1        | 1.4        | 1.3                          |

Similarly, in relation to the stage of the medication use process, some differences were observed across the years (**Table 3-14**). The highest percentage of comments and suggestions regarding medication experiences were reported at the administration stage, followed by the prescription stage. At the administration stage, responses fluctuated from 43% to 64.4% across the years. However, at the prescription stage, the proportion of responses fluctuated from 12.7% to 30.5%.

Table 3-14: Medication-related comments reported by patients by stage of the medication use process over three years.

| Stage of medication use process                                    | 2017, n (%) | 2018, n (%) | 2019, n (%) | Total across the three years |
|--------------------------------------------------------------------|-------------|-------------|-------------|------------------------------|
| Q59 Was there anything particularly good about your hospital care? |             |             |             |                              |
| Administration                                                     | 34 (48.6)   | 35 (53)     | 56 (63.6)   | 125 (55.8)                   |
| Prescription                                                       | 21 (30)     | 8 (12.1)    | 12 (13.6)   | 41 (18.3)                    |
| Dispensing                                                         | 1 (1.4)     | 5 (7.6)     | 2 (2.3)     | 8 (3.6)                      |
| Monitoring                                                         | 3 (4.3)     | 3 (4.5)     | 3 (3.4)     | 9 (4)                        |
| Related to medication discussion                                   | 8 (11.4)    | 12 (18.2)   | 14 (15.9)   | 34 (15.2)                    |
| Not clear                                                          | 3 (4.3)     | 3 (4.5)     | 1 (1.1)     | 7 (3.1)                      |
| Total                                                              | 70          | 66          | 88          | 224                          |
| Item response rate (%)                                             | 0.5         | 0.5         | 0.7         | 0.6                          |
| Q60 Was there anything that could be improved?                     |             |             |             |                              |
| Administration                                                     | 138 (41.6)  | 154 (49.4)  | 139 (47)    | 431 (45.9)                   |
| Prescription                                                       | 90 (27.1)   | 74 (23.7)   | 81 (27.4)   | 245 (26.1)                   |
| Dispensing                                                         | 9 (2.7)     | 5 (1.6)     | 14 (4.7)    | 28 (3)                       |
| Monitoring                                                         | 8 (2.4)     | 9 (2.8)     | 3 (1)       | 20 (2.1)                     |
| Other related to medication discussion                             | 75 (22.6)   | 63 (21)     | 53 (17.9)   | 191 (20.3)                   |
| Nor clear                                                          | 12 (3.6)    | 7 (2.2)     | 6 (2)       | 25 (2.7)                     |
| Total                                                              | 332         | 312         | 296         | 940                          |
| Item response rate (%)                                             | 2.4         | 2.3         | 2.4         | 2.4                          |
| Q61 Any other comments or suggestions?                             |             |             |             |                              |
| Administration                                                     | 101 (46.8)  | 82 (44.6)   | 94 (50.5)   | 277 (47.3)                   |
| Prescription                                                       | 61 (28.2)   | 53 (28.8)   | 47 (25.3)   | 161 (27.5)                   |
| Dispensing                                                         | 9 (4.2)     | 11 (6)      | 4 (2.2)     | 24 (4.1)                     |
| Monitoring                                                         | 4 (1.9)     | 1 (0.5)     | 3 (1.6)     | 8 (1.4)                      |
| Other related to medication discussion                             | 35 (16.2)   | 27 (14.7)   | 29 (15.6)   | 91(15.5)                     |
| Not clear                                                          | 6 (2.8)     | 10 (5.4)    | 9 (4.8)     | 25 (4.3)                     |
| Total                                                              | 216         | 184         | 186         | 586                          |
| Item response rate (%)                                             | 1.6         | 1.4         | 1.5         | 1.5                          |

### 3.8.3 Variables associated with submission of a medication-related comments

#### 3.8.3.1 Association between demographic characteristics and submission of a medication-related comment

A comparison of demographic characteristics between those who reported any medication-related experience and those who did not identified statistically significant relationships with age, ethnicity, and gender (Table 3-15).

Table 3-15: Comparison of demographic characteristics between those who submitted a medication-related free-text comment and those who did not.

| Characteristic                           | Medication-related comment, n (%) | Others, n (%) | P-value |
|------------------------------------------|-----------------------------------|---------------|---------|
| Age                                      |                                   |               |         |
| • 16 to 35 years                         | 177 (5.6)                         | 2967 (94.4)   | <0.05   |
| • 36 to 50 years                         | 321 (6.1)                         | 4911 (93.9)   |         |
| • 51 to 65 years                         | 429 (4.3)                         | 9610 (95.7)   |         |
| • 66 to 80 years                         | 418 (3)                           | 13534 (97)    |         |
| • 81 years and older                     | 216 (3.4)                         | 6179 (96.6)   |         |
| Ethnicity                                |                                   |               |         |
| • White Irish                            | 1405 (4)                          | 33630 (96)    | <0.05   |
| • Other ethnic background                | 166 (5)                           | 3184 (95)     |         |
| Gender                                   |                                   |               |         |
| • Male                                   | 574 (3)                           | 18853 (97)    | <0.05   |
| • Female                                 | 1005 (5)                          | 19013 (95)    |         |
| Main person completing the questionnaire |                                   |               |         |
| • The patient                            | 1181 (4.1)                        | 27757 (95.9)  | >0.05   |
| • A friend or relative of patient        | 158 (3.8)                         | 3977 (96.2)   |         |
| • The patient with the help of someone   | 222 (4.1)                         | 5256 (95.9)   |         |

Note: P<0.05 is set as statistically significant.

The age distribution between the two groups was found to be statistically significant, with a slightly higher proportion of those aged 16 to 35 years and 36 to 50 years having submitted a medication-related comment than those in other age groups. There was a statistically significant association between gender and submission of a medication-related comment, with females being more likely to submit a comment. Regarding ethnicity, the difference between the two groups was found to be statistically significant, with a greater proportion

of those who identified with a minority ethnic background submitting a comment than those who identified as White Irish. However, there was no statistically significant association between submission of a comment and the person who completed the questionnaire.

#### *3.8.3.2 Association between general hospital characteristics and submission of a medication-related comment*

There was a statistically significant association between medication-related comment submission and type of admission, with those who experienced an emergency admission being more likely to comment than those who experienced a planned admission (**Table 3-16**). There was no association between submission of a comment and whether a person admitted through the ED remained in the ED or was transferred to a ward.

Table 3-16: Comparison of general hospital characteristics between those who submitted a medication-related free-text comment and those who did not.

| Characteristic                                                                                                     | Medication-related comment, n (%) | Others, N (%)        | P-value |
|--------------------------------------------------------------------------------------------------------------------|-----------------------------------|----------------------|---------|
| Type of admission                                                                                                  |                                   |                      |         |
| • Emergency                                                                                                        | 1129 (4.4)                        | 24783 (95.6)         | <0.05   |
| • Planned                                                                                                          | 322 (3.6)                         | 8633 (96.4)          |         |
| • Other                                                                                                            | 79 (4.1)                          | 1829 (95.9)          |         |
| Emergency department stay                                                                                          |                                   |                      |         |
| • Remained in emergency                                                                                            | 36 (4.8)                          | 711 (95.2)           | >0.05   |
| • Transferred to hospital ward                                                                                     | 1056 (4.1)                        | 24454 (95.9)         |         |
| Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand? |                                   |                      |         |
| • Yes                                                                                                              | 893 (3.3)                         | 26209 (96.7)         | <0.05   |
| • No                                                                                                               | 377 (11.2)                        | 2983 (88.8)          |         |
| • Did not need explanation                                                                                         | 228 (3.4)                         | 6516 (96.6)          |         |
| Were you given any written or printed information about what you should or should not do after leaving hospital?   |                                   |                      |         |
| • Yes                                                                                                              | 554 (2.8)                         | 19196 (97.2)         | <0.05   |
| • No                                                                                                               | 899 (6)                           | 14045 (94)           |         |
| • I did not want or need any written or printed information                                                        | 44 (2)                            | 2146 (98)            |         |
| Did a member of staff tell you about medication side effects to watch for when you went home?                      |                                   |                      |         |
| • Yes                                                                                                              | 378 (2.3)                         | 16086 (97.7)         | <0.05   |
| • No                                                                                                               | 836 (8.1)                         | 9455 (91.9)          |         |
| • I did not need explanation                                                                                       | 202 (2.9)                         | 6832 (97.1)          |         |
| Overall rating of hospital experiences                                                                             | Mean (SD) 7.56 (2.7) *            | Mean (SD) 9.29 (2) * | <0.05   |

\* Tested using independent T-test; Note: P<0.05 is set as statistically significant.

People who reported not receiving any explanation regarding the purpose of their medications, those who reported not receiving verbal or written information and those who were not told about medication side effects to watch out for when they went home appeared more likely to submit a free-text medication-related comment than others ( $p=0.000$ ). There was an association between medication-related comment submission and the overall rating of hospital experience, with a lower mean hospital experience rating (7.56, SD 2.7), indicating a less positive experience compared to others who did not submit a medication-related comment (mean 9.29, SD 2).

### *3.8.3.3 Association between demographic characteristics and submission of a negative or positive medication free-text comment*

Of the 1577 submitted comments related to medication, 1237 (78.4%) were identified as negative, 137 (8.7%) were positive, while the remaining were including neutral medication comments. There were a statistically significant associations between the submission of a positive comment versus the remainder of survey respondents (i.e., did not submit a medication-related comments or submitted a neutral or negative one) and age and gender. Adults and female patients were more likely to submit a positive comment (**Table 3-17**).

However, there were statistically significant associations between the submission of a negative medication-related comment versus the remainder of survey respondents (i.e., did not submit a medication-related comments or submitted a neutral or positive one) and age, ethnicity and gender. A greater proportion of those aged 16 to 35 years and aged 36 to 50 years were more likely to submit a negative comment than other age groups. Across the ethnicity and gender variables, those belonging to an ethnic minority group and females were more likely to submit a comment. Conversely, there was no statistically significant association between the person who completed the questionnaire and those who did or did not submit a negative comment.

Table 3-17: Comparison of demographic characteristics between those who submitted of a negative medication free-text comment, submitted a neutral or positive medication comment, and other respondents.

| Characteristic                           | Submitted a positive medication experience comment, n (%) | Other respondents, n (%) | P-value | Submitted a negative medication experience comment, n (%) | Other respondents, n (%) | P-value |
|------------------------------------------|-----------------------------------------------------------|--------------------------|---------|-----------------------------------------------------------|--------------------------|---------|
| Age                                      |                                                           |                          |         |                                                           |                          |         |
| • 16 to 35 years                         | 16 (0.5)                                                  | 3128 (99.5)              | <0.05   | 143 (4.5)                                                 | 3001 (95.5)              | <0.05   |
| • 36 to 50 years                         | 29 (0.6)                                                  | 5203 (99.4)              |         | 260 (5)                                                   | 4972 (95)                |         |
| • 51 to 65 years                         | 38 (0.4)                                                  | 10001 (99.6)             |         | 338 (3.4)                                                 | 9701 (96.6)              |         |
| • 66 to 80 years                         | 34 (0.2)                                                  | 13918 (99.8)             |         | 313 (2.2)                                                 | 13639 (97.8)             |         |
| • 81 years and older                     | 19 (0.3)                                                  | 6376 (99.7)              |         | 165 (2.6)                                                 | 6230 (97.4)              |         |
| Ethnicity                                |                                                           |                          |         |                                                           |                          |         |
| • White Irish                            | 121 (0.3)                                                 | 34914 (99.7)             | >0.05   | 1095 (3.1)                                                | 33940 (96.9)             | <0.05   |
| • Other ethnic background                | 16 (0.5)                                                  | 3334 (99.5)              |         | 135 (4)                                                   | 3215 (96)                |         |
| Gender                                   |                                                           |                          |         |                                                           |                          |         |
| • Male                                   | 48 (0.2)                                                  | 19379 (99.8)             | <0.05   | 440 (2.3)                                                 | 18987 (97.7)             | <0.05   |
| • Female                                 | 89 (0.4)                                                  | 19929 (99.6)             |         | 795 (4)                                                   | 19223 (96)               |         |
| Main person completing the questionnaire |                                                           |                          |         |                                                           |                          |         |
| • The patient                            | 113 (0.4)                                                 | 28825 (99.6)             | >0.05   | 929 (3.2)                                                 | 28009 (96.8)             | >0.05   |
| • A friend or relative of patient        | 10 (0.2)                                                  | 4125 (99.8)              |         | 116 (2.8)                                                 | 4019 (97.2)              |         |
| • The patient with the help of someone   | 13 (0.2)                                                  | 5465 (99.8)              |         | 177 (3.2)                                                 | 5301 (96.8)              |         |

Note: P<0.05 is set as statistically significant.

#### *3.8.3.4 Association between general hospital characteristics and submission of a negative or positive medication free-text comment*

There were no statistically significant associations between those who submitted a positive medication comment versus other respondents and type of admission, emergency department stay, people who reported not receiving any explanation regarding of the purpose of their medications, not receiving written information and overall rating of hospital experience (**Table 3-18**). On the other hand, there were statistically significant associations between those who submitted a positive medication comment versus other respondents and being told about how to watch out for medication side effects. People who reported not being told about how to watch out for medication side effects were more likely to submit a positive medication comment.

Table 3-18: Comparison of general hospital characteristics between those who submitted of a negative medication free-text comment, submitted a neutral or positive medication comment, and other respondents.

| Characteristic                                                                                                     | Submitted a positive medication experience comment, n (%) | Other respondents, n (%) | P-value | Submitted a negative medication experience comment, n (%) | Other respondents, n (%) | P-value |
|--------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|--------------------------|---------|-----------------------------------------------------------|--------------------------|---------|
| Type of admission                                                                                                  |                                                           |                          |         |                                                           |                          |         |
| • Emergency                                                                                                        | 94 (0.4)                                                  | 25818 (99.6)             | >0.05   | 878 (3.4)                                                 | 25034 (96.6)             | <0.05   |
| • Planned                                                                                                          | 32 (0.4)                                                  | 8923 (99.6)              |         | 254 (2.8)                                                 | 8701 (97.2)              |         |
| • Other                                                                                                            | 4 (0.2)                                                   | 1904 (99.8)              |         | 67 (3.5)                                                  | 1841 (96.5)              |         |
| Emergency department stay                                                                                          |                                                           |                          |         |                                                           |                          |         |
| • Remained in emergency                                                                                            | 4 (0.5)                                                   | 743 (99.5)               | >0.05   | 28 (3.7)                                                  | 719 (96.3)               | >0.05   |
| • Transferred to hospital ward                                                                                     | 86 (0.3)                                                  | 25424 (99.7)             |         | 823 (3.2)                                                 | 24687 (96.8)             |         |
| Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand? |                                                           |                          |         |                                                           |                          |         |
| • Yes                                                                                                              | 105 (0.4)                                                 | 26997 (99.6)             | >0.05   | 669 (2.5)                                                 | 26433 (97.5)             | <0.05   |
| • No                                                                                                               | 13 (0.4)                                                  | 3347 (99.6)              |         | 326 (9.7)                                                 | 3034 (90.3)              |         |
| • Did not need explanation                                                                                         | 14 (0.2)                                                  | 6730 (99.8)              |         | 183 (2.7)                                                 | 6561 (97.3)              |         |
| Did a member of staff tell you about medication side effects to watch for when you went home?                      |                                                           |                          |         |                                                           |                          |         |
| • Yes                                                                                                              | 60 (0.4)                                                  | 16404 (99.6)             | <0.05   | 271 (1.6)                                                 | 16193 (98.4)             | <0.05   |
| • No                                                                                                               | 48 (0.5)                                                  | 10243 (99.5)             |         | 689 (6.7)                                                 | 9602 (93.3)              |         |
| • I did not need explanation                                                                                       | 16 (0.2)                                                  | 7018 (99.8)              |         | 153 (2.2)                                                 | 6881 (97.8)              |         |
| Were you given any written or printed information about what you should or should not do after leaving hospital?   |                                                           |                          |         |                                                           |                          |         |
| • Yes                                                                                                              | 73 (0.4)                                                  | 19677 (99.6)             | >0.05   | 405 (2.1)                                                 | 19345 (97.9)             | <0.05   |
| • No                                                                                                               | 51 (0.3)                                                  | 14893 (99.6)             |         | 737 (4.9)                                                 | 14207 (95.1)             |         |
| • I did not want or need any written or printed information                                                        | 6 (0.3)                                                   | 2184 (99.7)              |         | 35 (1.6)                                                  | 2155 (98.4)              |         |
| Overall rating of hospital experiences                                                                             | Mean (SD)*<br>9.2 (1.9)                                   | Mean (SD)*<br>9.2 (2)    | >0.05   | Mean (SD)* 7.42<br>(2.7)                                  | Mean (SD)* 9.28 (2)      | <0.05   |

\* Tested using independent T-test; Standard deviation (SD); P<0.05 is set as statistically significant.

There was a statistically significant association between those who submitted a negative medication comment versus other respondents and type of admission, with those who experienced an emergency admission being more likely to submit a comment than those who had a planned admission. However, there was no such statistically significant difference between those in the emergency department versus ward stay.

Furthermore, there were statistically significant associations between the submission of a negative medication comment versus other respondents and being provided an explanation for the purpose of their medication, receiving written information, and being told about how to watch out for medication side effects. People who reported not receiving any explanation regarding the purpose of their medications, those who reported not receiving written information and those who were not told about medication side effects to watch out for when they went home were more likely to submit a negative medication comment. There was an association between the submission of a negative medication comment versus other respondents and the overall hospital experience rating, with a lower mean rating for their hospital experience corresponding to a higher likelihood of submitting a negative comment.

### *3.8.3.5 Factors associated with submission of a negative or positive medication comment*

In the multinomial logistic regression analysis, the independent variables incorporated were overall rating of hospital admission, age group, ethnicity, gender, type of admission, provision of explanation of the purpose of medication, provision of a written information, and monitoring of the side effects.

The likelihood of submitting a negative medication comment compared to other respondents was significantly associated with several independent variables. These variables included the overall hospital experience rating, receiving written information, being told about how to watch out for medication side effects, age group and gender. As shown in **Table 3-19**, the strongest association was with individuals not being told about how to watch out for medication side effects, with a higher likelihood of comment submission for those individual. Additionally, individuals who did not receive written information or explanations about the purpose of their medication were more likely to submit a negative comment. Adults aged 36-50 years were more likely to submit a negative comment, whereas

individuals aged 66 and older were less likely to submit any comment. Across the variables overall hospital experience rating and gender variables, those who had a good experience and males were less likely to submit a negative comment.

Table 3-19: Factors associated with submission of a negative medication comment.

| Independent variables                                                                                              | Odd ratio           | Wald test      |    |         | 95% Confidences interval<br>(odds ratio scale) |
|--------------------------------------------------------------------------------------------------------------------|---------------------|----------------|----|---------|------------------------------------------------|
|                                                                                                                    |                     | Wald statistic | df | P-value |                                                |
| Overall rating of hospital experience<br>(Rating form 1, very poor to 11, very good)                               | 0.8                 | 226.4          | 1  | <0.001  | 0.80-0.84*                                     |
| Type of admission                                                                                                  |                     |                |    |         |                                                |
| • Emergency                                                                                                        | (Used as reference) | -              | -  | -       | -                                              |
| • Planned                                                                                                          | 1.14                | 2.46           | 1  | 0.12    | 0.97-1.34                                      |
| • Other                                                                                                            | 1.22                | 1.90           | 1  | 0.17    | 0.92-1.62                                      |
| Were you given any written or printed information about what you should or should not do after leaving hospital?   |                     |                |    |         |                                                |
| • Yes                                                                                                              | (Used as reference) | -              | -  | -       | -                                              |
| • No                                                                                                               | 1.30                | 11.79          | 1  | < 0.001 | 1.12-1.52*                                     |
| • I did not want or need any written or printed information                                                        | 1.15                | 1.39           | 1  | 0.24    | 0.91-1.45                                      |
| Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand? |                     |                |    |         |                                                |
| • Yes                                                                                                              | (Used as reference) | -              | -  | -       | -                                              |
| • No                                                                                                               | 1.59                | 28.20          | 1  | < 0.001 | 1.34-1.89*                                     |
| • Did not need explanation used as a reference)                                                                    | 1.27                | 3.81           | 1  | ≤0.05   | 1.00-1.61                                      |
| Did a member of staff tell you about medication side effects to watch for when you went home?                      |                     |                |    |         |                                                |
| • Yes                                                                                                              | (Used as reference) | -              | -  | -       | -                                              |
| • No                                                                                                               | 2.08                | 65.19          | 1  | < 0.001 | 1.74-2.48*                                     |
| • I did need explanation (used as a reference)                                                                     | 1.15                | 1.39           | 1  | 0.24    | 0.91-1.45                                      |
| Ethnicity                                                                                                          |                     |                |    |         |                                                |
| • White Irish                                                                                                      | (Used as reference) | -              | -  | -       | -                                              |
| • Other ethnic background                                                                                          | 1.16                | 2.07           | 1  | 0.15    | 0.95-1.43                                      |
| Age                                                                                                                |                     |                |    |         |                                                |
| • 16 to 35 years                                                                                                   | (Used as reference) | -              | -  | -       | -                                              |
| • 36 to 50 years                                                                                                   | 1.33                | 5.63           | 1  | 0.02    | 1.05-1.68*                                     |

|                      |                     |       |   |                       |            |
|----------------------|---------------------|-------|---|-----------------------|------------|
| • 51 to 65 years     | 1.03                | 0.07  | 1 | 0.79                  | 0.82-1.29  |
| • 66 to 80 years     | 0.69                | 9.98  | 1 | $1.58 \times 10^{-3}$ | 0.55-0.87* |
| • 81 years and older | 0.64                | 10.83 | 1 | < 0.001               | 0.50-0.84* |
| Gender               |                     |       |   |                       |            |
| • Male               | (Used as reference) | -     | - | -                     | -          |
| • Female             | 1.51                | 36.49 | 1 | < 0.001               | 1.32-1.73* |

\* Set as statistically significant.

However, the likelihood of submitting a positive medication comment compared to other respondents was significantly associated with some independent variables. These variables included the age group and gender. As shown in **Table 3-20**, the strongest association observed was with gender, showing females had a higher likelihood of submitting positive comments. Conversely, older individuals, specifically those aged 66-80 years, were less likely to submit a positive comment.

Table 3-20: Factors associated with submission of a positive medication comment.

| Independent variables                                                                                              | Odd ratio           | Wald test      |    |         | 95% Confidences interval<br>(odds ratio scale) |
|--------------------------------------------------------------------------------------------------------------------|---------------------|----------------|----|---------|------------------------------------------------|
|                                                                                                                    |                     | Wald statistic | df | P-value |                                                |
| Overall rating of hospital experience<br>(Rating form 1, very poor to 11, very good)                               | 1.02                | 0.11           | 1  | 0.74    | 0.92-1.12                                      |
| Type of admission                                                                                                  |                     |                |    |         |                                                |
| • Emergency                                                                                                        | (Used as reference) | -              | -  | -       | -                                              |
| • Planned                                                                                                          | 0.91                | 0.19           | 1  | 0.66    | 0.59-1.40                                      |
| • Other                                                                                                            | 0.70                | 0.48           | 1  | 0.49    | 0.26-1.92                                      |
| Were you given any written or printed information about what you should or should not do after leaving hospital?   |                     |                |    |         |                                                |
| • Yes                                                                                                              | (Used as reference) | -              | -  | -       | -                                              |
| • No                                                                                                               | 0.73                | 1.97           | 1  | 0.16    | 0.48-1.13                                      |
| • I did not want or need any written or printed information                                                        | 0.65                | 0.69           | 1  | 0.41    | 0.23-1.80                                      |
| Did a member of staff explain the purpose of the medicines you were to take at home in a way you could understand? |                     |                |    |         |                                                |
| • Yes                                                                                                              | (Used as reference) | -              | -  | -       | -                                              |
| • No                                                                                                               | 0.67                | 1.23           | 1  | 0.27    | 0.33-1.36                                      |
| • Did not need explanation used as a reference)                                                                    | 0.77                | 0.39           | 1  | 0.53    | 0.33-1.76                                      |
| Did a member of staff tell you about medication side effects to watch for when you went home?                      |                     |                |    |         |                                                |
| • Yes                                                                                                              | (Used as reference) | -              | -  | -       | -                                              |
| • No                                                                                                               | 1.52                | 3.18           | 1  | 0.07    | 0.96-2.40                                      |
| • I did need explanation (used as a reference)                                                                     | 0.73                | 1.03           | 1  | 0.31    | 0.39-1.35                                      |
| Ethnicity                                                                                                          |                     |                |    |         |                                                |
| • White Irish                                                                                                      | (Used as reference) | -              | -  | -       | -                                              |
| • Other ethnic background                                                                                          | 1.08                | 0.06           | 1  | 0.80    | 0.60-1.95                                      |
| Age                                                                                                                |                     |                |    |         |                                                |
| • 16 to 35 years                                                                                                   | (Used as reference) | -              | -  | -       | -                                              |
| • 36 to 50 years                                                                                                   | 1.08                | 0.05           | 1  | 0.82    | 0.56-2.08                                      |
| • 51 to 65 years                                                                                                   | 0.87                | 0.18           | 1  | 0.67    | 0.46-1.64                                      |

|                      |                     |       |   |         |            |
|----------------------|---------------------|-------|---|---------|------------|
| • 66 to 80 years     | 0.48                | 4.58  | 1 | 0.03    | 0.25-0.94* |
| • 81 years and older | 0.74                | 0.71  | 1 | 0.40    | 0.36-1.50  |
| Gender               |                     |       |   |         |            |
| • Male               | (Used as reference) | -     | - | -       | -          |
| • Female             | 2.06                | 12.70 | 1 | < 0.001 | 1.38-3.06* |

\* Set as statistically significant.

### 3.8.4 Qualitative analysis

The thematic analysis generated five themes and 13 subthemes. It should be noted that none of these quotes have been altered, and they are presented verbatim (which may involve typos and the use of colloquialisms) **Figure 3-2.**

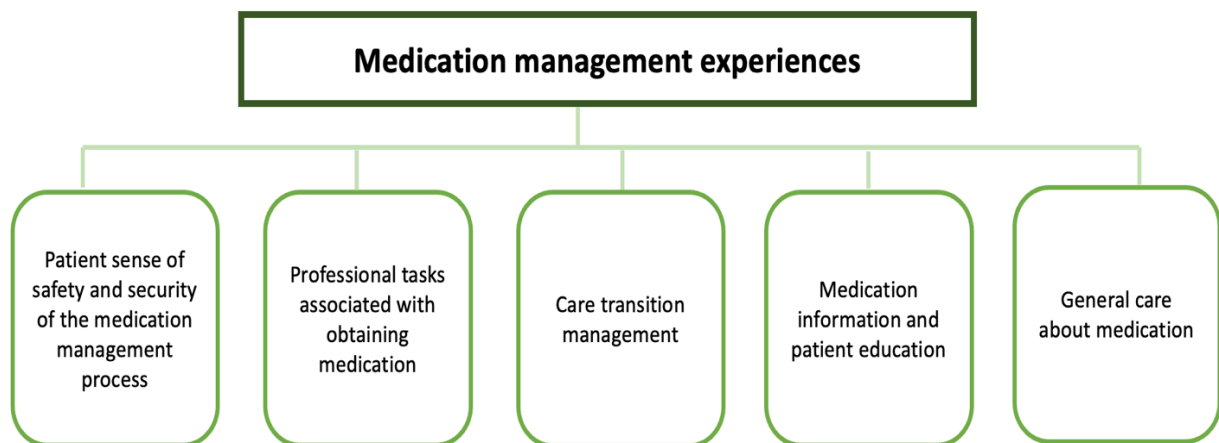


Figure 3-2: Medication-related free-text comment themes.

#### **Theme 1: Professional tasks associated with obtaining medication**

This theme encompassed various aspects of the process of receiving medication. Five sub-themes were identified within this theme: the efficacy or appropriateness of medication, medication supply (including the use of patient's own medication), requests for medication, MRP including side effect, complication or medication misuse, and timing of prescription, dispensing or administration of medication.

##### **Efficacy or appropriateness of medication**

Throughout their hospital stay, particularly in-ward and at the point of discharge, patients frequently expressed concerns about the efficacy of their medication including pain medications. Some patients reported that the painkillers failed to provide effective relief, leading to hours of severe pain. Discharge procedures also drew criticism, with patients often feeling like they were discharged without a comprehensive pain management plan and medication. Moreover, the strength of prescribed medications was another area of concern.

Patients frequently reported that the pain management provided was insufficient, resulting in persistent discomfort.

*“I have gallstones and none of the painkillers I got in ER worked, I was in serious pain for hours” ID: 24489*

*“The pain control was poor in the later stages of my stay and the prescription for follow up pain control was inadequate until adjusted by my GP”*

*“I was not given adequate pain relief during the night as there were no doctors available to prescribe” ID: 28533*

*“Was sent home without proper pain relief as a very vulnerable person left to sort myself out. I had to ask for a prescription for pain killers when leaving hospital and I was only given pain killers for 2 days” ID: 77795*

*“I did not receive adequate pain relief in A and E. As I had been taking (Med.) at home and no relief” ID: 33868*

*“I felt I had to ask for pain relief (tablets) as with being in a ward you are given relief every 4/6 hrs” ID: 69068*

### **Medication supply including use of patient's own medication**

Patients shared negative experiences related to medication supply during their transition from the hospital to the community. Patients frequently reported issues with the supply of medication during their hospital stay, which was particularly impacted on weekends or after-hours. In some cases, hospitals did not have the required medication in stock, leading to patients or their families having to bring personal medication from home or to travel to get it. Moreover, patients were sometimes discharged with only enough medication for a very short period, causing difficulties when additional medication was needed during holidays or when discharge timings were inconvenient for obtaining medication from pharmacies. This forced them to seek external pharmacies that were open, causing additional stress and inconvenience.

*"I wasn't given pain relief medication (just over the counter)" ID: 36587*

*"Give enough tablets for 24hrs so that could get to local chemist" ID:5967*

*"I was given no medication only prescription which meant we had to go straight to the pharmacy as it was a Sunday" ID: 23879*

*"My family had to travel to Dublin the next day with list of my medication as Dublin had nothing on me" ID: 76361*

*"I was discharged from hospital on a Sunday I was given new tablets when in the hospital. When I was leaving hospital I was only given tablets for Sunday evening. Monday was a bank holiday and I had great difficulty getting a chemist open" ID: 30120*

*"I wasn't offered any help or medication I didn't bring my own as I didn't think I had to" ID: 36904*

### **Request for medication**

Patients frequently reported challenges related to requesting medication during their hospital stay. Some patients felt that they were often required to ask for pain relief that was supposed to be provided at regular intervals. There were also instances in which requests for pain relief were questioned or forgotten by hospital staff, leading to prolonged pain and discomfort. In some extreme cases, patients reported that they had to leave their beds and seek out medical staff for medication due to prolonged wait times. Some patients indicated that their requests for medication were either ignored or outright denied, even when they were visibly in pain. A few patients reported not receiving their prescribed medication for their conditions for several days, causing further distress.

*"If your down to get pain meds every four hours after operation. why do you have to keep asking for them. its like the hospital is trying to save money" ID:709*

*"I had to keep asking nurses for pain relief but they kept forgetting to bring the medication" ID:8019*

*"In A&E during the night, I asked for pain relief. It took an hour before I got it, after asking 3 times. I was on a stretcher in front of the desk where three doctors and one nurse were sitting who totally ignored my request" ID: 76577*

*"When the doctor (Dr. Name) came around with his entourage I told him that I had not received my medication for two days he was taken aback" ID: 8645*

### **Medication related problems**

This sub-theme highlighted the experience of medication causing harm and patients' descriptions of their experiences of receiving medications that caused damage to their bodies, including side effects or allergies, and experiencing medication errors and other complications. Several patients reported experiencing medication-related problems including adverse reactions to specific medications.

Patients highlighted several medication-related issues, including adverse reactions, lack of information about side effects, and concerns about medication quantities issued at discharge. Some patients experienced medications having the opposite effect of what was intended or exacerbating existing conditions. Concerns were also raised about the lack of detailed discussions about potential side effects, leading to unexpected health issues and patient anxiety. Patients sometimes had to stop taking prescribed medications due to severe adverse effects that were not initially explained.

*"I had a bad reaction to (Medication), and despite this, I was given a (Medication) painkiller, which was very unpleasant." ID:4492*

*"I know I am old but I was ok before taking (Med.) to help me go wee but tablet had reverse reaction I suffer from (Cond. Type) was told the tablet would help but it didn't." ID: 33762*

*"As I am allergic to (Drug) and was given some in the A&E on my admission, I had a very bad reaction which caused me to stay in the hospital at least 4 days longer, and I was not happy with that." ID: 1189*

*"After the first difficult night with my husband he was sediated by (Med). He remained heavily sedated for over 3 weeks - confined to bed and (Proc. Name). None of this was discussed with me or his family." ID: 81279*

*"Sent home with a serious amount of meds. which made me worse!" ID: 67024*

### **Timing of prescription, dispensing or administration of medication**

This sub-theme relates to the waiting time and delays associated with medication management.

Patients frequently reported issues related to waiting for medication during their hospital stay and at discharge. Delays in medication administration were a common concern, with patients often experiencing waiting times of up to several hours for their medication. These delays also extended to the dispensing of medication at night, with some patients reporting receiving their medication very late at night. Inconsistency in the timing of medication administration was another reported issue, with medication being dispensed at varying times during the day. This inconsistency could potentially disrupt the effectiveness of the medication and cause additional discomfort for the patients.

*"Timing of administration of medicines varied widely from day to day" ID: 39603*

*"IV meds given sometimes an hour late" ID: 63398*

*"sometimes I had to go to the nurses station as my meds wre up to 3 hours overdue" ID: 71344*

*"Nurses giving out tablets after midnight after I was asleep - one night." ID: 63731*

*"Dispensing of night medication often very late i.e. 10-10.30 am" ID: 37825*

Patients often referred to a lack of adequate staff, particularly during peak times and weekends, which were perceived to cause the problem described above, for example resulted in prolonged waiting times for medication.

*"The only complaint I have is delay in getting pain medications, sometimes it took a long time. I do understand though that at weekends there is a major shortage of nursing staff"* ID: 27267

*"More staff, never got pain medication on time as there was never enough nurses"* ID: 29122

Upon discharge, patients reported long waiting times for prescriptions and a lack of explanation regarding their medication or noted that they were discharged with limited medication that was only enough for a few days before they needed to acquire a new prescription from their doctor. In addition to the delay in medication administration described above, respondents also reported delays in the prescription process itself, with patients often left waiting for physicians to sign off on their medication orders.

*"On discharge awaiting hours for prescription and explanation re medication"* ID: 31122

*"The doctors (surgeons) hardly spoke to me, they did not explain what was wrong or what to do after I was discharged. My prescription was only for a few days so I was out of pain killers until my doctor made me one, which needs a 24 hour waiting time."* ID: 37648

*"An inordinate amount of time and bed availability can be wasted waiting for a consultant/doctor to sign a prescription for medicine on discharge. I once waited from 9am till 5 pm"* ID: 2677

Additionally, staff shortages not only led to delays in medication administration but also overlapped with issues in medication supply, self-medication and requests. Patients often had to wait extended periods, despite making multiple requests. Furthermore, these shortages affected timely discharge and patients' ability to collect their medication.

*"Doctor came sometime after 6.00pm by that stage I had medicated myself"* ID: 69316

*"Be discharged by 5pm to allow for collecting (Med.) from pharmacy"* ID: 25036

*"More staff would help. The doctors and nurses in A&E were run off their feet and although they tried their best I had to ask 4 times for my medication and still had to wait 2 more hours in extreme pain"* ID: 30413

*"Staff should be more organised when discharging patients, on occasions I waited around waiting on prescriptions etc." ID: 31951*

## **Theme 2: Patient sense of safety and security of the medication management process**

This theme explored various aspects related to how patients perceived their safety and the security measures in place during medication management. Two sub-themes were identified within this theme: the observation or experience of healthcare professional medication errors and concerns about healthcare professional competence (including attitude, behaviour, knowledge, and skill).

### **Observation or experience of healthcare professional medication errors**

Patients reported several instances of medication errors that occurred during their hospital stay. Reports of medication errors included errors in prescription, dispensing, administration and documentation by healthcare providers. These included incorrect dosing, prescription omissions and the administration allergenic substances, often only caught by patient vigilance. Discrepancies between verbal instructions and written prescriptions, language barriers and inaccurate record-keeping were reported to exacerbate the problem. Errors in discharge prescriptions, sometimes involving dangerous dosage changes, heightened patient anxiety and eroded their trust in the healthcare providers.

*"On one occasion I was given the wrong dose of medicine & on another I was told one med had been stopped, when it was not, if I was not aware what med I should get I would have been messed up." ID: 25906*

*"Night staff poor english, give out wrong drugs sometimes." ID: 24693*

*"Hope you look at my records - given (Med) wasn't checked that I'm allergic to same - given tablets that set me hallucinating, twice" ID: 63762*

*"On discharge no letter given, 2 mistakes on prescription written by Doc." ID: 9414*

*"Several errors on discharge prescription including a doubling of strength of (Medication) despite not tolerating that dose in past. Once highlighted the errors were resolved with the registrar but shouldn't have happened" ID: 2678*

*"Yes, the nurses mixed me up with someone else's tablets when I wasn't on any medication I nearly took them." ID: 24578*

### **Healthcare professional competence (attitudes or behaviours, knowledge and skill)**

Patients reported significant concerns about healthcare providers' competence, attitudes, and behaviours. Issues included non-responsive behaviour during emergencies, neglect during pain episodes and leaving medication unsupervised by patients' bedsides. Furthermore, perceived inexperience, dismissive behaviour and apparent lack of knowledge about medication administration raised doubts about provider competence.

*"Medical staff blatantly not answering their bleep/page/mobile when patient or family member have query before/after discharge from hospital (i.e. home care query, incomplete prescription" ID: 1637*

*"I was left in pain and without medication in casualty after being diagnosed with (CONDITION NAME). I had to shout for help and I was left on my own without attention for over two hours" ID:1806*

*"Doctor should find the right reason before giving any medicines. How can he prescribe something if he isn't sure what's the problem is? " ID: 10524*

*"Many times doctors were using google search on their phones in front of me to know what medication I was taking. I found this to be unsettling and reduced my confidence in them" ID: 77824*

*"I'm not happy to remember a male nurse who was giving me an (Med.) very indifferent. He was very unpleasant, he was doing his work as punishment and painfully" ID: 30951*

### **Theme 3: Care transition management**

This theme focused on the process of transitioning patients between different healthcare settings, particularly during discharge from the hospital. Two sub-themes were identified within this theme: prescription not being given to the patient at discharge and medication errors at discharge or admission.

#### **Prescription not being given to the patient or delayed at discharge**

Patients highlighted significant issues with the transition from hospital care to home care, primarily due to inadequate communication and prescription management. Problems included incomplete or incorrect prescriptions at discharge, lack of timely preparation of discharge documents, and inconsistencies between patient instructions and reports to primary care. Additionally, inadequate communication between hospital staff and primary care physicians resulted in confusion and potential medication errors.

*"I was discharged with incomplete prescriptions, which meant I went a further two days without pain relief, and my family had to make 4 trips to the hospital to get a correct prescription - 4 prescriptions later." ID: 63112*

*"no discharge letter ready - no medicine list ready after some days at home - tablets changed by practice doctor + later dosages changed." ID: 29381*

*"Some of my GP prescription medications were not prescribed on the hospital drug administration Kardex" ID: 34817*

*"Communication between patient and staff and staff and staff was very poor ..... Even the prescription I was sent home with contradicted what the doctor wrote in his report to my GP" ID: 23429*

*"Follow up with my GP was another difficulty as he did not seem to have adequate information re my admittance to hospital and medications I was then to take." ID: 36461*

### **Medication errors at discharge or admission**

Patients expressed serious concerns about medication errors during admission or discharge transitions, which can have serious health consequences. These errors included miscommunication about medication regimens, prescribing incorrect or harmful medications, and omitting necessary medications from discharge prescriptions. Instances of inadequate instructions accompanying prescriptions and dismissal of patient concerns about their medications were also reported. There were also reports of medication errors due to miscommunication between hospitals during patient transfers.

*"I was then sent a prescription by post with a post it note attached saying - Avoid alcohol. 4 weeks post discharge I received another phonecall about the infection telling me I needed a prescription - doctor in question had no idea I had already received prescription by post and taken antibiotics" ID: 31991*

*"Due to the antibiotics being omitted from the prescription my mother suffered (Cond. Name) 5 days after discharge from hospital." ID: 38436*

*"Information on discharge prescription was incorrect, when brought to attention of nurse it was brushed off as correct, but on further insistence proved prescription incorrect. Because written by doctor, nurse felt it had to be correct. Patients need to be heard. Doctors and nurses not beyond getting details incorrect" ID: 63867*

*"Check and review prescribed medication carefully. I was given scripts for two antibiotics upon discharge and suffered severe side effects. Stopped immediately, read the package inserts and slapped my head. Returned to the hospital for a new script and proceeded successfully" ID: 69076*

*"I was transferred from Vincent's to tallagh with a bit of confusion and was nearly given wrong medication as staff in tallagh didn't read notes I brought this to the nurses attention and she read my notes and gave me the antybotic I was not allergic to" ID: 30360*

*"I was transferred to another hospital and when I arrived there was some confusion about the amount of medication I was taking." ID: 8782*

This theme intersected with the delay in providing prescriptions, which subsequently impacted the timing and administration of medications to patients. These delays could lead to the administration of incorrect medication. This theme also highlighted instances of miscommunication and a lack of information about medications during both admission and discharge processes.

#### **Theme 4: Medication information and patient education**

This theme highlighted the necessity of educating patients about their medicines and ensuring that both patients and their families are actively involved and heard in all healthcare decisions. Two sub-themes were identified within this theme: inadequate information about medications and patient and/or family being involved and heard.

##### **Inadequate information about medications**

Patients have reported significant concerns about the medication information and patient education process from admission to discharge. A common issue was the lack of explanation or discussion about changes in medication, including adding new drugs or altering existing ones. This lack of communication led patients taking incorrect dosages or the wrong medication altogether, resulting in adverse health outcomes. Patients also expressed frustration at the lack of communication about their medication between healthcare providers themselves. Instances of doctors changing medication or care plans without adequate documentation or informing the nursing staff were reported. Furthermore, language barriers between foreign nurses and patients created additional challenges in understanding medication instructions.

*"I was given extra (Condition Name) tablet without and explanation or discussion" ID: 1315*

*"I could not be sure about answer I gave to what drugs I had taken each day as some looked different to ones at home and I was often sleepy" ID: 3142*

*"Some of my answers may seem odd as on medication and treatment as my meds change they cannot give me a definite answers" ID:11080*

*"Needs to be a better communication between Doctors and nurses. Doctors may make a change to care/medication and do not write a note in the medical notes and do not tell the nurse. On the doctor rounds the team talk amongst themselves rather than to the patient" ID: 12448*

*"Communication skills for foreign nurses i.e. medication questions. I did not understand what they were saying" ID: 32691*

Finally, discharge processes were also a significant source of concern. Patients reported being rushed out of the hospital without receiving crucial information about their home medication regimen. They emphasised the importance of receiving written information or handouts that explained the medications they were prescribed, along with their purpose and any potential side effects.

*"I would like the doctor who is looking after my care to explain my medication on my discharge. As I was recently discharged on wrong medication and had to be admitted for a week due to their mistake. No doctor would admit to me about mistake" ID: 1413*

*"Medicines etc should be given in written form. Too much reliance on oral communication."*  
ID:8340

*"My husband was on quite a lot of medication when he left on quite a lot of medication when he left hospital but no one explained to me (as his main carer) what the medications were for" ID: 14385*

### **Patient and/or family being involved and heard**

Patients and their families emphasised the importance of their active participation in medication-related decisions and information sharing. Family members, particularly those who will be responsible for aftercare, should be consulted before discharge to ensure that they have a thorough understanding of the patient's medication regimen and the reasons behind it. However, patients and families have reported that discharge information often lacked depth, leaving carers with prescriptions but no additional medical advice or follow-up information. Patients also expressed frustration when their input was not taken into account and when they were not actively involved in medication-related decisions. This lack of direct engagement led to patients feeling uninformed about their treatment plans and medication regimens.

*"Patient should be told in advance of operation what pain meds will be given so that an informed decision can be made as to whether meds are suitable and not likely to make patient sick" ID: 9345*

*"That (Specialist Doctor) should speak more directly to the patient, not to (Doctor). It was to them he was asking questions about what medication I was on, etc. As I said, it was not my usual (Specialist Doctor) that was on duty; he was on holidays. But I feel whoever is doing duty for him should read back my file. It's quite frustrating. " ID: 3763*

*"It is very important when giving information to elderly/confused patients that a family member be present or given that information independently, so they too can be aware of*

*planned treatment and medication. So frustrating when the family member states 'I can't remember' ID: 1543*

*"Family members (next of kin) should be consulted before discharge or patient, particularly for aftercare and the taking of medicines, reasons for it" ID: 66314*

### **Theme 5: General care about medication**

This theme focused on aspects of the overall care provided to patients during the medication management process. This theme involved two sub-themes: privacy and suitability of medication administration locations and accommodating the cognitive and physical effects of medication.

#### **The privacy and suitability of medication administration locations**

Concerns were raised about the lack of privacy in places where medications are administered. Patients expressed concerns about the lack of privacy in and suitability of areas where medications were administered, with concerns raised about hygiene practices. Issues ranged from public discussions of personal medical information to inappropriate intrusion into personal spaces. Patients also pointed out the lack of privacy in certain situations, such as receiving medication or having their medical condition discussed in public settings, which led to a lack of confidentiality and privacy.

*"Patients with cancer or those receiving (Medication) in public areas should be admitted directly to a ward to avoid infection." ID: 36198*

*"there was no privacy when the patient's diagnosis, care and medication was being discussed and so everyone on the ward would have been aware of everyone else's condition" ID: 3864*

*"More privacy when medication administered" ID:12075*

*"The nurse came into the room without knocking on the door while I was getting dressed to give me prescriptions despite the door being closed" ID: 71554*

*"I was instantly given (Medication), (Medication) and despite the fact I was on a trolley on the corridor my provacy and dignity was respected at all times" ID: 2436*

### **Accommodating the cognitive and physical effects of medication**

The experiences shared by patients underscored the need for healthcare providers to account for the effects of medication on patients' cognitive and physical states when planning and implementing care procedures. Patients expressed concern about the behavioural changes caused by certain pain medications, suggesting that healthcare providers should be more cognisant of these potential effects. This included understanding the potential impacts of medication on the patient's behaviour, managing the timing of medication administration to minimise sleep disturbance, and ensuring that the administration of high-risk medications is properly supervised.

*"Distribution of tablets after midnight - this disturbs sleep very badly in an environment where it is already difficult to sleep. Then more tablets/samples at very early hours(ie 6am) - perhaps these times could be made more sleep friendly." ID: 29728*

*"Patients returning from heavy anesthesia while they receive a verbal briefing, they invariably will not take it all in. So possibly a short written note outlining what was covered in the operation and what was covered in the briefing would allow the patient, if they do not recall, to ask the team when next visited." ID: 29201*

*"Greater care needs to be shown when it comes to administering controlled drugs (pain meds). If the patients situation worsens as a result of these meds, action should be taken immediately. If the patient is not coherent then the family can be more involved in the care and treatment" ID: 13447*

*"A member of the finance team arrived at my bedside when I had only just woken up from (Medicine). I had already stated in admissions that I was a public patient and was willing to pay there and then for my one night stay but they would not accept the payment. This ruined my hospital experience as I was not feeling up to talking to someone about finance at that time. ID: 14329*

### 3.9 Study thematic framework

This section provides an overview of the most important areas for improvement in the inpatient medication management experience from admission to discharge, as derived from the analysis of the survey data (**Figure 3-3**).

- **Professional tasks associated with obtaining medication**

This refers to the structured processes and protocols that healthcare professionals follow to ensure that the right medications are prescribed and provided to patients. The emphasis on the tasks at both admission and discharge ensures continuity of care. The focus could be on the accuracy and the timing of medication administration, dispensing, prescription and on supplying enough medication.

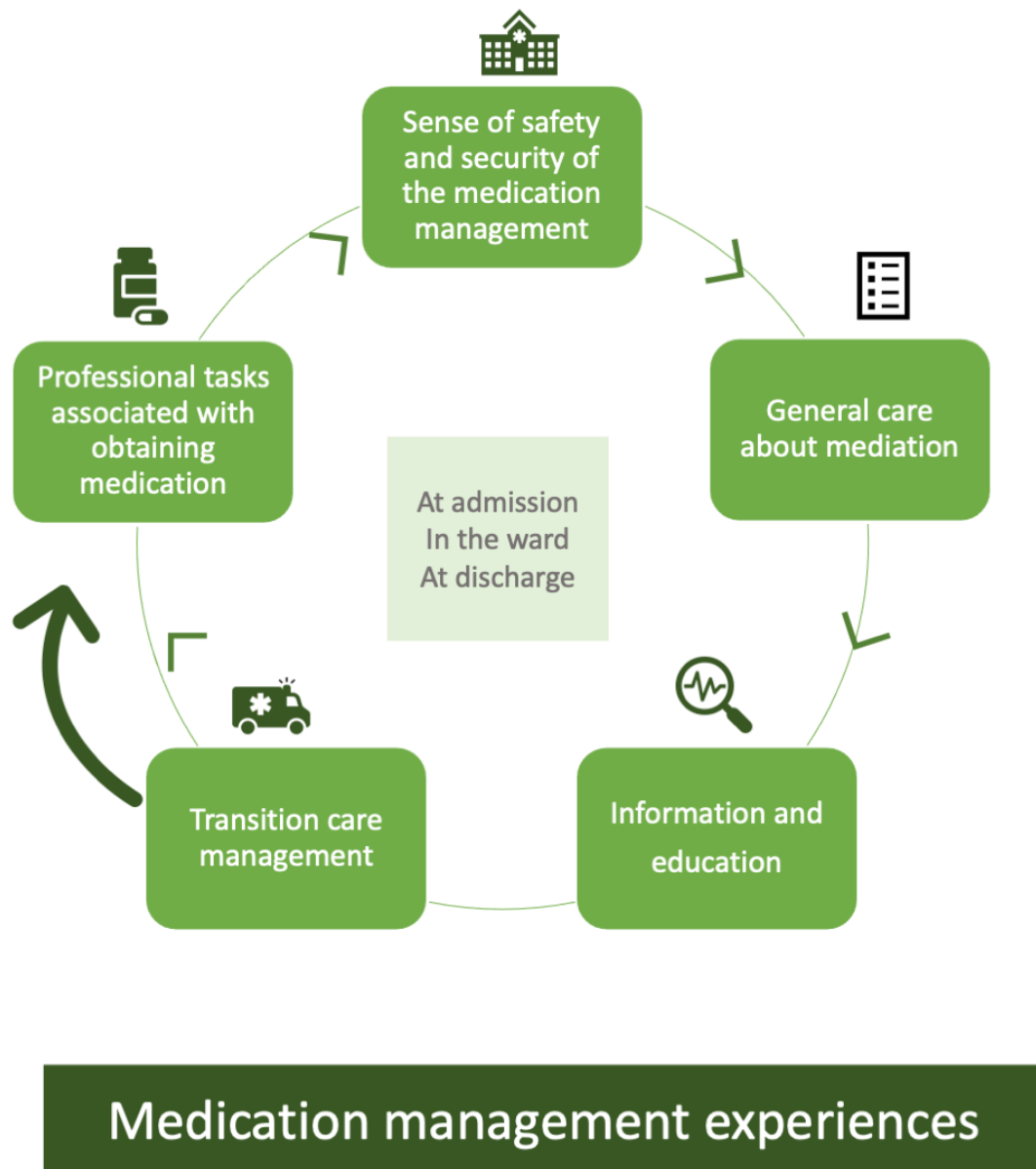


Figure 3-3: Thematic framework of medication management experiences.

- **Sense of Security and Safety of Medication Management**

The focus should be on precise medication reconciliation, which involves reviewing the patient's current medications to ensure that these medications are continued or adjusted

appropriately during hospitalisation. Additionally, it is crucial to ensure that patients are discharged with the right medications, clear instructions and information about any necessary adjustments made during their hospital stay.

- **Medication information and patient education**

Ensuring that patients receive and comprehend the information about the purpose, dosages, and potential side effects of their medications is essential, and this information should be effectively communicated to them.

- **Transitional care management**

Transitional care emphasises the importance of maintaining continuity in patient care as they progress between various stages or healthcare settings. This approach is founded on the belief that well-coordinated and thoughtfully planned transitions lead to improved patient outcomes, decreased medication errors, fewer complications and reduced delays in medication management during transitions of care.

- **General care about medication**

Improving overall medication care involves addressing aspects such as maintaining patient privacy, ensuring the appropriateness of medication administration locations and considering both the cognitive and physical effects of medications.

In the next section 3.10, the integration of qualitative and quantitative findings will be discussed and described. This approach facilitates a comprehensive understanding of the research topic by correlating numerical data with contextual insights.

### 3.10 Integrations of quantitative and qualitative findings

Quantitative analysis revealed that approximately 4% of respondents contributed free-text comments regarding medications. Among these respondents, a bad experience was associated with a greater likelihood of submitting a negative medication-related comment. The qualitative part of the study helped to explain more about the patient's concerns through theme “professional tasks associated with obtaining medication”. Among the concerns highlighted, some patients said they didn't feel their medication was good enough, which made them feel uncomfortable for a long time. They mentioned having to ask for pain relief repeatedly, even though they thought they should have received it regularly. Some patients

also said their requests for medication were ignored or denied, even when they were clearly in pain. Another big problem was the long waits for medication. Patients often had to wait for several hours to get their medication, which was frustrating for them. Furthermore, under the theme of “general care about medication”, the qualitative data showed that patients were concerned about the privacy and cleanliness of the places where they got their medication. Respondents weren't happy with how clean or suitability of the medication administration areas. Miscommunication during the transition of care under the theme of “care transition management” was another frequently raised issue, causing delays in receiving discharge prescriptions or leading to medication errors upon admission or discharge. These concerns help to explain the overall low rating of hospital experience. Along with these issues, discomfort and concerns about the safety and security of the medication management process, particularly regarding inaccurate record-keeping that could lead to medication errors, may have also contributed to the lower overall hospital experience ratings reported by those submitting negative medication comments. These concerns, occurring from admission to discharge, explained the patterns observed in the quantitative data, which indicated a high frequency of issues both during inpatient stays and at the point of discharge.

The quantitative results of the study highlighted a deficiency in the provision of medication explanations, with patients often reporting a lack of understanding about the purpose of their medications. They frequently did not receive verbal or written information and were not informed about potential side effects to watch out for upon returning home. Also, there was an association between not receiving information, explanations, or being informed about side effects, and submitting a negative comment. Qualitatively, under the theme "patient sense of safety and security of medication management process", respondents often reported negative comments about healthcare providers' attitudes and behaviours, which hindered the proper explanation of the purposes of medications and the answering of patients' questions about them. Additionally, the high workload and busy schedules of staff were reported to affect their ability to adequately explain medications. During discharge, several people reported delays in the discharge process, which reduced the time available to explain the possible side effects of medications or to provide important information about them. Furthermore, within the theme of "medication information and patient education," the absence of adequate information and discussion regarding changes in medication was identified as a significant factor contributing to numerous medication complications, such

as errors or incomplete prescriptions, observed both during inpatient stays and at the point of discharge.

The quantitative data from this study revealed that younger adults were more prone to submitting negative comments compared to older adults, suggesting an association between younger age and the likelihood of providing such feedback. Qualitative data described the reasons behind these negative comments, identifying concerns related to the medication management process. Taken together, these findings highlighted the area for improvement in patient care, particularly for younger individuals.

A summary of the quantitative results and qualitative findings, followed by the main integration points presented in **Figure 3-4**.

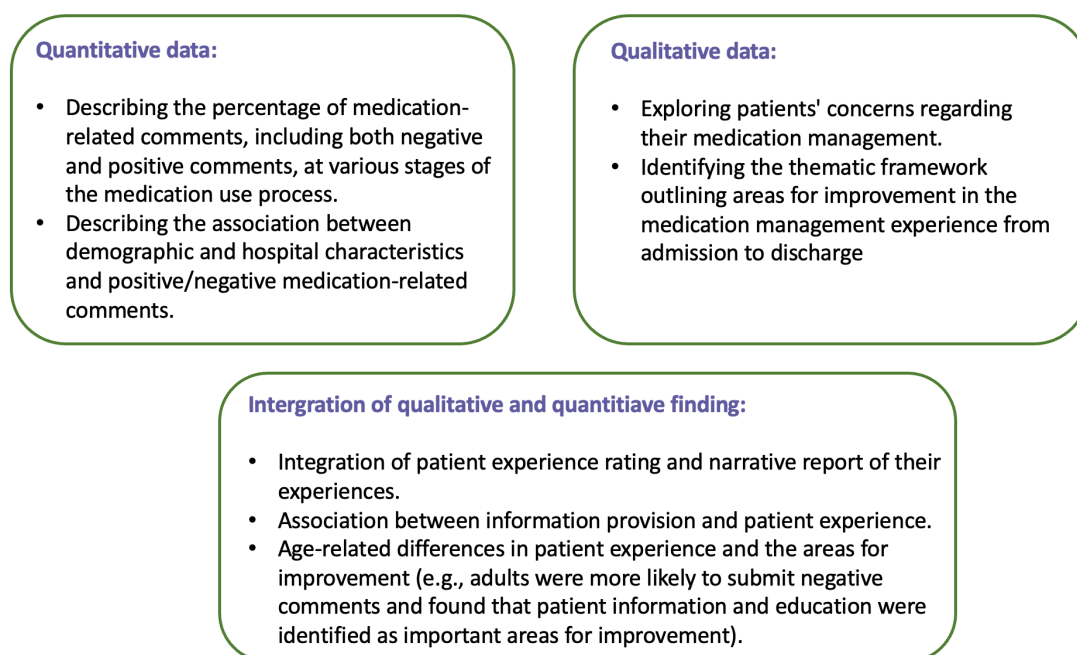


Figure 3-4: Integration of quantitative and qualitative findings.

### 3.11 Discussion

### 3.11.1 Key findings

The results identified that 4% of the respondent's provided comments related to medication. Most of these comments were negative, while a small proportion were either positive or neutral. The frequency of medication-related comment was consistent across different years of the NPES survey. The close-ended questions in this questionnaire involved only for questions related to medication experiences including questions about whether patients received explanations about the purpose of their medications, if they were provided with written information, and if they were informed on how to monitor potential medication side effects.

Our study found significant differences between the submission of medication-related comments and both demographic characteristics and general hospital characteristics. People who reported not receiving any explanation of the purpose of their medications, not receiving written information and not being told about how to watch out for medication side effects were more likely to submit a negative comment. In the regression analysis, age, gender, receiving written information, being told about how to watch out for medication side effects and overall hospital experience rating were significantly correlated with submitting a negative medication comment compared to submitting other comment. A stronger correlation was observed among patients aged 16 to 65 years, who exhibited a higher likelihood of submitting negative comments.

The qualitative data analysis uncovered various themes and sub-themes that provide valuable insights into understanding the reported medication-related experiences. The dominant themes that emerged from comments related to medication included aspects of professional tasks associated with the patient obtaining their medication, the patient's sense of safety and security in the medication management process, transitional care management, medication information and patients' education, and general care about medication.

### 3.11.2 Comparison with existing literature

The evidence in the literature supports the importance of exploring the medication experiences in older people in different health care settings [157, 172, 257, 272]. Yet, little is known about the in-patient medication experiences of younger adults. However, an experimental study aimed to investigating the influence of age on medication side effect recall compared younger patients (average age = 20.3) to older patients (average age = 73.5)

[281]. The side effects were categorised into three levels of severity: mild, moderate and severe. They found no age-related differences in the free recall of side effects and noted that older adults remembered more severe side effects compared to mild effects. However, when it came to recognising severe side effects in a later test, older adults were less successful than their younger counterparts [281]. This experimental study did not find an age association and differed from our study in the healthcare setting and focus. While their study exclusively examined the recall of side effects across different age groups, our research aimed to understand the association between age and medication-related experiences in inpatients. Our study found that people aged 16 to 35 years and aged 36 to 50 years were more likely to submit a negative comment than other age groups. Another study focused on the older patients conducted by Holmqvist *et al.*, [169] found that older patients had more difficulties interpreting their medications' effectiveness and side effects. Knowing whether the current treatment was right for them was difficult because they were unsure how they would feel without the medications [169]. This may explain the lower likelihood of older patients to submit negative medication-related comments in the current findings. Another reason explaining the lower submission of negative comments by older adults may be that they are more accepting of minor side effects or problems as they attribute them to their age and the belief that medications for their age group are intended more to alleviate symptoms rather than cure underlying conditions. If medications seemed effective, there is evidence that older people hesitated to ask about medication review evaluation, fearing that changes in their treatment could make them feel worse [169]. Additionally, they exhibited higher adherence to their prescribed medications after hospital discharge compared to younger adults [168]. Given that older adults were less likely to submit negative experiences, and our study found that younger adults were more likely to submit negative experiences, could suggest that younger adults in our study may have perceived complaining as an effective avenue for bringing about change and improving healthcare outcomes.

The bivariate analysis only identified an association between ethnicity and the submission of negative comments. People from a minority ethnic group were more likely to submit a negative comment than those who were white Irish. However, this became non-significant in the regression model. None-the-less, this suggests the need for further analysis within this data and in other studies to better understand the medication-related experiences and outcomes of minority ethnic group in Ireland. It's possible that language and cultural barriers could be a contributing to this.

The respondents expressed the need for enhanced management during the discharge process. These findings further contribute to the existing literature on post-discharge medicine management for older patients [157, 272, 282-284]. Our findings are consistent with qualitative studies that have found patients experiencing confusion about their medication, often not recognising the details and reasons for changes made to their medication regimen during their hospital stay [166, 167, 171]. However, these studies focused only on older patients aged >65 years at discharge. The reported confusion experienced by respondents in our study may have been due to a lack of explanations about medication at discharge. Older patients frequently voiced concerns about delays during the discharge process [157]. A significant number of these older individuals reported dissatisfaction with the discharge procedure, primarily due to perceived delays. These delays were typically linked to the time needed for pharmacy preparations and the subsequent waiting period for medication delivery to the ward. Some participants also believed that the timing of discharge was influenced by how busy the ward was [157]. We identified similar concerns in both older and younger adults, with a higher frequency of negative comments among the younger adults. We observed that young adult patients were more likely to report negative comments including their perception of uncertainty about the timing of discharge and their experience of delays in receiving their prescribed medications. The delay or absence of prescribed medications upon discharge has several negative consequences. Firstly, it prolongs the period of discomfort and pain for patients who require immediate relief. This delay in receiving necessary pain relief compromises patient comfort and can hinder their recovery process. Secondly, it places additional burden and stress on the patient's family, who must navigate the challenges of managing their family's health needs without the prescribed medications. A study by Tobiano *et al.*, [172] found that many older patients expressed a strong appreciation for the printed list of medications furnished by the pharmacist, characterising it as beneficial, informative, well-structured and a valuable service provided by the hospital at the time of discharge [172]. The current study identified similar concerns in both older and younger adult patients, with a higher frequency of negative comments among the younger adults. This suggests that medication management experiences could be consistent across different age groups and that there is a need for further exploration of medication-related concerns in young adults. We found that respondents who submitted negative medication-related comments were more likely not to have received written information, not to have been told about medication side effects and not to have received an explanation about the medication's purpose. These findings indicate that patients value being given an

explanation for the purpose of their medications, written information about their medications and information about how to watch out for medication side effects. Tomlinson *et al.*, [272] explored the experiences of older patients regarding their medications after discharge and identified that deficiencies in medication discussions and communication about regimens (often lacked detail, did not adequately address their questions ) negatively impacted their self-management abilities at home [272]. This highlights a critical gap in communication between healthcare providers and patients regarding medication-related issues.

Patient-centred care has recently gained significant importance due to its role in ensuring that patients receive care aligned with their needs and preferences [285, 286]. This approach emphasises improving communication between patients and healthcare providers, facilitating effective information exchange and understanding. Moreover, patient-centred care promotes shared decision-making, enabling patients to actively participate in their healthcare decisions, which has been associated with improved outcomes [285]. The current study's findings support the positive impact of patient-centred care on enhancing the quality of care and improving patient outcomes, particularly in medication management. Many patients in our study emphasised the significance of actively participating in medication-related discussions and having their concerns acknowledged. This suggests a need for further engagement of patients and their families in healthcare decisions. Another qualitative study identified that active involvement in decision-making alongside their caregivers, as well as receiving clear written instructions regarding medications before discharge, could improve the overall satisfaction of older patients with the hospital discharge experience [170].

### 3.12 Implications for practice and research

**Practice-**The results of this study, which focused on the medication-related experiences of adult inpatients in Ireland, reveal several crucial implications for healthcare and medication management practices.

- Enhancing the communication and patient education

The significant correlations between negative comments and the lack of adequate explanation about medication purposes, absence of written information and lack of guidance on monitoring side effects suggest a pressing need to enhance communication and educational practices. Healthcare providers should prioritise explaining the purpose of medications, providing written information and offering guidance on monitoring

potential side effects not only for older patients but also for younger adults. In practice, communication strategies should be implemented to enhance medication knowledge for older and younger adults [163]. Several studies addressed the communication strategies in older patients at transitions of care, which included individualised discharge summaries, pharmacists' interventions, and improvements in older patients' medication knowledge through medication education [163, 287-289]. The findings from the current study suggest the need to improve communication strategies for both younger and older patients. Implementing individualised discharge summaries that incorporate medication instructions is crucial, especially for older patients. Their belief that clear, written, plain language discharge summaries substantially enhance disease management highlights the importance of this practice [288]. However, it is worth noting that such discharge summaries can also prove invaluable for improving medication management among younger adults. Furthermore, encouraging the active involvement of pharmacists in delivering consistent information and education about discharge medications can help enhance medication knowledge in younger adults. Older patients reported that receiving consistent information and education about discharge medications from pharmacists improved their understanding of medication information [287]. Additionally, in line with the needs expressed by older patients for written medication information [163], our findings also underscore the importance of extending this practice to younger adults. This suggests the necessity of developing strategies to provide written information at the time of discharge.

- Improve the transitional care management

The current study indicates a need to improve coordination and communication during care transitions. Healthcare providers should ensure that patients receive clear instructions about their medication regimen, including any changes made during their hospital stay. During the transition care phase, the occurrence of medication-related errors is often attributed to inaccuracies in the medication histories taken by physicians during patient admission [290]. This highlights the critical role of medication reconciliation in mitigating these errors. Pharmacists play a crucial role in reducing medication-related errors and the associated risks and complications during admission [290]. Another valuable service that significantly contributes to improving transitional care are integrated medicines management service, which focus on medication-related

aspects during admission [289]. This service is provided by pharmacists who are responsible for medication reconciliation upon admission, conducting patient-centered medicine consultations (including discussions regarding newly prescribed, discontinued and altered medications) and establishing a comprehensive medication plan at discharge. This method has proven to be effective in reducing medication-related issues [289].

**Research-**The findings from this study provide valuable insights for future research aimed at enhancing patient experiences and outcomes in medication management for all adult inpatients, including both younger and older patients. Our findings suggest that the concerns and needs of younger adults align with those of older patients, as reported in previous studies [157, 169, 272]. Therefore, future research should focus on developing strategies that cater to the medication management needs of all adult age groups, ensuring a comprehensive and inclusive approach. This suggestion is supported by earlier findings regarding medication side effect recall, which found no significant difference in age for medication recall between older and young adults [281]. Moreover, a recent systematic review conducted by Ozavci *et al.*, [163] identified limited exploration of older patient experiences with medication management communication upon admission and during hospitalisation [163]. Based on our findings, we recommend further research in these settings without focusing on age as a factor.

### 3.13 Strengths and Limitations

It is essential to mention that the data used for this study were collected for a different purpose, as mentioned in Section 3.7.1.1, and were not explicitly intended to explore the issue of medication management. Instead, the primary focus of the NPES was to investigate the general experiences of patients who were hospitalised as inpatients. To overcome this limitation, this study employed a secondary analysis of qualitative and quantitative data using the GRAMMS framework to support the rigorous design and assess the quality of mixed-methods studies [277]. The mixed-methods analytical approach adopted in this research is a strength, as it enabled the identification of broad quantitative patterns in responses and allowed for a comprehensive qualitative analysis to explore the underlying themes driving these evaluations. This approach proved valuable in identifying areas of patient concern and priority. Additionally, it shed light on the issues that patients perceived

to require improvement, as discussed earlier in 3.11, with a specific focus on medication management experiences.

Due to the nature of secondary data analysis, not all aspects related to medication management may have been fully identified or explored [291]. Free-text comments serve as a valuable data source, ideal for content, thematic, and narrative analyses, especially when collected longitudinally [292]. However, in the current study, the open-ended questions in the NPES did not specifically inquire about medication management. Consequently, our qualitative analysis depended on unprompted mentions of medication management from inpatients in response to three general questions. It's possible that many patients had varied medication experiences but chose not to comment on them. Furthermore, it should be acknowledged that this study may be limited by the inability to follow up with patients who did not provide free-text responses. This means that the information obtained from the study may be restricted to only those patients who actively participated and provided their feedback. Patients who did not provide free-text responses may have had different experiences or perspectives regarding medication management, and their insights were not captured in the analysis [135], which could affect the completeness and accuracy of data [274]. Another drawback associated with analysing existing data is the potential disconnect between the researchers conducting the analysis and those who initially collected the data. Often, these two groups of individuals are distinct, which means that the analysts may lack awareness of specific nuances or intricacies in the data collection process that could hold vital significance in interpreting certain variables within the dataset [293]. To mitigate this limitation, the PhD student and their supervisor proactively reached out to the HIQA. Through this direct communication, they were able to clarify any uncertainties or ambiguities regarding the dataset.

The novelty of this study lies in its exploration of medication management experiences in Ireland. While previous studies have primarily used national surveys to address patient experiences, our research delves into a specific aspect of healthcare. The utilisation of a survey was particularly advantageous due to its large sample size [135]. One of the key strengths of employing secondary data analysis is the ability to tap into extensive existing datasets that are readily accessible for health research purposes [293]. This approach allows for the examination of a wide range of variables and trends that might not be feasible with smaller, primary datasets.

### 3.14 Conclusion

This study has provided an in-depth explanation of adult patient's experiences of inpatients medication management. Younger adult patients were more likely to submit a negative medication-related comments compared to older age groups. They expressed concerns about gaps in understanding the purpose of their medications not receiving written information, and a lack of awareness regarding potential side effects to watch out for at home. It was found that there is a compelling need for enhanced communication and patient education strategies concerning medication management in hospitals, especially given their substantial influence on patient experiences and overall satisfaction. These findings offer valuable insights for healthcare providers and policymakers to enhance the quality of care and patient satisfaction in medication management during their hospital stay and in the post-discharge period. There is a need to develop health communication strategies aligned with Ireland's healthcare objectives and patient safety initiatives, ultimately fostering a better-informed public and enhancing medication safety awareness.

### 3.15 In the next chapter

Following the current finding, the next chapter will present the results from a content analysis study that explores how medication-related harm has been reported in Irish newspapers and investigates the relationship between age and this reported medication-related harm.

**Chapter 4 : Medication-related harm and  
the newspapers - what has been  
communicated to the public in Ireland: A  
systematic content analysis.**

## 4.1 Introduction

Ensuring patient safety and improving healthcare outcomes are essential objectives for healthcare systems and policymakers. To achieve these aims, it is crucial to create public awareness and knowledge about the risks and benefits associated with medications and measures to optimise their safety [294]. Mass media can facilitate changes in health-related behaviours. The information presented through media channels, in terms of both its quantity and type, have potential to influence individuals' beliefs, attitudes, and perceived norms, consequently impacting their behavioural choices, both directly and indirectly [180, 295]. In this context, the mass media, including newspapers, are popular and reliable source of health information for the general public [194, 295]. Newspapers are important in the dissemination of health-related news due to their wide readership and easy accessibility.

A previous survey has shown that patients usually using media sources to seek information about medications and to learn about new medicines and their effects [296]. Even though health information is readily accessible on online platforms. Nevertheless, a study conducted by Mollema *et al.* [297] reported that traditional media significantly influenced the content shared online and, interestingly, that both online and offline articles exhibited a similar distribution of topics and information [297]. In a 2019 systematic review, the characteristics and outcomes of studies on the use of traditional media channels, including television, radio, newspapers and magazines, for public communication about medicines were investigated [194]. Among the included studies, newspapers emerged as the most frequently utilised media type (reported in 24 out of 57 studies). The main themes identified in the media coverage were primarily focused on vaccines, with 13 studies addressing this topic. Interestingly, only one study addressed the issue of administration including medication errors in the context of public communication about medicines [194].

Despite the growing evidence of the media's influence on perceptions about patient safety, especially medication safety, data on this topic is limited [298]. A previous study conducted in Canada evaluated newspaper coverage of certain new drugs and focused on the descriptions of the drugs' benefits and risks and whether important contextual information were provided. [299]. The results showed that a high percentage of newspapers (68%) did not mention any potential negative effects of the drugs and that they highlighted the benefits nearly five times more often. Furthermore, the newspaper articles lacked quantitative information that could have provided readers with a better understanding of the drug's

effectiveness and likelihood of experiencing adverse effects [299]. However, an analysis of newspaper coverage of paediatric medication errors and adverse drug events (ADEs) in different countries revealed that the media presented this information fairly, suggesting its potential to contribute to the development of a public awareness [298]. The finding mainly reported the patient incidents without any description of the medication related harm. A recent content analysis that addressed how media attention correlates with public awareness of adverse drug reactions (ADRs) in the United Kingdom (UK) for hormonal contraception found that media attention increases patient awareness of ADRs [300]. [300]. In another study that focused on how newspapers in the UK and the United States (US) reported medication adherence, it was found that information on adherence is not commonly reported or adequately covered, despite being widely available in the medical literature [183]. They found that approximately one-third discussed the negative consequences associated with non-adherence. The majority (62%) of these articles emphasised that non-adherence led to worse health outcomes [183].

Newspapers are widely recognised as effective channels for health communication; however, existing research on the coverage of medicines in newspapers has primarily focused on publications from the US, the UK [183, 194, 298] and Australia [190, 301]. In a content analysis-based study, Isik *et al.*, [198] examined medical errors reported in Turkish newspapers from 2012 to 2015. They found that most of the medical errors were the result of medical staff negligence, particularly those that involved medication administration, with physicians reportedly responsible for 74.1% of the errors [198]. Approximately half of these medical errors (51.7%) led to fatalities, while 25.0% resulted in permanent damage or injury. It was also found that most of the individuals affected by the medical errors were in two age groups: 0–16 years (39.8%) and 17–33 years (31%). Although this study explored the prevalence of medical errors across different age groups, it did not focus on medication specifically or investigate any potential associations between age and medical errors [198].

Little is known about how medication-related harm (MRH) is communicated to the public through newspapers in Ireland. MRH can be defined as any unintended or unexpected incident or accident that leads to patient harm due to medication. This lack of knowledge could impede patient safety initiatives and limit the effectiveness of healthcare policies designed to mitigate MRH. As Ireland's healthcare landscape continues to evolve, it becomes crucial to assess how information about MRH is presented to the public and whether the information aligns with healthcare objectives and patient safety initiatives. The

manner in which information about MRH is conveyed through newspapers can significantly influence how people perceive and understand medication use and safety.

Given the potential impact of age on the occurrence of MRH, age has been considered as a key aspect in this study. In **Chapter 3**, age has been identified as a factor that can influence how individuals experience and manage medications. Understanding how MRH is presented in relation to age groups can provide valuable insights into whether certain age groups may be more vulnerable to or affected by MRH.

To the best of our knowledge, no existing literature has described the content published in newspapers regarding MRH in Ireland. Therefore, the aims of this study were to describe how MRH is reported in Irish newspapers and its association with age. The outcomes of this study can be used to develop a deeper understanding of the messages that the public may consume about the effect of age on MRH.

## 4.2 Aim and objectives

The aim of this study is to describe how MRH and its association with age has been reported to the public in Irish newspapers during a selected period.

Understanding this will better explain how the print media portrays MRH, providing insight into an influence on the public's understanding towards medication safety. This information could then be utilised in designing effective health strategies that align with Ireland's healthcare objectives and patient safety initiatives.

**The following specific objectives were developed to achieve this aim:**

### **Quantitatively analysis**

- Systematically design a search strategy and apply it to a relevant database to select newspaper articles.
- Describe the nature of the reported MRH and its reported impacts.
- Describe the age and other reported characteristics of those who experienced MRH.
- Describe the change in MRH coverage over the selected period (2019, 2009, 1999).

**Qualitatively analysis**

- Qualitatively analyse the newspaper content to describe and categorise the nature of the reported MRH.

**Quantitative and qualitative findings integration**

- Integrate the qualitative and quantitative findings to better understand the content reported to the public.

**4.3 Methodology****4.3.1 Rational for the choice of research design**

The rational for the choice of research design and study design was similar to the rational adopted in the Chapter 3 Section 3.4.

**4.3.2 Justification from previous literature for the approach taken**

In 2019, a systematic review investigated studies published on the use of traditional media, including newspapers, other print media, television and radio, for public communication about medications [194]. The reported research methodology most frequently employed within the included studies was content analysis, followed by randomised clinical trials, surveys and focus groups. This systematic review highlights that the most common design used in studies exploring newspaper reporting of medication matters was content analysis [194]. Previous studies have used content analysis to examine medication safety issues reported in the media [186, 190, 198, 299, 302]. Hinchcliff *et al.* [190] analysed the most frequently read daily newspaper over five years to investigate the reporting of medication errors in Australia using a quantitative content analysis approach [190]. Cassels *et al.* [299] conducted an analysis of newspaper coverage regarding the nature, benefits and potential risks of five new prescription drugs that had attracted significant media attention. Additionally, they determined whether clinical or surrogate outcomes were mentioned and aimed to understand the presentation of such information. Their content analysis utilised 24 of Canada's largest daily newspapers [299]. Noto *et al.* [302] described Brazilian print media using major newspapers and magazines in all Brazilian state capitals based on a new time

frame (2000) to encompass all possible drug-related issues (e.g., health, legislation, education, public policies and public security). They analysed the newspaper coverage using a content analysis approach [302]. Chisnell *et al.* [186] investigated the nature of the representation of statin medications in a selection of British newsprint media. This involved assessing the number, timing and thematic content of the articles, followed by a descriptive analysis examining the frequency of statin coverage. This means they used both qualitative (thematic content) and quantitative (descriptive analysis) analyses [186]. Isik *et al.* [198] identified the types of and reasons for medication errors occurring in medical institutions that have been reflected in media coverage. They conducted a content analysis of five Turkish newspapers to accomplish this [198]. Limited methodological details about the content analysis approaches or frameworks used were reported in these studies (**Table 4-1**).

Table 4-1: Overview of approaches and analyses employed in previous studies addressing medication harm in newspapers.

| Authors                                          | Aim                                                                                                                                                                                                   | Study design     |
|--------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| Cassels et al., 2003 <sup>[299]</sup>            | To examine the newspaper coverage of the nature, benefits and harms of five new prescription drugs.                                                                                                   | Content analysis |
| Chisnell et al., 2017 <sup>[186]</sup>           | To investigate the nature of the representation of statin medications in the newsprint media.                                                                                                         | Content analysis |
| Hinchcliff <i>et al.</i> , 2012 <sup>[190]</sup> | To investigate the frequency, style and reliability of newspaper reporting of medication errors.                                                                                                      | Content analysis |
| Isik et al., 2016 <sup>[198]</sup>               | To identify the coverage of medication error types and reasons in Turkish newspapers.                                                                                                                 | Content analysis |
| Noto et al., 2006 <sup>[302]</sup>               | To describe the Brazilian print media based on a new time frame (2000) and to encompass all possible drug-related issues (e.g., health, legislation, education, public policies and public security). | Content analysis |

Nearly all the identified studies that explore newspaper data have employed a content analysis approach for data analysis. Additionally, document data are frequently utilised in health research, encompassing media analyses that concentrate on written materials such as newspapers and magazines. One common method of analysing these documents is content analysis, which pertains to a document's content [274]. Content analysis can be divided into quantitative and qualitative content analysis. Quantitative content analysis involves systematically identifying and counting characteristics to draw inferences from the data

[274]. On the other hand, qualitative content analysis, specifically thematic content analysis, involves comprehensive descriptions to provide a map of content across the dataset in health document research. It is common for studies examining media representations to combine qualitative and quantitative analytical methods [303]. Hence, the qualitative and quantitative content analysis is adopted for the analysis in this Chapter.

In content analysis, the main two methods for coding are deductive and inductive. Deductive coding uses coding frames from previous studies, while inductive coding generates a new coding frame that emerges from the study data [304, 305]. The deductive approach is used for theory testing based on previous knowledge and moves from the general to the specific [274].

The framework applied in **Chapter 3** explores the medication management experiences of adult inpatients in Irish hospitals. It also aims to understand the medication-related challenges these patients encounter. A shared objective between this study and **Chapter 3** is to investigate medication-related issues in Ireland and comprehend the associated challenges.

However, the two studies vary in their settings. **Chapter 3** focuses on hospitalised patients, discussing the healthcare system within the hospital based on comments from patients or their family caregivers. On the other hand, this Chapter sought to understand medication harm and its reporting in Irish newspapers. It noted that individuals did not generate these reports but rather they were produced by journalists.

Thus, the same framework is re-applied in the latter setting to aid in analysing Irish content concerning medication harms and to see if there is any similarity between the two settings in the medication management challenges described.

### 4.3.3 Study design

In this study, however, a content analysis-based study was adopted to collect quantitative and qualitative data and comprehensively describe media coverage of MRH in Irish newspapers. This study employed a sequential mixed-methods design, as described in **Chapter 3**.

The Good Reporting of a Mixed Methods Study (GRAMMS) framework was adopted to ensure the study was rigorously designed and reported [277]. This framework consists of six

items that guided our assessment of the mixed methods design (**Appendix III**), was described in detailed in **Chapter 3**, Section 3.6. The study included two phases that were completed sequentially, and then integrated to meet the study aim, more details are shown in Error! Reference source not found.

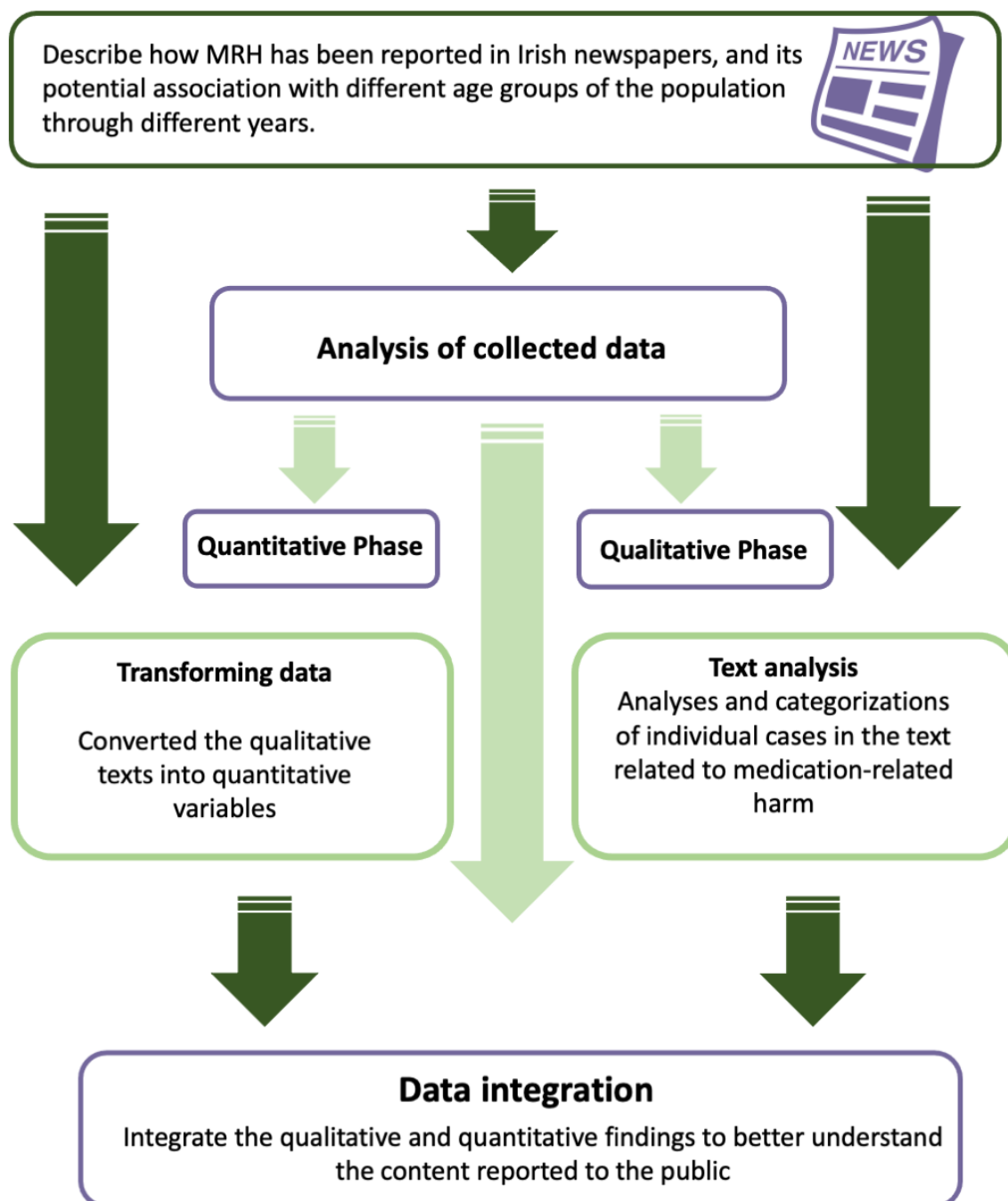


Figure 4-1: Sequential mixed-methods design adopted in content analysis.

## 4.4 Methods

### 4.4.1 Newspaper selection

The newspaper articles included in the study were sourced from the online version of the LexisNexis database [306], a comprehensive international newspaper database that encompasses a wide range of news types and origins. This online database was chosen due to its availability and ease of access through the Trinity College Dublin (TCD) Library. Only print media (newspaper) sources were considered in this study. These are defined by The Press Council of Ireland as either national or local newspapers [307].

### 4.4.2 Search strategy and eligibility criteria

A systematic approach was applied to the data collection to ensure that Irish newspaper articles that contained relevant information about MRH were retrieved. The central concepts that guided the search were “medication”, “harm” AND “patient” (**Table 4-2**) and their synonyms, which were adopted from two previously published studies [183, 298]. After the search strategy was designed, Boolean operators were applied to combine the three concepts. To enhance the search strategy, the symbol ( ! ) was used with the concept "medication" to account for word variations, such as "medic!," which included medication(s), medical, and medicine(s) [183].

Table 4-2: Search strategy concepts and their synonyms.

| Concept    | Synonyms                                                                                                                                                                 |
|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Medication | medic! OR drug OR pill OR dose OR prescription OR prescribing OR treatment OR dispensing                                                                                 |
| Harm       | harm OR error OR “adverse reaction” OR “adverse event” OR “adverse effect” OR adherence OR compliance OR interaction OR “side effect” OR “overdose” OR allergy OR injury |
| Patient    | patient OR person OR individual                                                                                                                                          |

Efforts were made to enhance the specificity of the search terms using an iterative approach, and this resulted in the exclusion of certain broader search terms. Initially, the search produced an excessive number of results due to the presence of these terms. Subsequently,

broad terms such as ‘damage’, ‘problem’, and ‘therap!’ were eliminated, and the number of results was considerably reduced. This refinement also resulted in more relevant information being obtained for the study. When the first 10 search results obtained using various search strategies were compared, it was found that omitting the broad terms improved the result relevance (see Appendix V for more details).

Several filters were applied (**Figure 4-2**) In terms of the time frame, the search was restricted to data from 1999, 2009 and 2019 to allow a comprehensive analysis of trends over multiple decades to be performed. Furthermore, the search was limited to retrieving articles published in English to ensure consistency in language for analytical purposes. To meet the study objectives, only articles published in Irish newspapers—from both the Republic of Ireland and Northern Ireland—were retrieved. However, to maintain a consistent scope, newspapers from Northern Ireland were subsequently excluded from the dataset through inspection of the newspaper titles.

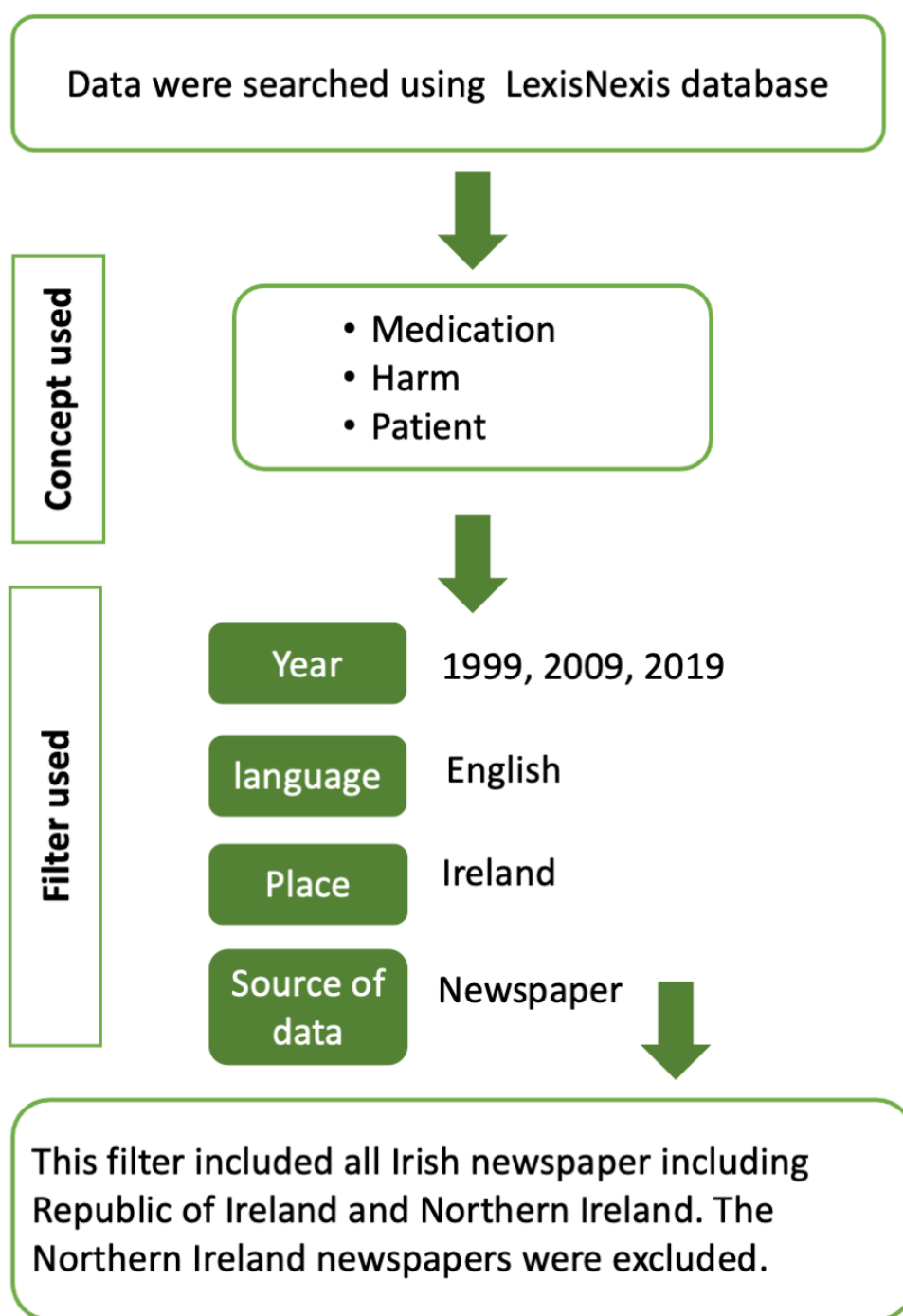


Figure 4-2: Flowchart showing the *systematic search strategy* employed in this study.

#### 4.4.2.1 Inclusion and exclusion criteria:

To be eligible for inclusion in this study, newspaper articles had to meet the following criteria:

- The article reported on MRH that affected an individual person or persons.

- The article was published in the Republic of Ireland.

**Conversely, newspaper articles that met any of the following criteria were excluded from this study:**

The article reported on diet, food or supplements as a treatment, on non-drug interventions (e.g. surgery, physical/psychological therapies) or on screening or testing.

The article reported on diseases that caused harm.

The article was published in medical (professional) newspapers.

The article solely described population health without addressing issues specifically affecting an individual person.

#### **4.4.3 Article selection and data extraction**

##### **Article selection**

The developed search strategy was applied to the LexisNexis database. Retrieved articles were downloaded as PDF files from the archive; each PDF file contained a maximum of 100 articles. Subsequently, the article titles were manually imported into an Excel form, and each article was assigned a unique identification number. These identification numbers were utilised within the data extraction form, which was structured to align with the inclusion criteria. The designed form consisted of six columns (**Figure 4-3**).

| Study_Identification_Number | Article_Name                                                                                                                                                                                                                                           | Publication                                                                    | People/Patient                                                                | Medication               | Harm                                              | Decision                             | Note                           |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------|---------------------------------------------------|--------------------------------------|--------------------------------|
|                             |                                                                                                                                                                                                                                                        | NOTE: exclude all articles published in medical newspaper or not in Irish news | NOTE: need here only specific patients or people, NOT the general population. | NOTE: only medication    | NOTE: INCLUDE only the harm causes by medication. | NOTE: INCLUSION needs to get 4 marks | Any comment                    |
|                             |                                                                                                                                                                                                                                                        | 0= excluded /1= included                                                       | 0= excluded /1= included                                                      | 0= excluded /1= included | 0= excluded /1= included                          | Inculde OR Exclude                   |                                |
| 1_1                         | The 'safer' PAINKILLERS experts fear are as risky as opioids; They're the alternative drugs doctors are handing out to avoid addiction. But evidence is mounting they could be just as dangerous - and may not even work ; The rise of generation GABA | 1<br>(Irish Daily Mail)                                                        | 1                                                                             | 1                        | 1                                                 | INCLUDE                              | (became anxious and depressed) |
| 2_1                         | Could your PILLS be making you ill?; It isn't just antibiotics that compromise your gut bacteria. Commonly used drugs to treat indigestion, diabetes and constipation                                                                                  | 1<br>(Irish Independent)                                                       | 0                                                                             | 1                        | 0                                                 | EXCLUDE                              |                                |

Figure 4-3: Designed form used in data extraction.

The designed form was used to review the newspapers and select the relevant ones for the study. For validation purposes, the supervisor (TG) reviewed 5% of the articles to ensure the accuracy of the inclusion process. These selected articles were discussed, and consensus was reached in cases of disagreement. Subsequently, the inclusion steps were completed. In cases where uncertainty arose about including a newspaper article, the supervisor was consulted, and a consensus was reached on whether the article met the inclusion criteria. In cases where multiple newspaper titles reported on the same story each article was included.

### **Data extraction**

The data extraction form was designed in Microsoft Excel to extract quantitative and qualitative data, which involved counting variables and coding quotes, respectively. More detailed information on the theme development can be found in Section 4.4.3.2.

#### ***4.4.3.1 Phase I: Quantitative data extraction***

During this phase, data were extracted using a quantitative content analysis approach. This involved converting the textual data into variables that could be used for quantitative analysis.

#### **The extraction form included the following variables:**

- Year of publication: The year in which the newspaper article was published.
- Newspaper title: The title of the newspaper in which the article was published.
- Demographic characteristics: The age and gender of the individual(s) who experienced MRH in the reported cases. The age group categories include child = under 16 years, young adult = 16–43 years, middle-age = 45-64, and old = 66 years and older.
- Medication class: The class or category of the medication(s) linked to the reported harm. Drugs were classified according to the anatomical therapeutic chemical (ATC) classification system and the defined daily dose (DDD)), which is a measuring unit that has become the gold standard for international drug utilization research [308].

- Degree of harm: This category included the classifications of fatal, permanent complication and other complication. The ‘other complication’ classification included MRH that led to severe harm and hospital admission but no evidence of permanent harm.

#### ***4.4.3.2 Phase II: Qualitative data extraction***

In this phase, data were extracted using a thematic content analysis approach. This process included identifying and categorising specific themes or patterns that emerged from the quotes extracted from the news articles.

### **4.4.4 Data analysis**

There were two units of analysis: (1) the newspaper article and (2) the patient case. In instances where an article featured multiple patient cases, we conducted separate analyses were conducted for each case.

#### ***4.4.4.1 Quantitative e data analysis***

A descriptive analysis was conducted to summarise the data collected from the entire dataset of newspaper articles using the SPSS statistical program (version 26, IMP SPSS). Frequency tables were utilised to present the data on the occurrence of different variables and provide a clear understanding of their distribution. These tables displayed the data on the frequency (by count numbers and percentages) and nature of the reported MRH, as well as the newspaper titles, reported drug class(es), demographics (age or gender) of those who experienced the MRH and degree of harm (i.e. fatal, permanent complication or other complication).

#### ***4.4.4.2 Qualitative data analysis***

##### **Thematic content analysis**

The content analysis was conducted in two phases. In the first phase, the transcripts were thoroughly read and studied to support familiarisation with the data. In the second phase,

directed content analysis was performed, and the data were deductively coded using the themes from the previous chapter's exploration of medication-related experiences (**Chapter 3**; Section 3.8.4, which provided a structured framework for the analysis [309]. The content analysis helped identify similarities and differences in the data based on the established themes between the current study and findings from **Chapter 3**.

These themes encompassed various aspects of medication management experiences and patient perspectives. These themes included:

**First**, professional tasks associated with obtaining medication, processes of medication administration, monitoring by healthcare professionals, medication supply, patient requests for medication, medication-related problems and the timing of prescribing, dispensing, or administering medication.

**Second**, theme that explored patients' sense of safety and security in the medication management process, addressing concerns about healthcare professional medication errors and issues related to HCP competence.

**Third**, transition care management theme including prescription not given to the patient at discharge and medication errors at discharge or admission.

**Fourth**, medication information and education theme addressing inadequate information about medications and patient and/or family being involved and heard.

**Fifth**, general care issues when using medication were discussed the Privacy and suitability of medication administration locations and the effect of medication on cognitive and physical functioning.

It should be noted that all presented quotes have not been altered and they are presented verbatim as they were submitted (which may involve typos and the use of colloquialisms).

#### 4.4.5 Ethical approval

This study was conducted on the online record newspapers (document data). This type of data management didn't necessitate ethics committee approval because the data didn't involve any personal information or confidentiality issues. All data sources were available within the public domain.

## 4.5 Results

Of 7,759 newspaper articles archived from the LexisNexis database, a total of 78 newspaper articles and 95 individual person cases were included in the study, as shown in **Figure 4-4**. There was no multiple articles across multiple newspaper titles on similar dates seem to cover the same story.

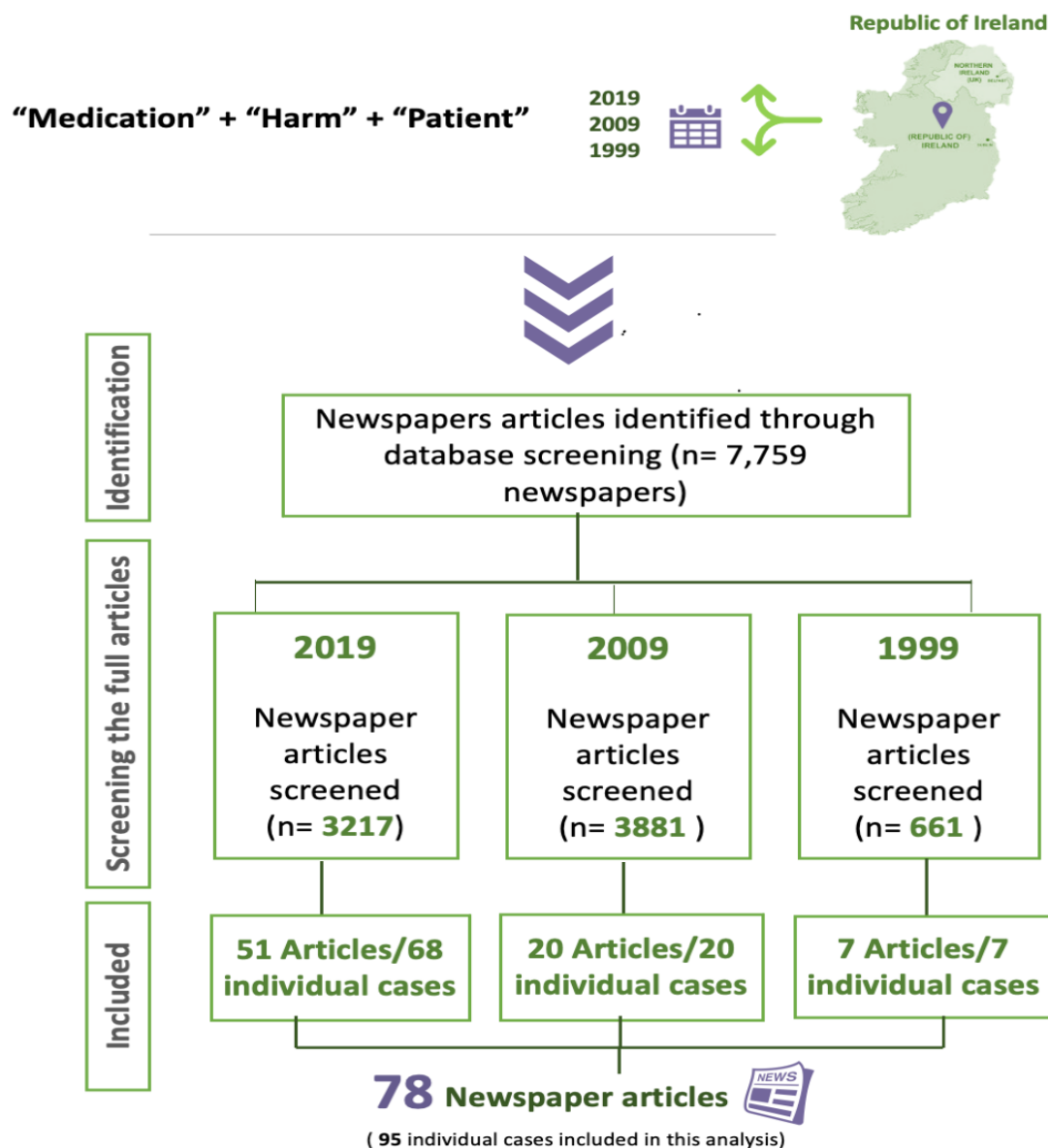


Figure 4-4: Selection process of included newspapers for analysis.

These articles were sourced from various newspaper titles, including "Bray People, Corkman, Drogheda Independent, Enniscorthy Guardian, Fingal Independent, Gorey

Guardian, Irish Daily Mail, Irish Examiner, Irish Independent, Irish News, Kerryman, New Ross Standard, Sligo Champion, Sunday Independent, The Herald, The Irish Times, Wexford People, Sunday Business Post, Sunday Tribune". The newspaper titles that most frequently reported cases of MRH were The Irish Daily Mail, The Irish Times, and The Irish Independent.

Some of the selected newspaper articles reported on more than one individual patient case. Notably, the 51 articles published in 2019 encompassed 68 individual cases. In contrast, the articles published in the remaining years reported only one individual case per article. The number of individual MRH cases reported in articles increased over time, with the highest number published in 2019. The percentage of articles reporting individual cases also exhibited an upward trend, rising from 7.4% in 1999 to 71.5% in 2019.

### 4.5.1 Quantitative results

#### *4.5.1.1 Characteristics of MRH across the years studied*

##### **Demographic characteristics**

The distribution of the reported MRH cases according to age group is presented in **Table 4-3**, and revealed distinct patterns across the age groups. Notably, the articles published in 2019 reported a significant proportion of MRH cases that spanned all age categories. Specifically, adults between 16 and 65 years were the subjects of a substantial proportion of the reported MRH cases, surpassing the other age groups. Conversely, in 2009, individuals aged 16–65 years and older constituted a smaller proportion of the reported MRH cases, whereas children constituted a similar proportion. In 1999, significantly fewer MRH cases were reported compared to the later years. Regarding gender, a higher proportion of the reported cases involved females.

Table 4-3: The main characteristics of the reported MRH cases across the studied years.

|                                                                       | 2019<br>(51 articles,<br>68 cases) | 2009<br>(20 articles,<br>20 cases) | 1999<br>(7 articles,7<br>cases) |
|-----------------------------------------------------------------------|------------------------------------|------------------------------------|---------------------------------|
| Newspaper title (n= 78 articles)                                      |                                    |                                    |                                 |
| • Irish Daily Mail                                                    | 33                                 | 0                                  | 0                               |
| • The Irish Times                                                     | 9                                  | 9                                  | 7                               |
| • Irish Independent                                                   | 5                                  | 4                                  | 0                               |
| • The Herald (Ireland)                                                | 1                                  | 0                                  | 0                               |
| • Sligo Champion                                                      | 1                                  | 0                                  | 0                               |
| • Irish Examiner                                                      | 1                                  | 1                                  | 0                               |
| • Sunday Business Post                                                | 0                                  | 1                                  | 0                               |
| • Sunday Independent                                                  | 1                                  | 2                                  | 0                               |
| • Sunday Tribune (Ireland)                                            | 0                                  | 2                                  | 0                               |
| • New Ross Standard (Ireland)                                         | 0                                  | 1                                  | 0                               |
| Age groups (n = 95 cases)                                             |                                    |                                    |                                 |
| • Child (< 16 years)                                                  | 6                                  | 4                                  | 0                               |
| • Young adult (16-44 years)                                           | 23                                 | 3                                  | 2                               |
| • Middle age (45-64 year)                                             | 21                                 | 3                                  | 1                               |
| • Old (> 65 years)                                                    | 6                                  | 4                                  | 0                               |
| • Not clear                                                           | 12                                 | 6                                  | 4                               |
| Gender (n = 95 cases)                                                 |                                    |                                    |                                 |
| • Male                                                                | 23                                 | 8                                  | 4                               |
| • Female                                                              | 39                                 | 12                                 | 3                               |
| • Not reported                                                        | 6                                  | 0                                  | 0                               |
| Medication classes (n= 95 cases)                                      |                                    |                                    |                                 |
| • Central nervous system                                              | 23                                 | 5                                  | 3                               |
| • Antiparasitic products, insecticides and repellents (antimalarials) | 9                                  | 0                                  | 2                               |
| • Antineoplastic and immunomodulating agents                          | 21                                 | 4                                  | 1                               |
| • Dermatological                                                      | 2                                  | 1                                  | 0                               |
| • Alimentary tract and metabolic                                      | 3                                  | 0                                  | 0                               |
| • Blood and blood forming organs                                      | 2                                  | 1                                  | 0                               |
| • Anti-Infectives                                                     | 3                                  | 2                                  | 0                               |
| • Genito urinary system and sex hormones                              | 1                                  | 0                                  | 0                               |
| • Cardiovascular system                                               | 1                                  | 0                                  | 0                               |
| • Musculo-skeletal system                                             | 0                                  | 1                                  | 0                               |
| • respiratory system                                                  | 1                                  | 0                                  | 0                               |
| • Systemic hormonal preparation and sex hormones                      | 0                                  | 0                                  | 1                               |
| • Medication classes not available                                    | 2                                  | 6                                  | 0                               |

## Medication classes

The distribution of medication class cases varied across different years. Among these, the most frequently reported medication classes were the central nervous system, antineoplastic, and antiparasitic agents (**Table 4-3**). In 2019, the number of cases within these classes surpassed those of other years (68 cases). In contrast, the year 1999 recorded a total of seven MRH cases spread across various medication classes without a predominant category.

Among the medication classes, the central nervous system medication class was the most frequently reported, with 16 cases in adults and seven cases in older people. Additionally, 14 and nine cases associated with antineoplastic and antiparasitic classes, respectively, were reported in adults.

### **Degree of harm**

The degree of harm reported was categorized as being (1) fatal (n=16), (2) leading to permanent (n=19) or (3) other medication-related complications (n=60) across different years. The reported harm encompassed a variety of problems, including physical symptoms like drowsiness, dry mouth, dizziness, nausea, hair loss, and vomiting. Additionally, there were instances of hypersensitivity reactions and negative effects on immunity. Cases of addiction and withdrawal were also reported, along with mental health and psychological effects (e.g. anxiety, depression, suicide attempts and hallucinations). Some articles reported permanent damage or consequences of MRH, such as organ damage (e.g. liver issues, eye damage or heart problems), birth defects, decreased fertility, impaired mobility, long-lasting psychological damage or chronic pain.

MRH resulting in death or permanent harm was reported less often than minor incidents that caused other harm. As shown in **Figure 4-5**, various types of harm were described in the articles, with those published in 2019 showing a particularly high occurrence of MRHs. While there was no notable difference in the number of reported fatal cases between 2019 and 2009, the number of other complications was high in articles published in 2019.

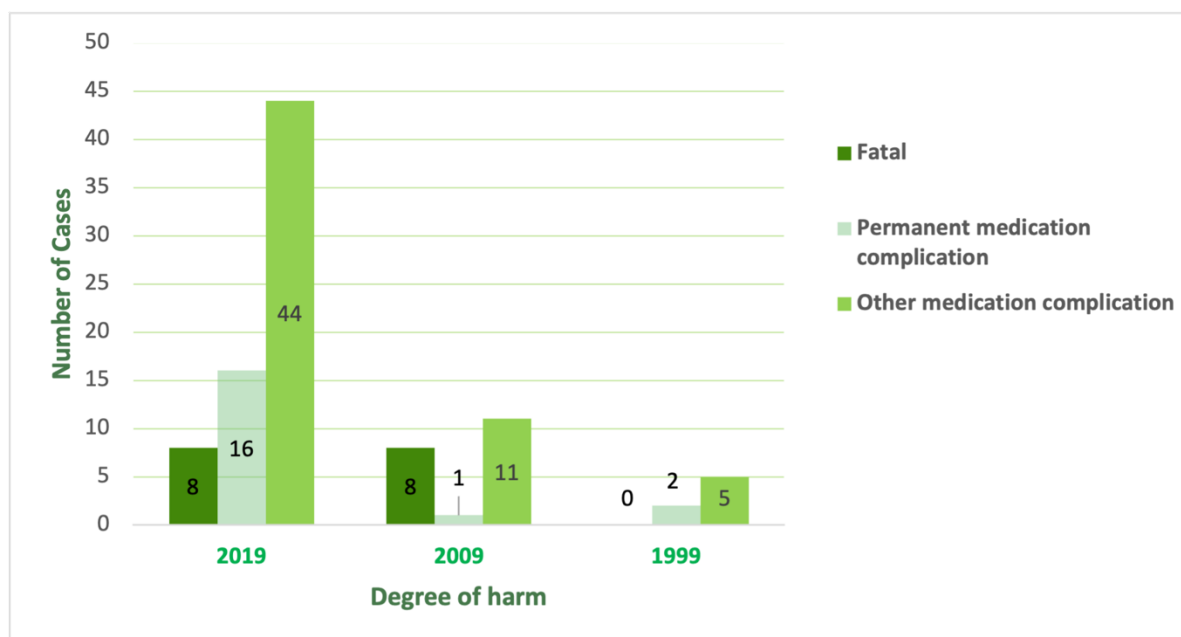


Figure 4-5: The degree of harm reported in articles published in the different years.

#### 4.5.1.2 Relationship between Age and MRH

Young adult and middle-aged individuals aged 16–44 and 45–64 years were found to be the frequently reported as being affected by all three types of MRH, accounting for 55.8% of all cases. These age groups contained six of the reported 16 fatal cases, with higher cases observed among young adults. Among the older population, there were also six fatal cases; however, there were only three reported cases of other complications in this age group. It should be noted that the patient's age was not reported in 22 cases (**Figure 4-6**).

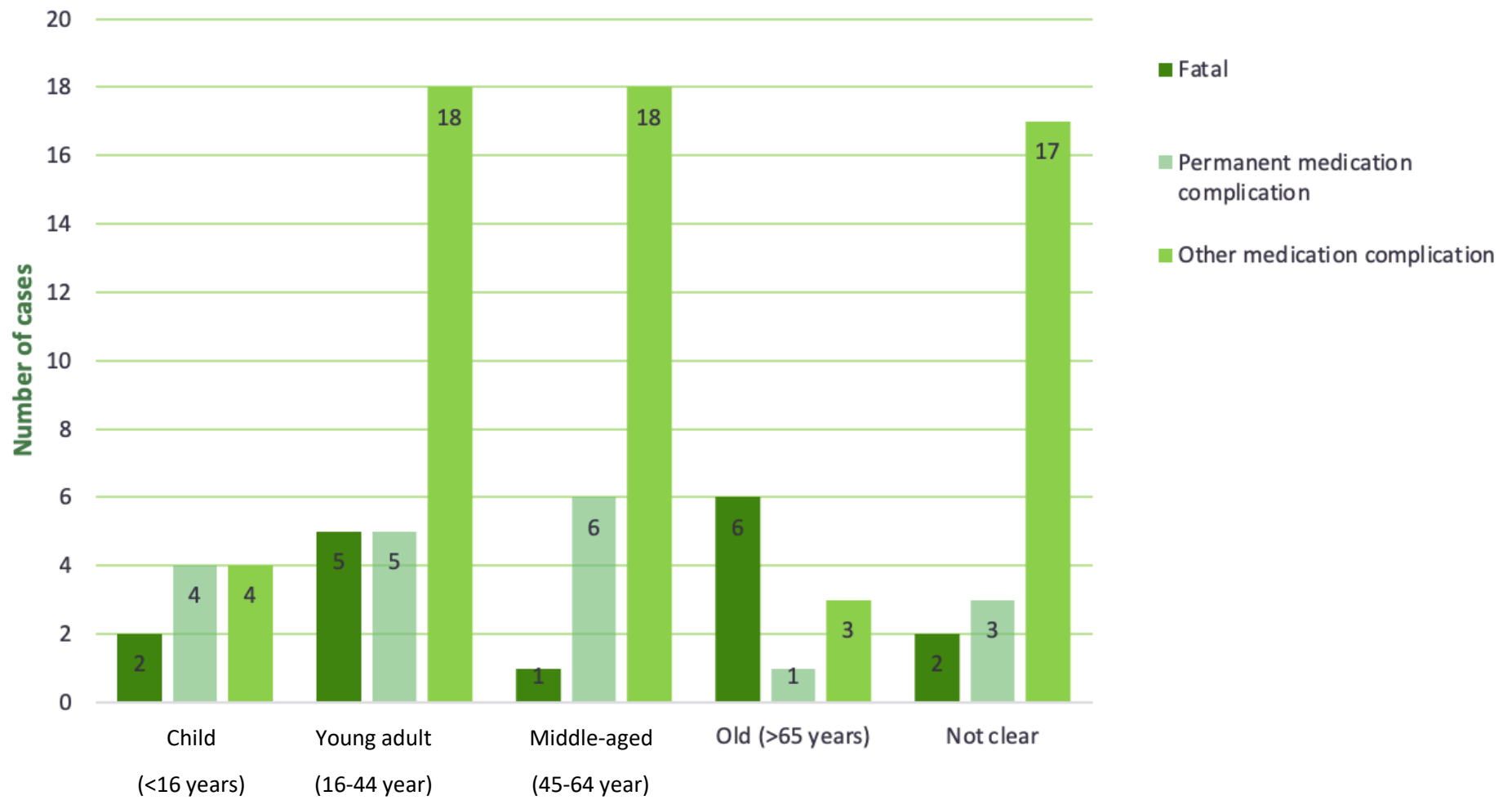


Figure 4-6: The degree of reported harm by age group.

## 4.5.2 Qualitative findings

### 4.5.2.1 Deductive themes and subthemes

The obtained newspaper article data were mapped to the following four of the five themes identified from the Chapter 3 (**Table 4-4**):

- Professional tasks associated with obtaining medication
- Patient sense of safety and security of the medication management process
- Medication information and patient education
- General care about medication

Table 4-4: The main deductive themes and sub-themes aligned with current study.

| Theme                                                                            | Subtheme                                                                                                        |
|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| <b>Professional tasks associated with obtaining medication</b>                   | Efficacy or appropriateness of medication                                                                       |
|                                                                                  | Medication supply (including the use of patient's own medication)                                               |
|                                                                                  | Requests for medication                                                                                         |
|                                                                                  | Timing of prescribing, dispensing, or administering of medication.                                              |
|                                                                                  | <b>MRP including side effect, complication and medication misuse</b>                                            |
| <b>Patient sense of safety and security of the medication management process</b> | <b>Observation or experience of healthcare professional medication errors</b>                                   |
|                                                                                  | Concerns about healthcare professional competence (including attitude, behaviour, knowledge, and skill)         |
| Transition care management                                                       | Prescription not given to the patient at discharge or delayed/facilitating community drug scheme administration |
|                                                                                  | Medication errors at discharge or admission                                                                     |
| <b>Medication information and patient education</b>                              | <b>Inadequate information about medications</b>                                                                 |
|                                                                                  | <b>Patient and/or family being involved and heard.</b>                                                          |
| <b>General care about medication</b>                                             | Privacy and suitability of medication administration locations                                                  |
|                                                                                  | <b>Accommodating the cognitive and physical effects of medication</b>                                           |

Abbreviations: Medication-related problem (MRP). Note: The themes and subthemes that were aligned with the MRH cases reported in the selected Irish newspaper articles are indicated in purple shadow and bold font. The white shadow indicates the themes and subthemes that were not applicable to the current study.

### Theme 1: Professional tasks associated with obtaining medication

The harm reportedly caused by medication varied, ranging from minor side effects to severe side effects that significantly affected individuals. The severe side effects extended beyond psychological consequences, reaching a level of concern that included changes in mental

function and, in some cases, even the risk of death. These side effects were associated with medications such as analgesics and anticancer and antimalarial medications.

*"Unfortunately I was one of the unlucky people who react badly to the chemo sessions and spent a lot of the time in hospital as the doctors tried to keep all the infections I was getting under control". ID: 12-17 (The Irish Times)*

*"And during six months of chemo I was weak and tired all the time. They helped some of the time, but gave me side effects such as a dry mouth". ID: 33-13 (Irish Daily Mail)*

The data revealed that there is a complex interplay among a patient's health background, health circumstances (complex health issues) and medication use. In some instances, issues such as unknown health conditions, lack of knowledge or personal problems resulted in overdoses. In all of these cases, the person took a dangerous amount of the medication for them and in some cases this proved fatal in some cases. The newspaper articles indicated to the public that medication misuse can have serious side effects.

*"A 66-year-old woman. She took the painkilling medication Tramadol which combined with her anti-depressant medication Mirtazapine with lethal results. (That doesn't mean she took a lot of tablets, it means they weren't being processed) the coroner said. (Because her liver was damaged, the medications were more likely to accumulate in her system. If your liver is damaged you cannot fight infection as well as the next person. It's a very important organ, so if it is damaged it affects a lot of your health,) the coroner said" ID:5-11 (The Irish Times).*

*"Judy, 70 (pictured) said she started vomiting blood after taking the painkiller 'like sweeties' for a knee injury. The drug caused four large ulcers in her stomach. One had eaten into an artery, causing a haemorrhage and she needed two blood transfusions" ID:20-3 (Irish Daily Mail)*

*"Hollie 26 year-old died on May 17, 2017, following an overdose of two drugs she was prescribed to treat her mental health problems, Naproxen and Fluroextine. She may have*

*taken 256 Naproxen tablets. Her family said at the inquest that she was regularly given a month's supply of different medications which they regularly took off her and handed back in small doses" ID: 68-2 (Irish Examiner)*

*"14-years girl. She took her own life from an overdose of a drug prescribed primarily for anxiety and blood pressure" ID: 42-10 (Sunday Tribune (Ireland))*

*"A blood sample from Ms Markey (85 year) was sent on to the State laboratory where blood levels of Surmontil were found to be 4.8 micrograms per litre well within the range of a lethal overdose . Nursing home director Katherine O Reilly said all drugs at the nursing home were pre-counted for the patients, and pre-packed by a local pharmacy in four week cycles" ID: 85-2 (The Irish Times)*

## **Theme 2: Patients' sense of safety and security of the medication management process**

The selected news reports collectively emphasised concerns about MRH caused by a range of factors, such as medication errors, system capacity issues and potential medical negligence. The articles presented evidence of patients making complaints or taking legal action to seek redress for the harm experienced. In some of these cases, there was a finding of negligence or fault on the part of the healthcare system. The prescribing issues described in these cases involved the choice of medication, omission of required medication and dosage of medication.

*"In Sgt Fedigan's case, it is understood that he will claim he should not have been prescribed Lariam for the tours he served abroad, after he reported symptoms of anxiety and depression.*

*But his counsel, Jerry Healy SC, said the Lariam he was given before, during and after a tour of duty in Chad in early 2009 had left him feeling very depressed and irritable, with headaches and nightmares". ID: 48-1 (Irish Daily Mail)*

*"The change was recommended by an investigation into the death of a patient and was welcomed yesterday by his family. He died of cardiac arrhythmia with a second factor of adverse drug reaction. We are delighted to have achieved something to safeguard patient lives in the future and to prevent other families going through the agony we have, said Barry Evans, brother of Colin yesterday". ID:48-7 (The Irish Times)*

*"Mary Moss was unaware that blood-thinning drugs, which she had been taking for years, were not included in a prescription given to her by Sligo General Hospital, her counsel said. The HSE admitted liability for the error, and apologised in court to Mrs Moss and her family. It said it sincerely regretted the impact on her life. Mr O'Neill said the hospital decided that her treatment would be changed to a different anticoagulant, but its staff failed to check her prescription records and include blood thinning drugs in her discharge prescription". ID: 87-2 (Irish Daily Mail)*

*"The Ombudsman s Office receives about two hospital-related complaints each week since its remit was extended in 2007. In her last annual report she highlighted how an elderly woman was heavily sedated, which affected her ability to communicate with her family over the last days of her life. She was given three times the dosage of anti- depressants she should have got because a mistake was made transcribing handwritten drugs records at Beaumont Hospital". ID: 59-18 (The Irish Times)*

*"Mrs Troute, a former bank employee from London who lives at Coosan, Athlone, Co Westmeath, is suing a nominee of Portiuncula Hospital and Dr Michael Brassil, an obstetrician who worked at the hospital in October 1995, for damages for personal injury due to negligence. He said that Mrs Troute was almost 34 years old when admitted to Portiuncula. The drug Syntocinon was administered to her to augment her labour. " ID:95-1 (The Irish Times)*

### **Theme 3: Medication information and patient education**

It was evident from the data that a significant gap exists in the process of providing patients with comprehensive medication information and education, particularly about potential MRH. The examined newspaper content revealed that there were instances where people were inadequately informed about the potential side effects of prescribed medications, leading to unexpected outcomes. The reports also highlighted concerns about insufficient medication information and a lack of clarity regarding side effects. This was found to be particularly relevant for younger individuals, who may lack the experience to fully grasp the implications of potential side effects.

*"14-year-old son .was prescribed the antidepressant Prozac. The psychiatrist had not met Jake before this consultation. "Jake had generalised anxiety, like most kids who were about to sit big exams, but he was not depressed and did not need medication. "At the pharmacy I didn't get the full package - I got a part of the full product...Stephanie said a patient information leaflet was not included with the drug....under 18 have an increased risk of side-effects such as suicide attempt, suicidal and hostility...If I had known what that drug was, I would never have given it to my child," Stephanie said....Stephanie welcomed this as she said the ruling 'death by suicide' didn't reflect her son's death, as she believes it was drug-induced" ID: 34-1 (The Herald (Ireland))*

*"I'm on 30 anti-virals a day for HIV but the fact that these could be damaging my liver has never been mentioned. I have severe joint ache and extensive fatigue - I feel like I'm 20 stone heavier - but I don't know if this is the side- effects of the HIV drugs or symptoms of hep C." ID:74-1 (The Irish Times)*

*"..... Natalia Buzzeo, 27, ...who went on pregabalin after being injured in a car crash....She was prescribed 150mg a day in hospital. 'The GP kept me on them for six years for the pain and even increased the dose,' says Natalia. 'No one at any point told me about any side-effects.' Yet Natalia says almost immediately she felt 'like a zombie'. 'I'd always been popular, but my personality changed - I fell out with people, lost" ID: 1-1 (Irish Daily Mail)*

*"I wasn't told anything about birth abnormalities, when it was first prescribed or after. I only noticed it made me less able to concentrate on lessons,' says Susan, who lives in Belfast.*

*'I answerut nothing more was said. I thought it was a passing query about whether I was eating my epilepsy medication and thought no more about it.' Caroline was very slow to develop, only starting to walk after 19 months. Her speech was also much delayed. In fact, her deep-set features, developmental delay and subsequent autism were classic signs of foetal valproate syndrome (FVS). My children will always struggle and I will always carry the guilt,' she says. 'I just wish I'd been warned'.ID: 46-1 (Irish Daily Mail)*

*" In terms of treating my hair loss, the drug worked brilliantly and the gaps on my crown filled in within three months,' he says. 'However, within weeks I lost interest in sex and my libido didn't return. I didn't connect it with finasteride as this side-effect was never mentioned. (SIDE-EFFECTS THAT JUST GO ON AND ON Two years ago, a desperate Ryan searched his symptoms online and came across post-finasteride syndrome (PFS) -a collection of symptoms that include sexual dysfunction, infertility, anxiety and depression, which persist long after finasteride is discontinued." ID:13-3 1 (Irish Daily Mail)*

*" Tom, 45, a former teacher. .... My relationship crumbled under the pressure of the sexual problems and I haven't had another relationship since,' he says. 'I had to give up teaching because of memory and fatigue problems. ('He did mention impotence could be a side effect, but being young I don't think I quite understood what this meant.)" ID:13-3 1 (Irish Daily Mail)*

#### **Theme 4: General care about medication**

The findings suggested that medication use, whether for treatment, pain management, or other purposes, significantly impacted an individual's physical activity and overall quality of life. These impacts ranged from experiencing severe side effects to misdiagnosing symptoms and severe disruptions in daily life and work. These stories highlighted the importance of careful medication management, thorough patient education, and the need for healthcare providers to consider the holistic impacts of medication on patients' lives.

*"Three years ago the drugs I was prescribed were making me feel like a zombie - I worked in customer services at the time and could barely speak coherently on the phone". ID: 2-3 (Irish Daily Mail)*

*"Jane Allan, 50,...fell ill within days of taking ciprofloxacin for a chest infection, with excruciating burning pain in her joints, bones and muscles. Five years on, she is still in pain and has had to give up work.....These drugs should always be the last line of defence. My life has been changed for ever, and I am not alone....However, Neal Millar, a consultant orthopaedic surgeon who gave evidence at the hearing, says the EMA's wording is as strong as anyone could realistically expect. Yet he, too, was disappointed by its failure to include advice to GPs to urgently refer patients affected by the antibiotics to specialists". ID: 17-1 (Irish Daily Mail)*

*"He told medics he had experienced mental foggiess, dizziness and memory loss. The symptoms, which were repeatedly misdiagnosed as depression, forced him to give up his job. drugs disrupted the patient's balance of gut microbes". ID:72-7 (Irish Daily Mail)*

*"They didn't help - they made me feel even more nauseous. It got to the point where I was vomiting after every meal. My life had become a nightmare". ID:44-3 (Irish Daily Mail)*

*"According to my husband Bob, I became short-tempered. It was impossible to go out for a meal, and tough visiting relatives when I couldn't eat without incident. I had to give up the auxiliary nursing work I was doing, too". ID: 44-3 (Irish Daily Mail)*

*"Chemotherapy made me feel really poorly. I couldn't walk because I had no energy and leg pain. I felt very lonely because all my friends carried on with their lives without me. I couldn't go out with them any more". ID: 33-13 (Irish Daily Mail)*

Some articles reported on people experiencing changes in their mental function, including dependence on medication use and suicidal symptoms.

*"I was taking so many painkillers that I was going zombie-eyed, my voice was slurred, and emotionally I was dropping lower and lower. I was 21 years old". ID: 10-5 (The Irish Times)*

*"became addicted to morphine and other prescription drugs for over seven years after a couple of major back operations. She eventually checked herself into rehab and recovered". ID:90-1 (Irish Daily Mail)*

*"Over-the-counter antihistamines did nothing and a stronger version from her GP, fexofenadine, led to dizziness and liver issues". ID:2-5 (Irish Daily Mail)*

The harmful effects of antimalarial drugs were reported among students.

*"in 2003, an inquest heard that another student, Vanessa Brunt, had returned from a gap-year trip in the Far East with a 'haunted expression in her eyes'. She had taken Lariam, and committed suicide at the age of 22". ID: 8-1 (Irish Daily Mail)*

*"death of student Alana Cutland - who threw herself from a small plane as it flew above the island - there is growing concern that her death might have been the result of a psychotic episode caused by the antimalaria tablets she was taking". ID: 801 (Irish Daily Mail)*

In the next section 4.6, the integration of the qualitative and quantitative findings will be discussed, and the key outcomes described. This correlation of the numerical data with the contextual insights allowed a more comprehensive understanding of the research topic.

## 4.6 Integration of quantitative and qualitative findings

Integrating the quantitative and qualitative data provides a comprehensive understanding of MRH and its implications. The quantitative data revealed that most reported MRHs were related to medication complications, with a smaller proportion leading to permanent complications or death. Qualitatively, these instances of complications were further examined within the theme "medication information and patient education", highlighting how inadequate information provided to patients regarding potential side effects could significantly impact their lives. This lack of communication contributed to cases where MRH affected patients' mental functions. The quantitative data revealed that the Irish study reported that young adults and middle-aged patients were frequently affected by medication-related harm (MRH). In contrast, the qualitative data provided a deeper understanding, highlighting concerns over inadequate medication information and unclear explanations about side effects. This issue was particularly pronounced among younger individuals, who might not have the experience or knowledge to comprehend the full scope of potential side effects.

In certain cases, within the theme of "patients' sense of safety and security of the medication management process" harm was linked to system capacity issues and potential medical negligence. Issues in prescribing, such as the choice of medication, omission of necessary medication, and incorrect dosage, were identified as contributing to serious medication complications. Moreover, under the theme of "general care about medication" there were reports indicating that medication complications could hinder physical and mental activities, potentially affecting an individual's ability to perform their job. In some instances, complications from medications could lead to death or cause permanent damage.

A notable finding from the quantitative analysis was that the majority of MRH cases were associated with central nervous system medications. Qualitatively, under the theme of "professional tasks associated with obtaining medication," the data provided context to these findings, revealing that some patients became addicted to these medications or misused them, resulting in complications or adverse interactions with other medications. This misuse was often exacerbated by patients not receiving sufficient explanations about potential side effects. Some instances of misuse resulted in fatalities, where factors like unknown health conditions, lack of knowledge, or personal issues led to overdoses. A summary of the quantitative results and qualitative findings, followed by the presentation of the main integration points in **Figure 4-7**.

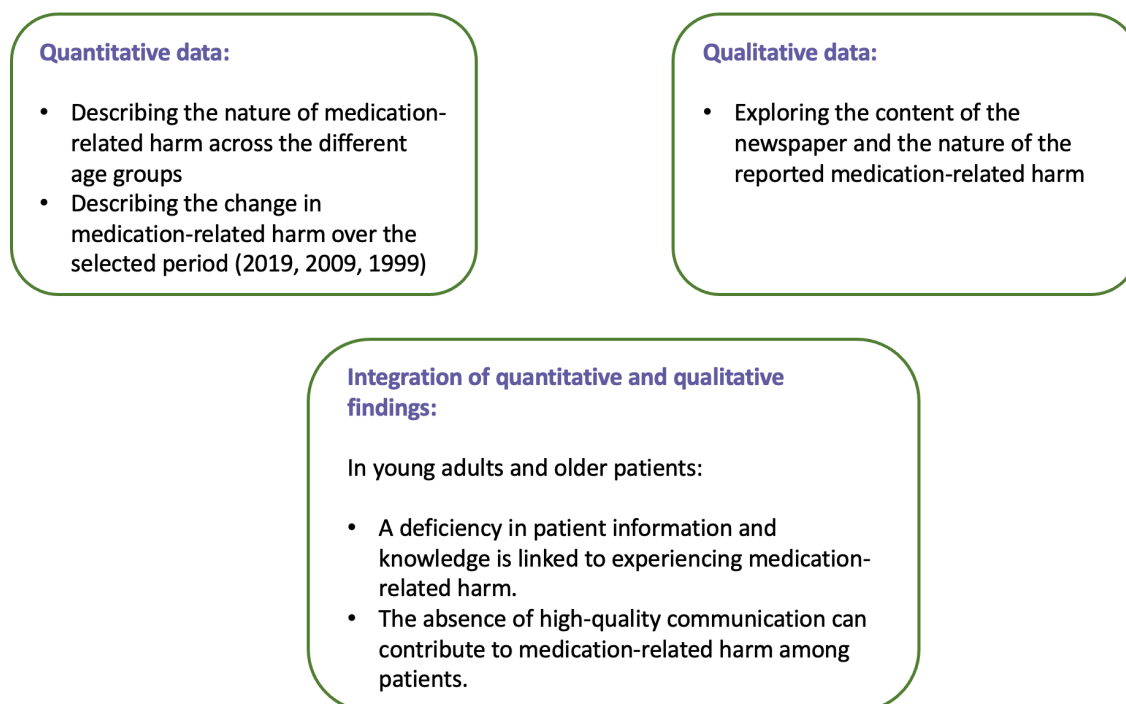


Figure 4-7: Integration of quantitative and qualitative findings.

## 4.7 Discussion

### 4.7.1 Key findings

In this study, 95 MRH cases were identified in 78 newspaper articles published in Irish newspapers during three specific years (1999, 2009 and 2019). Non-fatal and non-permanent types of harm were most frequently (56%) reported in the newspaper articles. Over time, newspaper coverage of individual MRH cases increased from 7.4% in 1999 to 71.5% in 2019, with the highest number of articles published in 2019. In relation to gender demographics, a greater percentage of the cases reported were observed to affect females over the different years. The most commonly reported medication classes associated with MRH were those related to the central nervous system, antineoplastic, and antiparasitic drugs.

In 2019, there were MRH cases in different age groups. More of these cases happened in adults between 16 and 65 years old compared to other age groups. Young adult and middle-

aged individuals aged 16–44 and 45–64 years were the most frequent subject of the reported MRH cases, with higher proportion of reported other medication-related complications compared to other harm categories. Middle-aged group had less frequently fatal cases. In contrast, older individuals also had same fatal cases and only three cases of other medication complications.

The qualitative findings suggested that the professional tasks associated with the patient's obtaining their medication, patient's perception of the safety and security of the medication management process, the provision of medication-related information and patient education and the general care regarding medication use were issues reported within the included newspaper articles.

#### **4.7.2 Comparison with existing literature**

This study identified 95 cases of MRH reported in Irish newspapers over the study years, providing findings that have not to date been identified. For example, Catalán-Matamoros and Peñafiel-Saiz, [194] conducted a systematic review of how the media has been used for public communication about medications in the last decade. It included studies from different parts of the world covering various types of medicines. Most of these studies were done in the United States (47 of them), with a few from other rich countries like Australia, the UK, Canada, and Italy [194]. Interestingly, there were no articles from Ireland included in this review. They searched the media coverage from 2007 to 2017.

The degree of harm reported in the current study shows that fatal and permanent damage was reported less frequently than non-fatal, non-permanent harm across all selected years. This contrasts with another content analysis of newspaper coverage, which found that approximately half of the reported medical errors (51.7%) resulted in death, and 25.0% of them resulted in either permanent damage or injury. Only 1.7% of the medical errors resulted in tangible damage [198]. These differences could be attributed to variations in harm definitions, as the latter study encompassed all types of medical harm, including diagnostic errors, and could also be influenced by differences in the populations. Another possible explanation could be the differences in the populations studied. The current study focused on cases in Ireland, while the second article looked at cases in Turkey, and there could be differences in healthcare practice and culture between these jurisdictions. In addition, there were variations in the time periods of the reported cases. The former study examined

different selected years (2019, 2009, 1999), whereas the latter study covered the years 2012 to 2015.

Furthermore, this study identified that most reported MRH cases affected adults, and fewer affected older adults or children. It's important to note that this observation about the relationship between age and MRH is based on description and not subjected to statistical analysis. Patient age information associated with medication-related issues is frequently absent from newspaper articles. A content analysis by Goodfellow *et al.*, [183] of the coverage of medication adherence by the UK and US newspapers found that only 28% of the analysed articles provided details about the specific age group of the patients. They found a discrepancy in the reporting of older populations between US and UK articles. In US articles, the older were represented in 14% of cases, while in UK articles, they were mentioned in 9%. [183]. Consistent with our finding, the median age of hospital patients who experienced any adverse effect increased by five years between (INAES-1 55 years in 2009) and INAES-2 (60 years in 2015) without any increase in the Charlson Index score of comorbidity burden [137]. The adverse event rate in hospitalised patients were more strongly related to complexity and co-morbidity than age alone [310]. Another content analysis conducted by Isik *et al.*, [198], described how medical errors were reported in Turkish newspapers. They found that most of the reported medical errors occurred in individuals aged 0 to 16 and 17 to 33, accounting for 70.8% of the cases [198]. The message available to the public through newspaper reporting are that MRH affects all ages, and that it affects younger and older adults similarly.

The highest proportion of reported MRH cases occurred among adults, particularly related to the use of central nervous system medications like analgesics and antidepressants, primarily in 2019. In recent years, following a rise in the incidence of depression, antidepressant medication usage has risen accordingly. In Ireland, there was change in some medication prescription over time. A repeated analysis conducted by Norris *et al.*, [311] found that the prevalence of strong opioid prescribing in Irish general medical services increased from 14.43% in 2010 to 16.28% in 2019, with the most significant increase observed in the  $\geq 65$  years age group. Tramadol was the most commonly prescribed analgesic during this period [311]. Our results found that central nervous system medication including analgesics were the most frequently reported drug class in newspapers. Furthermore, our qualitative findings identified that individuals experienced addiction, misuse, and overdose

associated with opioid analgesics, including tramadol and morphine and that this harm was often influenced by the person's background and medication miss use.

The findings suggested that people were concerned about the safety and security of medication management because medication errors made by healthcare professionals. This finding accords with the finding from a Turkish content analysis of newspaper coverage, which also determined that physicians were the primary cause of medical errors in 74.1% of cases [198]. The newspapers coverage, in this study, shed light on a critical aspect of healthcare where patients reported experiencing MRH without prior awareness of potential side effects of the medication they used. Patients reportedly often found themselves devoid of pertinent information either from their healthcare providers or pharmaceutical companies, leaving them unable to make informed decisions about their treatments. The consequences of this lack of education were far-reaching. The harm caused by medication side effects was not limited to temporary discomfort; rather, some instances led to permanent health implications or death. Hinchcliff *et al.*, [190] identified the frequency and types of medication errors matters reported. This study identified articles that reported on medication errors problems occurring within hospitals (the most common) and outside the hospital such as prescription activities of General Practitioners [190]. They found that poor staff communication and poor communication between general practitioners, pharmacists, and patients, often results in the incorrect dispensing or prescribing of medication. The authors concluded that there was a need to increase the public's understanding and awareness of medication safety issues [190]. The absence of proper patient education and information in these cases was not only detrimental to the patients' well-being but also posed significant risks to the health of their unborn children. This is an important issue, especially in the context of medication prescriptions, to prevent potential MRH. We discovered several cases across all age demographics where patients were not adequately informed about the potential side effects when prescribed medication, including antidepressants. In Ireland, a study by McCool *et al.*, [312] conducted over a five years (2016 to 2020) examined antidepressant medication usage among Irish medical card holders. Their study highlighted a substantial increase in antidepressant initiation prescriptions, the annual rate peaking in 2019 with a rate of 0.83 per 1000 prescriptions [312]. The interesting point is the concert between the finding from the newspaper coverage study which reports the individual MRH and the literature which identified the trends in antidepressant prescribing.

Given that no similar study has been conducted on MRH in Ireland or elsewhere, it is difficult to compare this study's findings to those of other studies. However, it is interesting to note that the increasing volume of articles reporting on this issue coincides with the recent increase in the prevalence of polypharmacy [1, 313].

Overall, the findings suggest that public messages from the included articles are that a lack of patient information and knowledge is connected with experiencing MRH, lack of good quality communication can result in MRH, error can happen in prescription, certain people or certain circumstances seem to put people at risk of MRH, e.g. liver damage.

#### 4.8 Implications for practice and research

**Practice**-Noticeable gap has been observed in the provision of medication information and patient education, as evidenced by both the current study and a newspaper article [190]. This suggests the need to enhance the communication of medication information, recognising its vital role for patients, both within healthcare facilities and in media coverage. It suggests that involving healthcare professionals in medical coverage, especially on social media platforms like Instagram and Snapchat, which are widely used across various age groups. Health practitioners can also use the study's findings to reflect on their role in disseminating health information responsibly and ethically, thereby contributing to public health objectives. Lastly, the general public will gain insight into the quality and comprehensiveness of MRH reporting, empowering them to make more informed decisions about their healthcare.

**Research**-Numerous studies have focused on examining medical issues in traditional print media [186, 302, 314], there is a pressing need to broaden the scope. Incorporating emerging platforms like social networks and various digital media can be beneficial. These platforms cater to a wider age demographic, offering a more comprehensive understanding of medication-related problems. In addition, suggests the need for patient safety researchers and advocacy groups to engage more strongly with the media as a strategy to increase the productive public discourse concerning MRH and gain support for evidence-based interventions.

The findings highlighted the necessity for improved medication processes, thorough review of patient history, and effective communication between healthcare providers and patients to prevent adverse drug events and to ensure optimal patient care.

### 4.9 Strengths and Limitations

This study has several limitations. First, the study was limited to a single country, Ireland. It is possible that different results would be obtained if the same type of study were conducted in another country. Second, the study was limited to the analysis of newspaper articles. It is possible that other media outlets, such as television and social media, may have different patterns of MRH coverage. Third, the absence of any accuracy checks or statistical testing for interrater agreement in selecting newspaper articles. Fourth, the LexisNexis database has limitations. It may not capture the full scope of all content and provide comprehensive coverage of all articles due to factors such as copyright restrictions [183, 298]. In addition, one limitation of this access was the unavailability of the option to sign in and save the search. To overcome this, the search strategy was maintained in a Word document and manually copied and pasted each time for conducting the search, which needed four visits to complete the data collection.

On the other hand, the strengths of this study include using mixed-methods approach for comprehensive understanding of how MRH has been reported to the public in Irish newspapers. For supporting that the study used the GRAMMS framework, for supporting the rigorous design and assessing the quality of mixed-methods studies [277]. Using this framework facilitated the identification of overarching quantitative patterns in responses and permitted an in-depth qualitative analysis to help explain the quantitative findings. In addition, the combination of deductive and inductive coding approaches enriched the depth of analysis by allowing for the exploration of both predefined and emergent themes, ultimately contributing to a comprehensive understanding of MRH and its associations in newspaper articles.

### 4.10 Conclusion

This study explored MRH as reported in Irish newspapers over three specific years (1999, 2009 and 2019). By undertaking a systematic content analysis, we found 95 individual MRH

cases reported in 78 newspaper articles. The reported MRH was categorised into three harm levels, and adults aged 16–65 years were found to have experienced the most cases of MRH. Over time, there was an increasing trend in the reporting of MRH cases in the studied newspapers. These findings offer a comprehensive understanding of how MRH is depicted in the media. They underscore the necessity for better dissemination of medication-related information to bolster patient safety and enhance our knowledge of medication management challenges and their impact on patient well-being.

#### **4.11 In the next chapter**

In the next chapter, a summary of the major results of this thesis is presented, as well as a triangulation of the findings in relation to age and recommendations for further studies and applications.

## **Chapter 5 : General discussion**

## 5.1 Introduction

This chapter discusses the findings presented in **Chapters Two to Four**. Key findings are summarised, then triangulated with each other and the current literature. The strengths and limitations of the thesis are also explored. Followed by implications for practices, policies, and researches, and recommendations are summarised from this thesis. Finally, then the challenges faced the doctoral studies are described, followed by the conclusion.

## 5.2 Summary of key findings

Patient harm is a common outcome of medication-related problems (MRPs), yet a significant number of these incidents, such as hospital admissions caused by medications, can be prevented. Therefore, exploring the association between age and medication-related problems in adults was the main aim of this thesis. This research question was addressed by employing systematic review and mixed methods.

**Chapter 2** presents the outcomes of a systematic review and meta-analysis investigating the relationship between age and medication-related admission (MRAs) in adult patients with the aim of identifying any statistically significant association. The results conclude that younger adults rather than older adults are at an increased risk of MRA. The findings suggest caution against an overemphasis in policy, practice or research funding on an exclusively older cohort to reduce or prevent MRA. It highlights the need for a deeper understanding of the independent risk factors contributing to MRA, and the development of associated policy and practice. Moreover, it is recommended that further research use a consistent approach to defining age categories. Additionally, when examining the association between age and MRA, adjustments for confounding factors should be considered.

A sequential explanatory mixed methods study conducted across Irish hospitals using secondary analysis of National patient experiences survey (NPES) undertaken to explore the medication-related experiences of adult inpatients are presented in **Chapter 3**. The study explored the association between age and the submission of free text comments describing

negative medication experiences, and it was found that younger patients (aged 16 to 65 years) were significantly more likely than older patients ( $\geq 65$  years) to submit a negative comment. An association was also identified between submission of a negative medication experience and overall rating of hospital experience, suggesting that those who experienced a medication-related problem had a poorer hospital experience overall. This study identified the challenges faced by adult inpatients with regard to medication during their hospitalisation and at discharge, highlighting the need for better medication processes and communication and several other potential areas for improvement, as discussed in Chapter 3, and again in Section 3.9.

In **Chapter 4**, the last research study, another sequential explanatory mixed methods study was presented. However, it was conducted to explore how the issue of medication-related harm (MRH) was presented to the public in Irish newspapers and whether there was any discernible association with age in the reported harms. This study revealed a higher number of reported cases of harm in newspapers among young adults and middle-age aged 16 to 64 years compared to other age groups. Furthermore, qualitative analysis found that the experiences of the public reported in the newspapers and those of inpatients collected in the survey were quite similar. The similarity was on the topic of medication related harm associated with a lack of patient knowledge about potential side effects, with some of the reported side effects affecting the patient's physical activity, mental function and impacting their life. It was also found that the patient's sense of safety and security about medication management can be negatively affected when medication error occurs, particularly when it is perceived that health care professionals may have been at fault. This underscores the importance of enhancing individual patient awareness about the potential benefits and risks of their medication use and providing explanations about potential MRPs within the adult age group.

An overview of the thesis objective including whether the age association was addressed or not, the setting and type of MRP across the different studies is in **Figure 5-1**.

# 1 Systematic review

Conducting a critical evaluation of the literature on the relationship between age and medication-related hospital admissions in adults.

## 2 Patient experience

Explore and understand the adult experience of actual medication management through their hospital journey

## 3 Media study

Examine the public reports regarding medication related-harm in newspaper

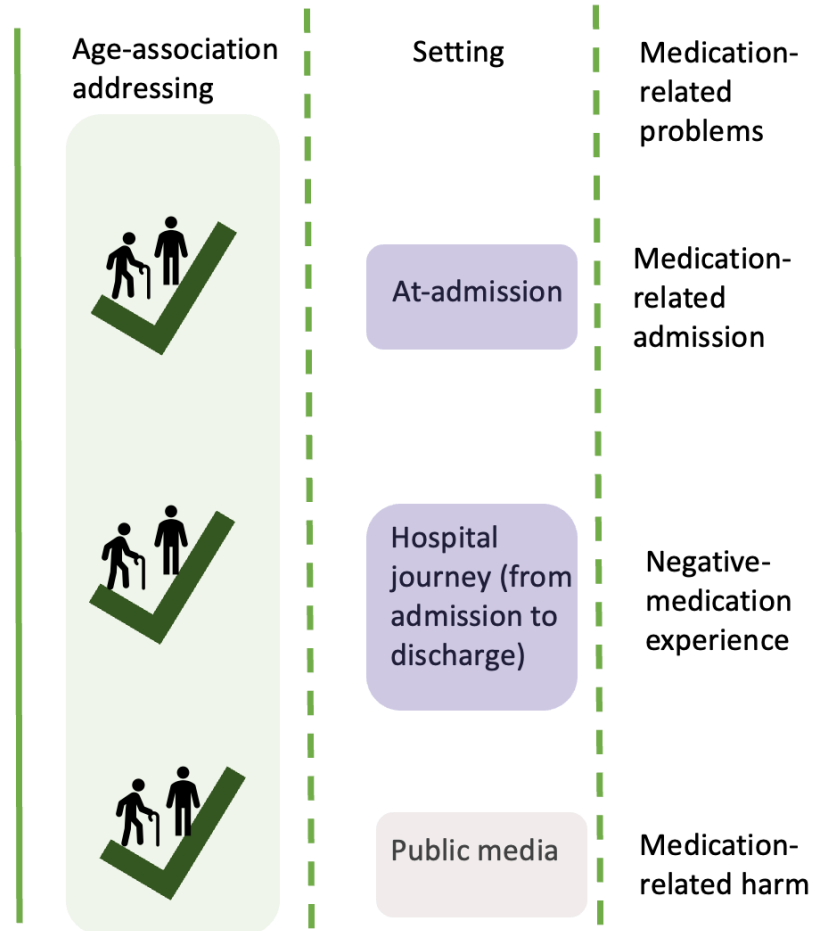


Figure 5-1: Summary of the main thesis objectives.

## 5.3 Triangulation of study findings

### 5.3.1 The relationship between age and MRP

The literature frequently relies on age as a risk factor for MRP [106, 107, 126, 212]. The findings from the secondary analysis of NPES survey data identified that younger adults were more likely than older adults to submit a negative medication-related comment. The findings from the mixed methods analysis of newspaper coverage of MRH identified that younger adults were the subject of most of the reported cases. Together, both of these findings indicate that younger adults both have unmet medication management needs, and are reported in the media to experience MRH, including fatal events. Therefore, these findings highlight the importance of addressing and meeting the needs of this cohort to enhance their medication management and their perception of their medication experience. The findings from these two studies undertaken in Ireland are consistent with the key finding from our systematic review that there is a statistically significant association between age and MRA in young adults, suggesting that younger people are as likely to experience MRAs as older people, having adjusted for a variety of confounders. This implies that age should not be considered an independent risk factor for MRA.

A more recent cross-sectional study conducted by Cahir *et al.*, [128] investigated the risk factors associated with adverse drug reaction (ADRs)-related hospital admissions in older patients aged  $\geq 65$  years Ireland [128]. They found that increased age was associated with a lower likelihood of ADR-related hospital admission [128]. Another Irish prospective observational study involving middle-aged patients (45-64 years), sought to identify the prevalence, severity, and preventability of ADR-related hospitalisations [73]. They found that middle-aged patients are indeed vulnerable to medication-related admission. However, they did not establish a significant association between age and the occurrence of MRAs in this age group [73]. Both of these observational studies were carried out in Ireland. While they focused on different populations, they both had a similar conclusion: age is not associated with MRAs.

This triangulated finding, with evidence from multiple sources, that both younger and older adults are vulnerable to MRP including hospitalisation, harm and negative experiences, has important implications for practice, policy and research, and these are elaborated on in Section 5.5 of this chapter.

***The key message: Both younger and older adults are vulnerable to MRP including MRA, MRH, and negative medication management experiences. Further research is needed to better understand the burden of these issues in younger age groups, as they may have a long-term impact as individuals age.***

### **5.3.2 Thematic framework arising from this thesis**

The mixed methods analysis of newspaper coverage of MRH, re-applied the themes, in the form of a conceptual framework, generated from the secondary analysis of the NPES. Both the NPES and the newspaper coverage studies employed mixed methods but differ in their aims and settings. It is interesting to find that four out of the five themes related to exploring medication experiences aligned with the findings from the newspaper coverage of MRH. Re-applying the conceptual framework in the newspaper coverage of MRH study was helpful to support analysis of the newspaper reports but it should be considered that the details of medication information between the two studies were different. The NPES was completed by patients themselves or their representative and the data provided more information about the medication experiences. The semi-structured survey guided patients to provide additional information through a combination of multiple-choice and free-text questions. The newspaper coverage of MRH articles reported the MRH from the journalist point of view or reported the story as the journalist understood it or as reported in legal cases. It was observed that the patient's insufficient or infrequent receipt of medication information, their concerns about safety and security, experienced medication side effect associated with obtaining medication, and the general impact of medication effects on physical or cognitive function were prevalent in both the newspaper coverage of MRH study and the secondary analysis of the NPES of medication management. This therefore provides evidence from multiple sources for improving the medication management process experienced by the Irish people and suggests the importance of finding ways to better prevent avoidable medication-related harm.

### **5.3.3 Patient education and MRP**

Two studies in this thesis found that patients did not always receive information regarding their medication and the potential side effects to look out for. The finding from the secondary analysis of NPES data described that patients have concerns about their medication

information and education from admission to discharge. The secondary analysis of NPES found that patients sometimes had to stop taking prescribed medications due to severe adverse effects not initially explained.

Furthermore, the mixed methods analysis of newspaper coverage of MRH indicated a parallel issue. Newspaper content frequently depicted situations where individuals were inadequately informed about the potential side effects of prescribed medications, ultimately resulting in unexpected health consequences. Newspapers found that lack adequate information about potential side effects, especially among younger individuals who may not fully comprehend the implications of these side effects. Most of adult people in the reported cases in newspaper converge did not receive adequate information about potential side effect to watch.

Together, both of these findings highlight a significant gap in providing patients with comprehensive medication information, thereby increasing the risk of adverse health outcomes. This triangulated finding, with evidence from Irish sources, suggests a lack of adequate information and education provision to both younger and older adult as it was.

The triangulated finding from both the NPES study and the newspaper coverage study suggest the need for greater information provision and education at the point of prescribing. This raises the question about how best to achieve this, and to do so in a way that meets the literacy needs of the Irish people. It is known that provision of simple messages is a helpful way to improve the patient's receipt of the correct information. Various strategies could enhance patient comprehension, including simplifying language for better understanding, repeating key information, and applying the 'teach-back' method. The 'teach-back' approach involved asking patients to reiterate the information they had received, fostering an iterative process that extends beyond mere information delivery [315, 316].

Both studies also suggested that a lack of adequate communication can lead to medication error. The NPES data reported that this lack of communication led patients to take incorrect dosages or the wrong medication altogether, resulting in adverse health outcomes. Where the newspaper converges of MRH study found that lack of information during medication dispensing prevented the patient from knowing what the drug was used for. This therefore provides evidence that patients do not receive the information they want or need about medicines when they are in hospital or in the community and identifies this as a potential contributor to medication-related harm.

Our findings from the secondary analysis of the NPES data highlighted the need to enhance education and communication specifically during hospital discharge, and the newspaper converge of MRH also captured that patient experienced harm due to medication error at hospital discharge. The discharge processes were also a significant source of concern. Patients reported being rushed out of the hospital without receiving crucial information about their home medication regimen. They emphasized the importance of receiving written information or handouts that explained the medications they were prescribed, their purpose, and any potential side effects. Several patients expressed concerns regarding medication information and patient education from admission to discharge. Evidence from the wider literature suggests that for older patients, inadequate explanations about medications at discharge can lead to medication omissions, incorrect dosages, and feelings of anxiety and confusion [157]. This lack of information often stemmed from healthcare professionals assuming that older individuals or their caregivers already completely understood medication details [157]. In a qualitative study, the medication management experiences of older patients at discharge were explored [272]. It was found that they had limited conversations about their medications both during hospital admission and at discharge. This lack of communication left participants and their family caregivers with unanswered questions about post-discharge procedures and potential side effects [272]. It highlighted that if medication discussions were not continued with patients after discharge, medications might remain unreviewed for extended periods. This limited opportunities for patients to be actively involved in the shared decision-making process, which should ideally accompany regular medication reviews [272]. The triangulated findings from this thesis highlight the need for patients and/or families, regardless of age, to be better involved and heard in their medication management. These findings align with the current patient safety literature's emphasis on involving patients as active participants in their healthcare. This practice helps to mitigate safety risks and promotes patient-centred outcomes [317, 318].

***The key message: There is a need to improve patient education about medication. It is recommended to provide clear, tailored information about medication use, encourage active patient involvement in their care, and use person-centred approaches to enhance engagement.***

### 5.3.4 Patient sense of safety and security of medication management

Several concerns about medication errors and healthcare providers' competence within the healthcare system were identified from both the NPES data and the newspaper coverage of MRH. The findings from the mixed methods analysis of newspaper coverage of MRH identified concerns around medication harm stemming from medication errors, system capacity issues, and potential medical negligence. These reports not only underscored the patient experience of harm but also demonstrated the extent to which patients sought legal redress. In several instances, there was evidence of negligence or fault within the healthcare system, with prescribing issues involving the choice of medication, omission of required medication, and incorrect dosage.

Both the newspaper coverage of MRH study and NPES study identified medication errors at multiple stages of medication management, including prescribing, dispensing, administration, and documentation errors. These errors, such as incorrect dosing, prescription omissions, dispensing of medication without provision of a patient information leaflet and administration of allergenic substances, were often identified. Issues such as discrepancies between verbal and written instructions, language barriers, and inaccurate record-keeping further heightened the problem. Particularly concerning were errors in discharge prescriptions that increased patient anxiety and diminished trust in healthcare providers. A previous study found that medication errors can manifest at various stages of the medication use process, including the prescription and administration phases [319]. Common, well-known reasons for errors include failure to communicate drug orders, writing the wrong medication, wrong drug selection, confusion over similarly named drugs, transcription errors and errors involving dosing units or weight [319]. Issues arising from the prescription and monitoring stages, particularly those involving the monitoring for adverse medication effects and prescribing wrong drugs, have been identified to be associated with preventable medication-related hospitalisations [99].

***The key message: These findings highlight the need for improvements in medication management, including a comprehensive review of patient's medical histories, enhanced medication reconciliation procedures, improved healthcare provider competence, and improved system capabilities to prevent MRP, such as ADE, and to ensure optimal patient care.***

### 5.3.5 General care about medication

Two studies' findings from this thesis highlighted medication's significant impact on patients' cognitive and physical activity and overall quality of life. The findings from the mixed methods analysis of newspaper coverage of MRH identified that medication use significantly affected individuals' physical and mental function and quality of life. From the experience of severe side effects to the misdiagnosis of symptoms, patients faced disruptions in their daily lives and work. These narratives underscored the imperative for better medication management, comprehensive patient education, and healthcare providers' consideration of the holistic impact of medications on patients' lives. However, the finding from the secondary analysis of NPES data identified a broader issue including the need for healthcare providers to consider the behavioural changes induced by certain medications, emphasizing the importance of understanding, and managing these effects. Patients called for better timing of medication administration, for example to minimize sleep disturbances or to enhance physical accommodation such as the need to be close to a bathroom, and enhanced supervision of high-risk medications. These findings illustrate the complex interplay between medication use and patients' physical and cognitive states. Therefore, the findings together suggest that healthcare providers should manage medication use more effectively and consider the broader impacts on patients' lives, reflecting a need for a holistic, patient-centred approach to healthcare.

*The key message: These findings collectively emphasise the importance of healthcare providers taking a more effective approach to medication management. They should consider the broader consequences of medication on cognitive, behavioural, and physical well-being, as these factors can significantly influence the overall patient experience. The NPES showed negative comments were linked to lower overall hospital experience ratings. This underscores the necessity for a holistic, patient-cantered approach to medication management.*

### 5.3.6 Pain management

Analgesics were identified as a problematic group of drugs both in the NPES and in newspaper reports of MRH. The finding from the secondary analysis of NPES identified that patients often expressed concerns about the (in)effectiveness of their medication, particularly painkillers. Many reported inadequate pain management, persistent discomfort, and instances where their requests for medication were ignored or denied. The findings from the mixed methods analysis of newspaper coverage of MRH identified that the most commonly reported harm was associated with analgesic and painkiller medication, where the person took a dangerous amount of the pain medication for them and in some cases this proved fatal. Most of these cases were due to a complex interplay between a patient's health background, health circumstances (complex health issues), and the medication use. This therefore provides evidence that patients need improved pain medication management, including assessing the effectiveness of prescribed painkillers, regular evaluation of pain management strategies, and monitoring of patient use of analgesics, having due regard to their medical history and health circumstances to prevent harm related. Ideally, pain management requires a multidisciplinary healthcare team to accurately address the individual patient's pain management needs and pain control [320]. Therefore, the healthcare system needs to pay closer attention to the patient's symptoms and complaints to provide the best healthcare possible and avoid any adverse effects or harm. Collectively, these findings emphasize the requirement for enhancements in medication management such as thorough review of the patient's history, enhanced healthcare provider proficiency, and improved system capabilities to prevent adverse drug events and to ensure optimal patient care.

***The key message: There is evidence that people need more effective pain management and for the therapeutic and adverse effect of analgesic to be better monitored and managed. Patient perceived that this could be achieved by managing the impact of painkillers, reducing long waiting times for receiving or requesting them, and improving patient knowledge and understanding of medication effects and potential side effects.***

## 5.4 Strengths and limitations of the thesis

### 5.4.1 Strengths of the thesis

This thesis boasts several strengths that contribute to a comprehensive understanding of the association between age and MRP from various angles. These multifaceted studies collectively make significant contributions to achieving the research's aims and objectives. Notably, the research methodology employed is robust. A systematic review and meta-analysis were utilised to assess whether age is a risk factor for medication-induced hospital admission in adults. Additionally, a mixed-methods approach was adopted to investigate the association between age and medication experiences in adult inpatients. The study also delved into understanding the messages received by the public about MRH, providing valuable insights into whether certain age groups might be more vulnerable to these harms. This thesis addresses a broad spectrum of MRPs, including MRAs, medication experiences, and MRH.

The combination of these approaches strengthens the findings, offering a comprehensive view of the association between age and MRP on both international and national scales. Moreover, the diverse settings explored in this thesis, ranging from admission to hospitalisation and discharge experiences, enhances the generalisability of the findings to multiple care settings. While the systematic review and the secondary analysis of NPES focused on adults aged  $\geq 16$  years, the newspaper coverage of MRH included all age groups. This broader age range sheds light on the potential occurrence of severe MRPs, even among children, as indicated by fatal cases reported. NPES does not directly address children but instead focuses on maternity experiences through a separate survey. This survey provides mothers with an opportunity to share their experiences with Ireland's maternity services, spanning from antenatal to postnatal care [260].

The evidence from all three studies, which employed methodological standards to enhance rigour in performance and reporting, is that both younger and older adults can experience MRP. Also, triangulating between the included studies adds another strength.

*The key message: The evidence from all three studies, which employed rigorous methodological standards, enhances the credibility of the findings. The systematic review used meta-analysis to determine correlations, the NPES data employed robust statistical tests like multiple regression analysis, and the newspaper coverage of MRH used mixed-methods to understand reported harm in individual cases. This combination of robust*

*methods, along with the triangulation of findings from these studies, provides comprehensive and valid evidence. Triangulation, involving the use of multiple methods or data sources, strengthens research findings by enhancing their validity and reliability [264].*

### 5.4.2 Limitation of the thesis

The finding from this thesis face limitations. In this thesis, none of the studies involved the patient or the public as members of the research team, although active partnership between members of the public and researchers has been found to improve the relevance and quality of research projects. Incorporating patient and public involvement in research can significantly enhance the quality and relevance of studies [321, 322]. By involving patients and the public, researchers can gain critical insights into lived experiences, priorities, and needs that may not be immediately apparent to healthcare professionals or academics. This involvement can lead to more patient-centred research questions, improved study design, and more relevant outcome measures. It can also improve the dissemination and implementation of research findings, as patients and the public can help communicate results in an accessible and meaningful way to a broader audience [321].

None of the studies in this thesis explore patient outcomes like mortality rate or quality of life. There is a need to investigate the relationship between age and patient outcomes associated with medication management. This thesis primarily concentrates on identifying age-related risk factors in the systematic review and exploring the connection between age and medication experiences and age-related MRH. However, it does not explore how age influences medication-related mortality, (re) hospitalisation, or quality of life, and other health outcomes.

Another limitation of this thesis is that it focusses on the adult patient aged  $\geq 16$  years, without including other age group such as children, except including them only in the newspaper coverage of MRH. In a prospective observational study, it was discovered that 87.7% of patients admitted to the paediatric ward, spanning from premature infants (born before 37 weeks) to adolescents (13 to 18 years), experienced at least one MRP [323]. The paediatric patients aged  $<18$  years were particularly susceptible to MRPs, with most of these issues being preventable [324]. In this thesis, we identified that newspaper articles reported

the medication-related death of children. This underscores the need to address these concerns and to further explore MRAs in children and the medication-related experiences of children and their parents or guardians around periods of hospitalisation.

***The key message: Further research is needed to explore MRA and the medication-related experiences of children and their parents or guardians around periods of hospitalisation.***

### 5.5 Implications for practice and research

The potential overemphasis on age as a risk factor for MRPs, including MRAs, could arise from the observation that older populations often have multiple health conditions (multimorbidity) and take multiple medications (polypharmacy), which can lead to increasing the risk of adverse drug interactions and reactions [325]. However, a prospective case-control multicenter study by Leendertse *et al.*, [9] identified several significant risk factors associated with preventable MRAs in older people aged  $\geq 65$  years. The study highlighted polypharmacy as the primary medication-related risk factor with preventable MRA, where age was not considered as a confounding variable. Additionally, they found that impaired cognition, existing comorbidities, impaired renal function, dependent living conditions (such as nursing homes, care homes, or home-based nursing care), and non-adherence to prescribed medication regimens were patient-related factors associated with preventable MRAs [9]. Even this single study, which was conducted in the Netherlands did not identify age as a risk factor for MRA in older people. Howard *et al.*, [100] conducted a study investigating the risk factors related to preventable MRAs. Their findings underscored the importance of effective communication and knowledge management in medication processes. Improving this area could potentially decrease the incidence of preventable MRAs. However, their research did not consider age as a significant risk factor [100].

Many policies aiming to enhance medication safety emphasise the importance of focusing on older patients, who are considered more susceptible to ADEs, medication error prescription and polypharmacy than younger adults [326, 327]. They propose strategies to refine the prescribing process so as to bolster medication safety in this demographic. These strategies include: (1) Building effective prescribing teams that work closely with older patients, ensuring they fully understand their medications' purpose, potential benefits, and

risks. (2) Enhancing the involvement and developing partnerships with older patients and caregivers, with shared decision-makers on the use of medication. (3) Enhancing the comprehensive understanding and awareness of older patients on their medication regimen [326, 327].

The insights garnered from this thesis when triangulated, point to the need for a wide-ranging exploration of potential influences associated with MRPs. It is imperative to understand that MRPs aren't confined to a specific age group, but rather, they can impact patients across the age spectrum. Both young and older patients may be equally vulnerable to these issues. Furthermore, enhancing the education and understanding of all patients, irrespective of their age, stands as a key strategy for improving medication safety and outcomes. By fostering a deeper comprehension of their treatment plans, patients can be empowered to actively participate in their healthcare, thus contributing to safer medication practices and better health outcomes.

Therefore, further research is suggested to address the association between age and other risk factors on medication outcome. Also, we suggest future studies exploring the association between age and MRAs should use standardised age brackets and age cut-offs. This is important because as detailed in **Chapter 2** the currently available literature is heterogenous in this regard, which limits the ability to pool data [323, 324] [34, 126].

*The key messages: Although many policies prioritize medication safety for older patients, this thesis emphasises that MRPs can affect patients across all age groups. Therefore, it's crucial to broaden the exploration of potential influences associated with MRPs. Improving patient education and understanding about medication use, regardless of age, is a pivotal strategy for enhancing medication safety and outcomes.*

*The systematic review identified variations in how age cut-offs were reported among the included studies, making it challenging to incorporate all of them into regression analysis tests. Additionally, there was a lack of comprehensive reporting of age-related information, hindering comparing results between studies. Consequently, this review recommends further research that employs a standardized age cut-off and provides comprehensive age-related information to facilitate more meaningful comparisons in future research.*

The following section presents recommendations grounded in the evidence and findings from the three studies in this thesis, after triangulation.

## 5.6 Recommendations

- The evidence presented in this thesis suggests that both younger and older adults are vulnerable to MRPs. Further research is needed to better understand the burden of medication-related issues in younger age groups, as these are currently relatively infrequently described and may have a long-term impact as individuals age. Providing optimal medication management care during young and middle adulthood is crucial to preventing worse medication-related outcomes in later years.
- The key themes that emerged regarding inpatient medication management experiences and newspaper coverage of MRH were patient sense of safety and security of medication management, professional tasks associated with obtaining medication, medication information and patient education, and general care about medication. These issues are associated with negative patient experiences and reports of MRH.
- There is a need to improve patient education about medication. It is recommended to provide clear, tailored information about medication use, encourage active patient involvement in their care, and use person-centred approaches to enhance engagement.
- These findings highlight the need for improvements in medication management, including a comprehensive review of patient's medical histories, enhanced medication reconciliation procedures, improved healthcare provider competence, and improved system capabilities to prevent MRP, such as ADE, and to ensure optimal patient care.
- These findings collectively emphasise the importance of healthcare providers taking a more effective approach to medication management. They should consider the broader consequences of medication on cognitive, behavioural, and physical well-being, as these factors can significantly influence the overall patient experience. The NPES showed negative comments were linked to lower

overall hospital experience ratings. This underscores the necessity for a holistic, patient-cantered approach to medication management.

- There is evidence that people need more effective pain management and for the therapeutic and adverse effect of analgesic to be better monitored and managed. Patient perceived that this could be achieved by managing the impact of painkillers, reducing long waiting times for receiving or requesting them, and improving patient knowledge and understanding of medication effects and potential side effects.
- The evidence from all three studies, which employed rigorous methodological standards, enhances the credibility of the findings. The systematic review used meta-analysis to determine correlations, the NPES data employed robust statistical tests like multiple regression analysis, and the newspaper coverage of MRH used mixed-methods to understand reported harm in individual cases. This combination of robust methods, along with the triangulation of findings from these studies, provides comprehensive and valid evidence. Triangulation, involving the use of multiple methods or data sources, strengthens research findings by enhancing their validity and reliability.
- Further research is needed to explore MRA and the medication-related experiences of children and their parents or guardians around periods of hospitalisation.
- Although many policies prioritize medication safety for older patients, this thesis emphasises that MRPs can affect patients across all age groups. Therefore, it's crucial to broaden the exploration of potential influences associated with MRPs. Improving patient education and understanding about medication use, regardless of age, is a pivotal strategy for enhancing medication safety and outcomes.
- The systematic review identified variations in how age cut-offs were reported among the included studies, making it challenging to incorporate all of them into regression analysis tests. Additionally, there was a lack of comprehensive reporting of age-related information, hindering comparing results between studies. Consequently, this review recommends further research that employs a standardized age cut-off and provides comprehensive age-related information to facilitate more meaningful comparisons in future research.

## 5.7 Challenges faced during the doctoral studies.

It is important to acknowledge the challenges facing these doctoral studies. This thesis faced challenges due to the introduction of new legislation in Ireland and the worldwide influence of the coronavirus (COVID-19) pandemic.

### 5.7.1 Implications of the General Data Protection Regulation and new Irish regulations

This thesis seeks to address the nature and risk factors associated with MRPs associated with hospitalisation by conducting epidemiological observational studies to describe medication-related burden and using validating tools to predict individual patients' risks of MRPs in Irish hospitals. Data from previous studies are employed and enriched by the PhD candidate for the purpose of this study. This enrichment was performed by manually extracting data from hardcopy or electronic hospital medical records. The process of data enrichment took place between December 2017 to May 2018. On May 25, 2018, the General Data Protection Regulation (GDPR), a new European Union framework on data protection and privacy law for personal information, came into effect (Regulation (EU) 2016/679 of the European Parliament and of the Council) [328, 329]. There was a lack of enforcement provisions in the previous regulation, so the GDPR was introduced to address this. The new regulation boosted the privacy of individuals and gave greater protection to their information, the core principle of this framework. The GDPR introduced a broad definition of personal data and defined it as sensitive personal information that encompasses names, home addresses, medication record numbers, diagnoses, dates of birth, email addresses and more to give individuals more protection over the use and storage of their personal information. The GDPR seeks to harmonise various countries' data protection laws, to simplify these laws and to make a law applicable to each country in the European Union.

On August 8, 2018, the Health Research Regulations (HRR), an Irish law, was signed by the Minister of Health and came into force. This regulation sets out suitable and specific safeguards as required under the GDPR so that personal data are processed in a manner that is lawful, fair and transparent to support health research, patient trust and desirable public confidence. The main principle and aims of the new regulation are to control and minimise

the use of personal data for health research and to govern the processing (possession, use, collection, access to, sharing, storage and destruction) of these data [330].

Data processing for the studies described previously faced several challenges due to the implementation of the GDPR and the HRR. The chief challenge involved the necessity of obtaining explicit consent for utilising subject data, which was one of the six main ‘suitable and specific’ measures mandated by the Irish government’s HRR. The GDPR, on the other hand, did not impact data processing, allowing personal data to be used in health research without explicit consent. However, explicit consent was mandated by the HRR regulations as the legal basis for processing sensitive health data and had a significant impact, leading to constraints on health research in Ireland for both ongoing and new studies. In cases for which obtaining consent was not feasible (such as retrospective studies), researchers were required to apply to a newly established National Consent Declaration Committee. There was a lag time between the enactment of the law and the establishment of this National Consent Declaration Committee function. Another challenge the study faced was the new legal requirement to anonymise all clinical data. This posed the risk of making it impossible to revert to identifiable data in case of missing data or the need for additional information [329].

Prior to the GDPR and the HRR, this project proceeded in accordance with the safeguards of the GDPR that commenced in May 2018. The GDPR did not prohibit health research, given that it was previously approved by the Joint St. James’ Hospital/Tallaght Hospital Research Ethics Committee. However, the introduction of the HRR in August 2018 invalidated any previously granted Research Ethics Committee approvals. It prohibited retrospective healthcare record review for research purposes in the absence of explicit written consent for each instance of data processing, even if the data were pseudonymised. Consequently, the continuation of this project became infeasible.

Given these uncertainties and time constraints, the PhD student's timeline could not accommodate these challenges. With a limited timeframe and multiple tasks yet to be completed, the PhD student focused on identifying research questions that did not necessitate personal subject data and were feasible within the given timeline. The scholarship for this thesis was funded, and the initial goal was to submit the thesis in 2022. The final decision was to terminate this project in April 2019, and neither the PhD student nor her supervisor would access the data again.

The PhD student and supervisor tried to identify another project with research questions that did not necessitate personal subject data using open data access (principal source of national data) in Ireland. The desired dataset would not contain any personal information (patient names, addresses or contact details). The PhD student dedicated approximately four to five months to developing the new research question and methods while awaiting approval. Unfortunately, the application was declined due to the necessity of seeking approval from the National Consent Declaration Committee.

That period was particularly challenging for the PhD student, who experienced significant lost work, time and effort. Moreover, during the data collection phase, the student suffered a hand injury resulting from prolonged laptop usage, necessitating hand surgery. Subsequently, a few months of physiotherapy were needed to restore normal hand movement. Collectively, these factors had a profound negative impact on the overall progress of the thesis.

### 5.7.2 Implications of COVID-19

Throughout this thesis, the COVID-19 pandemic created significant global disruptions. These disruptions led to the implementation of restrictive public health measures and imposed time constraints.

The COVID-19 pandemic presented a series of formidable challenges that significantly impeded the progress of the PhD student's research project. First, the progression of fieldwork was substantially disrupted as the COVID-19 pandemic-imposed travel restrictions and raised safety concerns, instigating anxiety and uncertainty for the student. In alignment with health and safety recommendations, Trinity College Dublin mandated transitioning to remote work in March 2020, shifting interactions between the student and her supervisor to online platforms. The implications of the pandemic extended beyond the logistical aspects of research, significantly impacting the PhD student's emotional well-being and leading to her decision to return to a more secure health environment in her home country of Saudi Arabia in May 2020. This geographical relocation, however, presented an additional barrier for the research, particularly concerning **Chapter 3**. Due to ethical constraints, transferring data from Ireland for processing in another country was prohibited. This unexpected predicament considerably influenced the research trajectory, necessitating

adjustments to accommodate these external constraints. The extended duration of quarantine significantly affected various aspects of the research journey. Notably, the pandemic's widespread impact on mental health and overall well-being was palpable, with the student grappling with uncertainty, isolation and stress, all of which contributed to a decline in focus, motivation and overall productivity. The shift to remote work blurred the boundaries between work and personal life, increasing the potential for burnout and reduced efficiency. Additionally, the adaptation to new online research techniques and virtual tools demanded extra time and effort. Finally, unforeseen personal health issues and other unexpected personal circumstances further compounded the challenges posed by the pandemic, creating a complex and unprecedented environment that profoundly impacted multiple facets of the PhD student's research journey.

## 5.8 Conclusion

This thesis primarily centred on exploring the connection between age and MRPs in adults. The findings indicated that age was an independent risk factor for MRAs, with both young and older adults vulnerable. However, younger adults are at a heightened risk compared to their older counterparts. This suggests the necessity for further research to identify and better understand other risk factors and to moderate the influence of age in interventions and strategies for identifying and managing MRAs in practice. The research also highlighted the challenges faced by adult inpatients during hospitalisation and discharge. It was found that adults aged between 16 to 65 years were more likely to provide negative comments about their medication experience. Moreover, a person's overall hospital experience was impacted by their medication-related experience. The adults faced numerous challenges, including concerns about professional tasks associated with obtaining their medication, the safety and security of medication management, transitional care management, receipt of medication information and patient education, and general care about their medication. There was an increase in the frequency of reporting of MRH cases in newspapers in recent time, peaking in 2019. The majority of MRH cases reported in Irish newspapers were associated with adult individuals and common themes identified from these reports included the impact of drug on individuals' health and individual's background.

The overarching message from this thesis is that age is a risk factor for MRP in young adults. This finding underscores that both younger and older patients experience MRP, emphasising the need to accommodate both age groups in strategies to identify and to manage MRPs. Furthermore, it highlights the importance of conducting further research to better understand the risk factors related to MRP generally and MRA specifically.

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