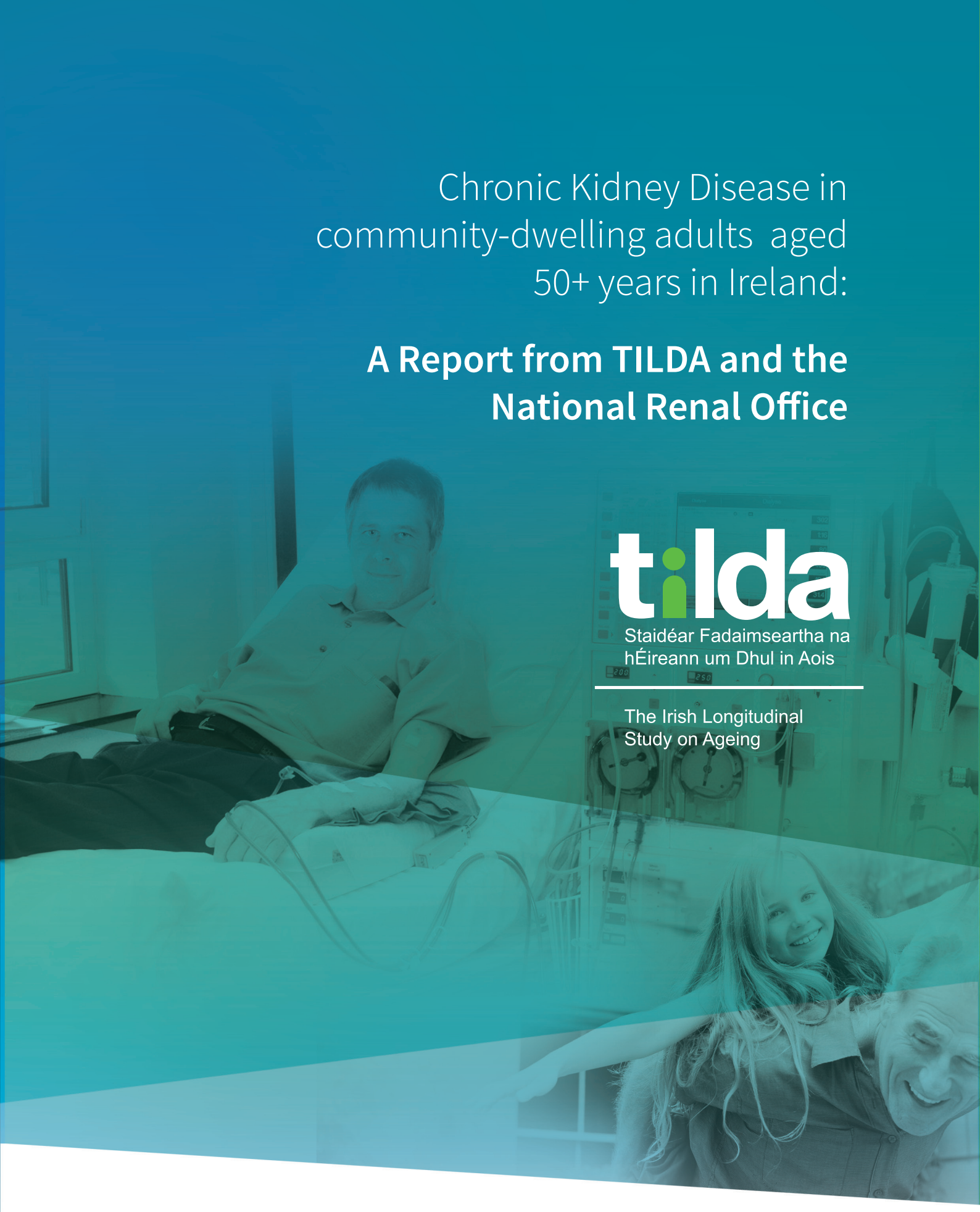
Chronic Kidney Disease in community-dwelling adults aged 50+ years in Ireland:

A Report from TILDA and the National Renal Office



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Staidéar Fadaimseartha na hÉireann um Dhul in Aois

The Irish Longitudinal Study on Ageing

Clár Éire Ildánach
Creative Ireland Programme

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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Chronic Kidney Disease in community-dwelling adults aged 50+ years in Ireland:

A Report from TILDA and the National Renal Office.

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On behalf of The Irish Longitudinal Study on Ageing (TILDA) and the National Renal Office of the HSE (NRO).

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1. Report Summary:

- The presence and severity of CKD identifies individuals who are at increased risk of adverse health outcomes and premature mortality; and as such, preventing and managing CKD constitutes a key aim of overall management. We conducted the largest longitudinal study performed in Ireland using data from TILDA to describe the clinical epidemiology of CKD in Ireland.

- Based on data from 2009-2011 to 2013-2015, CKD prevalence in adults aged 50 years and over in Ireland is rising . While this is likely to be primarily related to ageing and improved survival in the general population, these trends highlight the importance of continued public health action to raise awareness and to improve the care and outcomes for people with CKD.

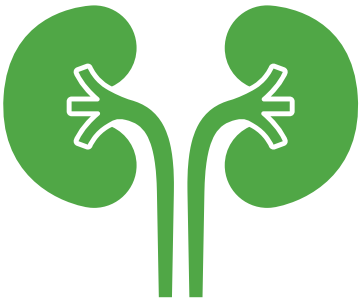
- Based on data from Wave 3 of TILDA (2013-2015) integrated with the last Irish Census estimates, the national prevalence of CKD Stage ≥ 3 is 15.6%, with increasing prevalence with age and in female sex. The estimated national prevalence was 4.9% and 35.8% in people aged 50-69 years and 70+ years, respectively, which translated to 50,496 adults aged 50-69, and 152,882 adults aged 70+ living with CKD in Ireland in 2016.

- The new eGFR formula (2022), which removes the race adjustment from the regression equation, yielded similar albeit slightly lower estimates of CKD prevalence/incidence.

- Hypertension was the most common CKD-related condition in the Irish adult population. The estimated prevalence of CKD in Irish adults aged 50+ years without diabetes and hypertension was 6.22 % based on Wave 1 data and 10.01% based on Wave 3 of TILDA. Age, blood pressure, HbA1c, BMI and hypertension were significantly associated with the presence and severity of CKD.

- Based on eGFR grading, 15.6% of the Irish population aged 50+ years have CKD and are at increased risk of adverse outcomes related to CKD including cardiovascular disease, premature mortality and the development of End Stage Kidney Disease (ESKD). More than 5% of the Irish population aged 50+ years have more advanced CKD by eGFR grading and are even more at risk of these adverse outcomes.

- Our study supports the previously observed association between ageing, impaired kidney function and kidney function decline over follow up. The incidence of CKD ≥ stage 3 was 16 per 1000 person-years which will likely contribute to substantial future demand on Nephrology services .



CKD PREVALENCE IN ADULTS AGED 50 YEARS AND OVER IN IRELAND IS RISING

2. Considerations and recommendations from the National Renal Office of the HSE.

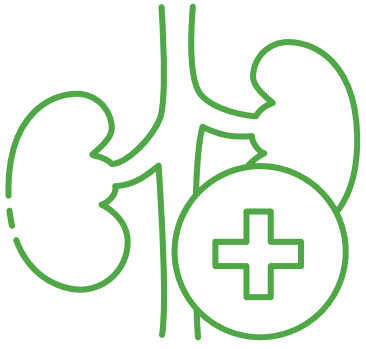
- This Report clearly identifies that although CKD is common in the general population of Ireland aged 50 years and over, most people are unaware that they have CKD. We advocate for increased public awareness campaigns since it is of paramount importance to highlight the significance of CKD in the general population. This is particularly the case in light of the risk of progression of CKD to more advanced stages, the associated cardiovascular disease and premature mortality risk, in addition to the risk of acute kidney injury and medication prescribing errors. Furthermore, contemporary treatment strategies have emerged to reduce the risk of progressive worsening of kidney function and cardiovascular risk such as the SGLT2 inhibitors, non-steroidal mineralocorticoid antagonists and GLP-1 analogues.

- CKD should not be viewed in isolation, but as an integral part of the management of the other long term conditions that the majority of people with kidney disease have, such as diabetes, hypertension, heart failure and cardiovascular disease. In fact these comorbidities and conditions may be even more relevant to an individual's current and future well-being since people with early stage CKD are much more likely to suffer premature death due to cardiovascular disease than to progress to end stage renal disease requiring dialysis or kidney transplantation.

- Our study suggests that 98% of TILDA participants with CKD aged 50 years and above were not aware of CKD. In addition the frequency of poorly controlled hypertension based on guideline treatment targets in patients with established organ damage in the form of CKD is alarming. The cardiovascular, cognitive and comorbidity implications of untreated hypertension in CKD could be highlighted and addressed by the inclusion of CKD in the primary care chronic disease management programme.

- CKD has huge cost implications for healthcare, as was highlighted by the recent Kidney Research UK report which highlights CKD as a public health emergency. [1]

- The National Renal office (NRO) proposes to use the clinical epidemiology data from this report to inform the design of the model of care and service development for early CKD in the community and to advocate for CKD to be part of the National Chronic Disease Management Program.



98% OF TILDA PARTICIPANTS WITH CKD AGED 50 YEARS AND ABOVE WERE NOT AWARE OF CKD

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Chronic Kidney Disease in Ireland: Evidence from TILDA

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Staidéar Fadaimseartha na hÉireann um Dhul in Aois
The Irish Longitudinal Study on Ageing

About Chronic Kidney Disease

Chronic Kidney Disease (CKD) is linked to an increased risk of heart disease and premature death. Treating high blood pressure and other risk factors for kidney disease can protect kidney and heart health, and prevent the need for dialysis.

Over the past 10 years, the number of patients treated by dialysis or kidney transplantation has increased by 30%. **This costs the State almost €1 million per day to treat.**

1 in 7 More than people aged 50+ and over have CKD in Ireland **(over 200,000 people)**

Chronic Kidney Disease is common

CKD is more common with increasing age and **among women**

Based on TILDA data collected from **2009-2011** and **2014-2015**, CKD is rising among adults in Ireland

People with **high blood pressure** or **diabetes** are up to 3 times more likely to have CKD

Risk Factors

About **50% of adults** with CKD have uncontrolled blood pressure

Early detection and treatment leads to better outcomes, including **prevention of the need for dialysis**

Monitoring for CKD requires regular **blood** and **urine checks**

Maintaining Kidney Health

Proper management of blood pressure and blood sugar levels can help keep **kidneys healthy**, in addition to maintaining a healthy weight

WORLD KIDNEY DAY
9th March 2023

Preparing for the unexpected, supporting the vulnerable

An Roinn Sláinte Department of Health
HRB Health Research Board
The Atlantic Philanthropies
HSE
Trinity College Dublin, Coláiste na Tríonóide, Baile Átha Cliath, The University of Dublin

3. Introduction

Chronic kidney disease (CKD) refers to the general term for persistent irreversible damage to kidney function which is associated with increased risk of experiencing significant morbidity and premature mortality. [2,3] CKD is a silent condition, which commonly goes undetected or is detected only as an incidental finding following routine laboratory testing.[4] Contemporary KDIGO criteria stratify patients into risk groups based on disease cause, abnormalities of kidney structure and function, and the degree of aberrant urinary albumin excretion according to the US National Kidney Foundation (NKF) grade.[5] Kidney function is estimated by the clearance of serum markers, namely Creatinine and/or Cystatin C which are combined with age and sex to produce an estimated Glomerular filtration rate (eGFR).4 However, once an individual is diagnosed with CKD, current clinical guidelines recommend stratification to assess disease severity, the implementation of adequate interventions to reduce progression, and the subsequent monitoring for associated complications[6]. Furthermore, the evidence emerging from the most recent clinical trials of contemporary interventions in CKD such as the SGLT2 inhibitors demonstrate a specific benefit to patients with CKD above and beyond blood pressure control and renin-angiotensin-aldosterone axis blockade.[7-10] This benefit applies both to patients with diabetes and without diabetes, and is proportionate to the degree of urinary protein excretion.[8] Initiation of disease modifying therapy in CKD could slow the progression, reduce cardiovascular disease risk and thus significantly improve outcomes. However, due to the silent nature of CKD, only a minority of individuals are diagnosed at early stages, limiting the practical implementation of these recommendations.

Therefore, recognising the scale of CKD and the distribution of the disease stages in Ireland is an important step to impact outcomes for people with CKD. Although screening for CKD to this point has not been advocated for by bodies such as the US Preventive Services Task Force, and other international bodies the independent benefit of SGLT2 inhibitors in CKD have rekindled the CKD screening debate internationally. Allowing for heterogeneity by region, the global prevalence of CKD is estimated at 9%. [2] Medicare data for the 2011 prevalent US population, estimated CKD prevalence amongst those aged 65 years and older at approximately 10% in contrast to 1% of the younger population, indicating that the ageing population carries the overall burden of CKD in the population.[11] Future trends in the demographics of the general population in Ireland will have significant implications for CKD, with an approximate doubling of the proportion of individuals aged over 65 years expected in the next 15 years, within which the largest increase is expected in those aged 80 years and over. [12] This will lead to considerable healthcare resource utilisation for Nephrology services.

While valid attempts have been made to report the prevalence of CKD in Ireland,[13,14] to date none have focused on a longitudinal cohort study based on a stratified random sample of the general population. Similarly, the incidence of CKD in the Irish general population has not been investigated to date and the Irish Longitudinal Study on Ageing (TILDA) provides the most suitable substrate in which to study this. The prevalence of CKD (defined as eGFR<60 ml/min) in Ireland has previously been estimated at 11.7% based on creatinine-estimated GFR (eGFRcreat) in a nationally representative registry of adults aged > 45 years (2007 Survey of Lifestyle, Attitudes, and Nutrition). [13] More recently, the National Surveillance System data of patients admitted to Irish health centres in the West of Ireland suggested an expected increase of CKD temporal trends of 1.5 % per year (from 6.7% in 2005 to 7.2% in 2014) in the Irish healthcare system. [14] However, as opposed to TILDA, a stratified random sample of the general population, cohorts based on healthcare utilisation are potentially subject to selection bias. In addition, creatinine estimated eGFR was used to estimate CKD frequency in both of these prior studies, and since serum creatinine may be influenced by muscle mass among other confounders, [15], in this report we also assessed CKD by serum Cystatin C. We therefore utilised both serum creatinine-based eGFR and serum Cystatin C based formulas.

This report arose from a need to inform future healthcare resource planning for CKD in Ireland by the National Renal Office of the HSE. In this report we map the epidemiological and clinical features of CKD in a population-based cohort, evaluate potential risk factors, and describe the true incidence and prevalence of CKD in Ireland using TILDA data, a large (n > 8,000) population-based longitudinal study.

4. Methods

4.1 Study population:

The Irish Longitudinal Study on Ageing (TILDA) was established at Trinity College Dublin to assemble comprehensive health, social and economic data from Irish adults aged 50 and over, at a national level. [16] TILDA recruited a stratified clustered sample representative of the community-living Irish population aged 50+. Random sampling of geographical clusters was used to select households (RANSAM sampling framework).[16,17] Data collection involved an in-home interview, a self-completion questionnaire (CAPI), and a comprehensive health assessment (HA) undertaken in the health center or in the respondent's home. Detailed descriptions of the recruitment protocol have been published previously. The baseline (i.e., Wave 1, 2009-2011) sample was 8,175 adults aged ≥ 50 years. Subsequently, 5751 participants completed the health assessment, carried out by trained nurses. The data is collected every two years (known as study Wave). All components of the above design were conducted at Wave 1 and were repeated at Wave 3 (2015-2016). Our analysis included participants who completed HA and had kidney function available at both Waves. All the participants provided informed signed consent. The Research Ethics Committee of Trinity College Dublin approved the study protocol. All experimental procedures adhered to the Declaration of Helsinki.

4.2 Assessment of demographics and risk factors for CKD:

TILDA included measurements of height and weight, which was used for calculations of BMI. Obesity was defined as BMI above 30 kg/m2. Hypertension and diabetes were defined by a physician/health-care professional diagnosis that was self-reported by the participant because CKD is most strongly related to these conditions. The identification of uncontrolled hypertension was additionally based on measured mean (average of two BP measurements) systolic blood pressure and/or diastolic blood pressure > 140/90 mmHg or >130/80 mmHg. Antihypertensive medication use included diuretics, beta-blockers, calcium-channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or other antihypertensive agents. The CKD awareness at TILDA Wave3 was based on (variable ph301_18) positive response to the question "last time we interviewed you reported any of the conditions on card? Chronic kidney disease" and the variable CHRkidney. Information on age, sex, smoking, and education attainment was based on self-report during the CAPI portion of TILDA. Education status was divided into primary/none, secondary, and higher/third.

4.3 Kidney Function and Outcome Definition and Analysis:

Plasma creatinine and cystatin C were measured with an enzymatic and a particle–enhanced immunonephelometric assay, respectively. The measurements were performed in the same blood sample, at the Clinical Laboratory, at Saint James Hospital, Dublin. The creatinine measurement method aligned with calibration to IDMS (Roche Creatinine plus ver.2, Roche Diagnostics, Basel, Switzerland).

We estimated eGFR from blood cystatin C and creatinine concentrations (eGFRcys-cre) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations, as recommended by KDIGO.18-22 Because some previous reports used the creatinine equation, eGFR using this marker was also calculated and reported, to allow the comparison of the selected outcomes. For the definition of CKD, we used a cut-off of 60 ml/min/1.73m2. Additionally, we quantified the frequency of the CKD categories, based on eGFR measurements expressed in ml/min/1.73 m2 and categorized as Stage 3a (eGFR 45-59), Stage 3b (eGFR 45-59), Stage 4 (eGFR 15-29) and Stage 5 (eGFR <15). Higher categories of eGFR were categorized as normal or Stage 1 (eGFR >90) or mildly reduced or Stage 2 (eGFR 60- 89).

Statistical analyses were performed in SAS V 9.4 (SAS Institute, Cary, NC). Clinical characteristics and summaries of outcomes were summarized as counts and percentages (proportions) for categoric variables, means with SDs for normally distributed continuous variables, and medians and quartiles for continuous variables with skewed distributions. Incidence rates of CKD were used to describe the follow-up results at Wave 3.

The comparisons in the participants characteristics according to CKD grades were made with ANOVA/Wilcoxon test for continuous variables, the differences according to ordinal variables was tested using the Cochran-Armitage trend test. A multivariable logistic regression model were used to test jointly the predictors of CKD risk identified in the univariate approach. To provide an estimate of the Irish prevalence of CKD, the observations from the TILDA were weighted to account for the complex design of TILDA[23] and age-categorized to the 2016 population according to the National CSO Survey (2016).[23] In this instance, longitudinal weights which account for participant attrition between Wave 1 and Wave 3 were used. The two-stage, stratified clustering sample design of TILDA was accounted for when computing confidence intervals and standard errors. Prevalence estimates and descriptive statistics were weighted for survey non-response, as well as non-attendance at the health assessment component of the study. Statistical analyses were performed using survey procedures in SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). Estimates from our study are nationally representative of the noninstitutionalized Irish population of adults aged 50 years or older. Prevalence estimates were applied to the 2016 census to obtain estimates of the number of individuals with CKD in Ireland in the year 2016. Two-sided p values less than 0.05 were considered statistically significant.

5. Results

5.1 Participant characteristics at TILDA Wave 1 and Wave 3:

Eight thousand one hundred seventy-five participants aged 50 years or older were enrolled in the TILDA Study between 2009 and 2011 (i.e., TILDA Wave 1). For the present study, we selected participants with kidney function estimates available. Based on weighted estimates the mean age of this population was 62.5 years at TILDA Wave 1, the median age was 60.5 years (range 50 to 95 years), 49% were male and 51% were female. While the follow-up of TILDA participants is still ongoing; in this publication, we report the findings from Wave 1 between 2009 and 2011, and Wave 3 between 2014 and 2015 during which blood samples were archived..

Table 1 shows the distribution of CKD-related factors and comorbidities within the TILDA dataset, with national estimates at both study Waves. During the follow-up period between the two time points, the population became older and included a significantly larger proportion of age sub-groups 60-69 and 70+. The median eGFR was within normal to mildly decreased values at both study waves. Hypertension was the most prevalent self-reported comorbidity, with a national prevalence of 34.5% and 36.9%, based on TILDA Wave 1 and Wave 3 respectively. Diabetic individuals comprised 7.5% of the population at Wave 1 and 8.8% at Wave 3, and the majority of those with diabetes had HbA1c in the range of suboptimal glycaemic control (their median HbA1c was 80 mmol/mol (9.5 %)). Both time points were similar with regard to the distribution of socio-economic factors, the proportion of smokers, and glycaemic control (based on haemoglobin A1c (HbA1c)). At study Wave 3 the participants were treated more frequently with antihypertensive (AHT) medications than at Wave 1 (34% vs 44%, $p<0.001$).

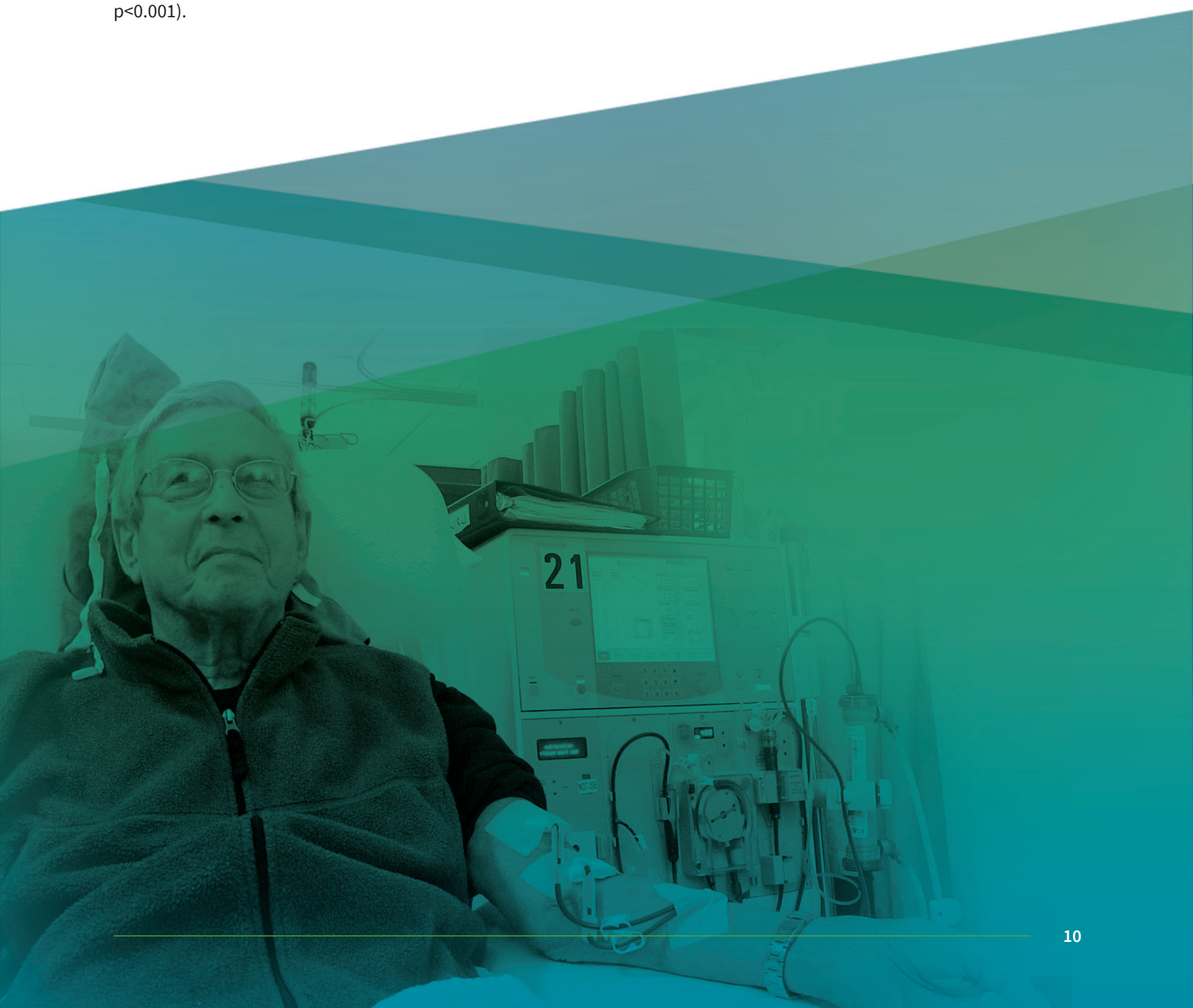


Table 1.
Clinical characteristics of TILDA participants. Distribution of CKD associated factors based on data from Wave 1 and Wave 3.

	2009-2011		2014-2015	
*Estimate***	**Unweighted**	**Weighted**	**Unweighted**	**Weighted**
Age, yr	62.0 (8.4)	62.4 (0.2)	66.5 (8.4)	66.9 (0.2)
Age, median, yr	61.0 (55, 68)	60.5 (0.2)	65 (60, 72)	64.9 (0.2)
Age group				
% 70+	20.1%	22.8%	33.2%	34.0%
Sex:				
% Male	46.6%	48.6% (0.8)	n.a.	n.a.
% Female	53.4%	51.3% (0.8)	n.a.	n.a.
Diabetes mellitus				
% Yes	6.2%	7.5% (0.5)	7.8%	8.8% (0.5)
HbA1c, mmol/l	32.0 (30.0, 35.0)	31.9 (0.07)	35.0 (33.0, 38.0)	34.7 (0.08)
Hypertension				
% Yes	34.3%	34.5% (0.9)	36.1%	36.9% (0.9)
Smoking				
% Current	13.7%	18.5% (0.8)	10.5%	14.3% (0.8)
% Former	40.1%	38.2% (0.9)	43.5%	42.6% (0.9)
% Never	46.8%	43.2% (0.9)	45.9%	43.1% (0.9)
Obesity				
% Yes	31.9%	32.1% (0.87)	32.1%	32.7% (0.88)
% No	68.1%	67.9% (0.87)	67.9%	67.3% (0.88)
Residence				
% Rural	46.6%	43.8% (1.0)	46.2%	43.4% (1.0)
% Dublin County	26.5%	29.0% (0.9)	27.1%	29.1% (0.9)
% Other City	26.9%	27.1% (0.9)	26.7%	27.3% (0.9
Education				
% Primary	22.16%	28.7% (0.9)	22.21%	28.6% (0.93)
% Secondary	41.53%	47.5% (0.9)	39.73%	45.4% (0.93
% Higher	36.31%	23.7% (0.7)	38.06%	25.9% (0.74
Insurance				
% Medical card	39.1%	45.7% (1.0)	46.9%	52.2% (1.0
% Medical insurance	50.5%	42.3% (0.9)	44.1%	36.6% (0.9)
% Not insured	10.2%	11.9% (0.6)	8.9%	10.1% (0.6)
AHT treatment				
% Yes	33.5%	34.4% (0.9)	42.7%	44.1% (0.9)
% No	66.5%	65.5% (0.9)	57.3%	55.8% (0.9)

**Diabetes and hypertension diagnosis were self-reported. AHT treatment includes diuretics, beta-blockers, calcium channel blockers, ACE inhibitors, Angiotensin receptor antagonists, other Renin-Angiotensin System agents, or other antihypertensives. This corresponds to ATC codes C02, C03, C0, C08, and C09

***The unweighted estimate data are mean (standard deviation), and median (1st quartile, 3rd quartile), and the weighted data are presented as an estimate and standard errors.

Abbreviations: AHT; anti-hypertensive, HbA1c; haemoglobin A1c

5.2 Prevalence of CKD Stage ≥ 3 according to CKD-EPI eGFR formulas with and without race adjustment

Various eGFR formulas are available to estimate kidney function.[15,18-22] Current guidelines recommend reporting kidney function using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations unless other equations are more accurate in a given population, and recommend the combination of creatinine and cystatin C (eGFRcys-cre) as more accurate than either eGFRcre or eGFRcys alone. Importantly, based on previous studies of cohorts of community-dwelling older adults, such as TILDA , the CKD-EPI equation was documented to outperform other formulae (such as Berlin Initiative Study (BIS), Full Age Spectrum (FAS), or Asian), when validated against measured GFR (mGFR) using iohexol clearance 20. Furthermore, using the CKD-EPI equations, eGFRcys-cre performed better than using either marker alone. Finally, the KDIGO recommendations advise utilizing eGFRcys or the eGFRcys-cre combination rather than eGFRcre when the urinary albumin:creatinine ratio (ACR) data are unavailable 5. For these reasons, our presentation of the results in the following sections will mainly focus on the CKD-EPI GFRcys-cre combination equation estimates.

In this section, we compare how using different CKD-EPI GFR formulae, based on either cystatin C and/or creatinine, and with- versus without- the race correction, translates to the differences in CKD prevalence, based on the analysis of our cohort at TILDA Wave 3. Figure 1a illustrates the proportion of CKD cases across four age categories (i.e., 50-59, 60-69, 70-79, and 80+ years) using the different CKD-EPI GFR equations. Estimates, based on standardised weights, are presented separately in Panel B. The average eGFRcys-cre estimated with the race correction was 78.8 mL/min/1.73 m2 (range: 11.6; 126.6), and the median was 80.8 (IQR: 68.1 - 91.4). For the cys-cre combination CKD-EPI formula eliminating the race correction from the eGFR equation, the average eGFR was 82.6 mL/min/1.73 m2 (range: 12.4; 129.0), and the median was 84.8 (95% CI: 84.1 – 85.6). When compared with eGFRcys-cre including the race correction in the equation, the new CKD-EPI formula with the race-adjustment removed generated slightly higher eGFR values across all four age sub-groups (the average difference was 4 mL/min/1.73 m2), which translated to marginally lower CKD prevalence of 2.10% in age category 50-59, 5.25% in age category 60-69, 19.18% in age category 70-79, and 49.80% in the 80+ age category (the overall CKD prevalence at Wave 3 of TILDA was 13.29% (95% CI: 11.89, 14.69)) (for comparison of different eGFR formulas see also Table 2).

At both time points and different age sub-groups, we observed similarly large differences between plasma cystatin C-based and plasma creatinine-based GFR estimates: the median cystatin C-based measure was 6.5 ml/min/1.73 m2 lower in males and 8.1 ml/min/1.73 m2 lower in females. Accordingly, the CKD prevalence was about 30-40% greater when using cystatin C-estimated GFR than the creatinine-estimated GFR (see Figure 1, Panel A and B), additionally the eGFRcys-cre combination equation yielded slightly lower kidney function estimates than eGFRcys.

Figure 1. Cross-sectional prevalence of CKD Stage ≥ 3 based on different CKD-EPI eGFR equations: (A) unweighted prevalence in the TILDA dataset, and (B) the estimated prevalence in the Irish population based on standardisation with sampling weights. The results are based on TILDA Wave 3 data. CKD-EPI refit refers to the GFR equation refitted to remove the race adjustment from the regression equation. Abbreviations: cys; cystatin C, cre; creatinine, EPI-eGFR; Chronic Kidney Disease Epidemiology Collaboration- estimated Glomerular Filtration Rate

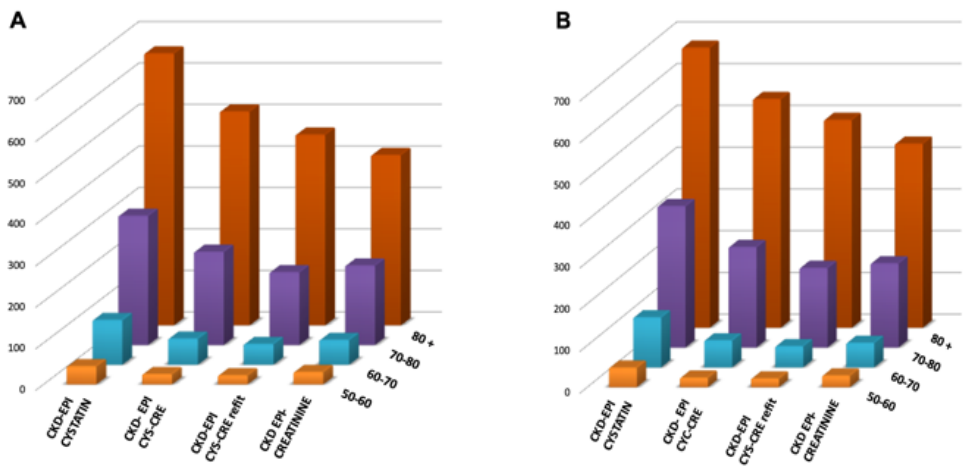


Table 2.
Cross-sectional prevalence of CKD in the Irish population based on different cystatin C and creatinine CKD-EPI eGFR equations. Data are based on TILDA Wave 3.

	Age sub-group			
% (95% CI)	**50-59 N=922**	**60-69 N=1596**	**70-79 N=918**	**80+ N=335**
All				
eGFRcyscre <60 ml/min	2.39% (1.36; 3,42)	6.58% (5.22; 7.93)	24.13% (20.85; 27.41)	54.8% (3.1)
eGFRcyscre*<60 ml/min	2.10% (1.12, 3.07)	5.25% (4.02, 6.48)	19.18% (16.16, 22.19)	49.80% (43.60, 56.00)
eGFRcre <60ml/min	2.79% (1.68, 3.89)	5.86% (4.60, 7.11)	20.2% (17.09, 23.38)	44.10% (37.96, 50.23)
eGFRcys<60ml/min	4.70% (3.13, 6.27)	12.03% (10.18, 13.89)	33.97% (30.38, 37.55)	67.12% (61.26, 72.98)
Male				
eGFRcyscre<60ml/min	2.40% (1.01, 3.78)	4.82% (3.18, 6.46)	23.10% (18.49, 27.72)	50.41% (41.60, 59.22)
eGFRcyscre*<60ml/min	2.23% (0.89, 3.58)	3.72% (2.25, 5.19)	18.27% (14.11, 22.43)	45.00% (36.18, 53.81)
eGFRcre<60ml/min	3.10% (1.51, 4.70)	5.13% (3.44, 6.82)	17.74% (13.55, 21.92)	39.78% (31.18, 48, 36)
eGFRcys<60ml/min	4.72% (2.44, 7.01)	9.00% (6.56, 11.43)	30.48% (25.55, 35.42)	63.64% (55.16; 72.12)
Female				
eGFRcyscre<60ml/min	2.39% (0.83, 3.95)	8.31% (6.17, 10.46)	25.16% (20.52, 29.79)	57.76% (49.56, 65.97)
eGFRcyscre*<60ml/min	1.96% (0.52, 3.39)	6.76% (4.80, 8.72)	20.08% (15.76, 24.41)	52.93% (44.59, 61.26)
eGFRcre<60ml/min	2.45% (0.91, 4.09)	6.57% (4.73, 8.42)	22.74% (18.23, 27.24)	46.92 (38.59, 55.24)
eGFRcys<60ml/min	4.68% (2.49, 6.86)	15.03% (12.22, 17.83)	37.44% (32.35, 42.53)	69.39% (61.73, 77.05)

Abbreviations: cys; cystatin C, cre; creatinine, eGFR; estimated Glomerular Filtration Rate eGFR, CI; confidence interval
*Indicates the eGFR formula refitted to remove race adjustment

5.3 Cross-sectional prevalence of CKD Stage ≥ 3 based on TILDA Wave 1 data:

Based on weighted estimates, the estimated national prevalence of CKD Stage ≥ 3 based on eGFR below the threshold of 60 ml/min/1.73 m2, was 11.73% (95% CI: 10.41, 13.05), using the race-adjusted CKD-EPIcys-cre equation. The prevalence was 34.81% (95% CI: 30.63, 38.98) in Irish individuals 70+. In men and women, the prevalence of CKD was 8.22% (95% CI: 6.77, 9.69) and 15.05% (95% CI: 12.97; 17.14), respectively; it increased with age in both sexes. (Table 3).

CKD Stage ≥ 3 was estimated among more than half (59.0% (95% CI: 48.76, 69.21)) of individuals aged 80 years or older, 26.65% (95% CI: 22.66, 30.64) of adults aged 70 to 79 years, 8.73% (95% CI: 6.96, 10.50) of adults aged 60 to 69 years, and 2.05% (95% CI: 1.31, 2.75) of adults aged 50 to 59 years. This was accompanied by a higher prevalence of diabetes and high blood pressure in older adults. The prevalence of CKD Stage ≥ 3 in individuals without these comorbidities was 52.79% (95% CI: 36.52, 69.05) of those aged 80 years or older, 17.55% (95% CI: 12.44, 22.67) of adults aged 70 to 79 years, 5.34 % (95% CI: 3.44, 7.24) of adults aged 40 to 59 years, and 0.94 (95% CI: 0.38, 1.50) of adults aged 50 to 59 years old (overall prevalence was 6.33 % (95% CI: 5.07, 7.59)).

Table 3.
Prevalence of CKD Stage 3 or greater according to age and sex. Data are based on TILDA Wave 1.

	N TOTAL*	N CASES	PREVALENCE %	WEIGHTED PREVALENCE % (95% CI)
MALE				
50-59	768	5	0.77	1.04 (0.28, 1.79)
60-69	616	36	6.33	7.08 (4.71, 9.46)
70-79	319	64	20.0	21.18 (16.12, 26.23)
80+	53	26	49.05	45.51 (29.82, 61.19)
TOTAL	1,756	140	7.97	8.22 (6.76, 9.68)
FEMALE				
50-59	899	25	3.05	3.03 (1.81; 4.26)
60-69	727	61	8.91	10.34 (7.70, 12.98)
70-79	325	91	28.00	31.68 (25.54, 37.82)
80+	64	40	61.53	65.85 (52.84; 78.87)
TOTAL	2,015	223	11.06	15.05 (12.97, 17.14)

Abbreviations: CI; confidence interval

*The weighted prevalence estimates have been calculated for 3,771 out of 3,774 participants in the final dataset, 3 individuals were excluded due to missing cluster/weights data.

5.4 Cross-sectional prevalence of CKD Stage ≥ 3 based on TILDA Wave 3 data:

The overall national prevalence of CKD Stage ≥ 3 at Wave 3 was 15.63% (95% CI: 14.15; 17.10) using the race-adjusted CKD-EPIcys-cre equation and was higher than estimates at TILDA Wave 1 as presented in Table 2. This was accompanied by a higher frequency of individuals within older age categories compared with Wave 1 (A total of 1253 TILDA participants were older than 70 years, representing approximately 33.2% of the sample size at Wave 3). The prevalence was 35.86% (95% CI: 32.55, 39.17) in Irish individuals 70+. The overall CKD prevalence was 13.06% (95% CI: 11.26; 14.84) in men and it was 18.05% (95% CI: 15.85; 20.25) in women (p-value for the difference <0.001).

The age-standardized CKD prevalence (separately in men and women) is summarized in Table 4. The estimated prevalence of CKD Stage ≥ 3 was more than half (54.86% (95% CI: 48.72, 61.00)) of individuals aged 80 years or older, 24.13% (95%CI: 20.85, 27.42) in adults aged 70 to 79 years, 6.60% (95% CI: 5.22, 7.93) in adults aged 60 to 69 years, and only 2.39% (95% CI: 1.37, 3.43) in adults aged 50 to 59 years. The prevalence of CKD Stage ≥ 3 in those without comorbidities (hypertension or diabetes) was 50.38% (40.71; 59.99) of individuals aged 80 years or older, 17.48 (95 % CI: 13.41; 21.55) of adults aged 70 to 79 years, 4.31% (95% CI: 2.80; 5.48) of adults aged 60 to 69 years, and 1.66% (95% CI: 0.69; 2.63) of adults aged 50 to 59 years (the overall prevalence was 10.01% (95% CI: 8.44; 11.58)).

Table 4.
Prevalence of CKD Stage 3 or greater according to age and sex distribution. Data are based on TILDA Wave 3.

	N TOTAL*	N CASES	PREVALENCE %	WEIGHTED PREVALENCE % (95% CI)
MALE				
50-59	429	12	2.80	2.40 (1.02; 3.79)
60-69	719	37	5.14	4.82 (3.18; 6.46)
70-79	453	97	21.14	23.11 (18,49; 27.72)
80+	155	78	50.32	50.41 (41.60; 59.22)
TOTAL	1756	224	12.75	13.06 (11.26; 14.86)
FEMALE				
50-59	493	12	2.43	2.39 (0.89; 3.95)
60-69	877	64	7.29	8.32 (6.17; 10.46)
70-79	465	110	23.65	25.16 (20.53; 29.79)
80+	180	95	52.78	57.77 (49.56; 65.97
TOTAL	2015	281	13.95	18.05 (15.86; 20,24)

Abbreviations: CI; confidence interval

*The weighted prevalence estimates have been calculated for 3,771 out of 3,774 participants in the final dataset, 3 individuals were excluded due to missing cluster/weights data.

5.5 Cross-sectional prevalence of CKD Stage ≥ 3: related comorbidities and their interaction with age on the odds of being diagnosed with CKD

5.5.1 Diabetes mellitus type 2

Diabetes is the most established causative factor for CKD, and new treatment options to slow progression and reduce morbidity and mortality are increasingly available. In line with previous findings, in our cohort diabetes was associated with increased odds of being diagnosed with CKD. Based on data from TILDA Wave 1, the national prevalence of CKD was 23.93% (95% CI: 17.19; 30.61) in Irish individuals aged 50+ with diabetes mellitus and 10.76% (95% CI: 9.47; 12.05) in non-diabetic individuals (OR= 2.62 (95% CI: 1.77, 3.86). The national prevalence was 25.21% (95% CI: 19.27; 31.13) and 14.70% (95% CI: 13.21, 16.19) respectively, based on the data from TILDA Wave 3 (OR=1.94 (95% CI: 1.40, 2.73)).

The risk of CKD at Wave 3 TILDA according to age (i.e., 50-59, 60-69, 70-79, and 80+) and diabetes status, is shown in Table 5. In age sub-groups < 80 years, this risk differed according to the presence of diabetes. Specifically, in the 60-69- and 70-79 year age groups, we observed, respectively, an increased CKD frequency, as compared with the estimates in non-diabetic participants. However, these associations were attenuated in the oldest sub-group (i.e., 80+ years) compared to younger individuals.

Table 5.
Prevalence of CKD Stage 3 or greater according to age and diabetes status. Data are based on TILDA Wave 3.

	N TOTAL*	N CASES	PREVALENCE %	WEIGHTED PREVALENCE % (95% CI)
WITHOUT DM	N=3475			
50-59	880	23	2.61	2.48 (1.39; 3.56)
60-69	1478	90	6.09	6.47 (5.05; 7.87)
70-79	820	170	20.73	21.20 (18.03; 24.48)
80+	297	154	51.85	55.72 (49.28; 62.16)
TOTAL	3475	437	12.57	14.70 (13.21, 16.19)
WITH DM	N=296			
50-59	42	1	2.39	0.98 (0.00; 3.10)*
60-69	118	11	9.32	7.91 (2.99, 12.82)
70-79	98	37	37.78	44.94 (32.88; 57.00
80+	38	19	50.00	48.63 (29.97; 67.30)
TOTAL	296	68	22.97	25.21 (19.27; 31.13)

Abbreviations: CI; confidence interval

*The estimate has wide CI intervals ad may be less accurate. The weighted prevalence estimates have been calculated for 3,771 out of 3,774 participants in the final dataset, 3 individuals were excluded due to missing cluster/weights data.

5.5.2 Hypertension

Similar analyses were conducted for the association between CKD Stage ≥ 3 and self-reported hypertension (HT) (see Table 6). The proportion of CKD cases in Ireland increased more than three times in people with prevalent HT, based on data from Wave 1 of TILDA (21.20 % (95% CI: 18.41, 24.00) vs. 6.74 % (95%CI: 5.45, 8.02), OR= 3.39 (95% CI: 2.14, 3.33)). Similarly, the odds of CKD were more than doubled in hypertensive individuals at TILDA Wave 3 (24.16 % (95% CI: 21.34, 26.95) vs. 10.64% (95% CI: 9.07, 12.21), OR= 2.67 (95% CI: 2.14, 3.33)). These associations were stronger in younger participants (with CKD being more than two times more prevalent in those with HT in age subgroups 50-69) versus the oldest age category (see Table 6). In the participants 80 years or older, age appeared the major determinant of CKD diagnosis. Similar patterns of association across age categories were observed at TILDA Wave 1 (data not shown). Additionally, considerable gender differences were found in the association between HT and CKD risk when controlled for age; the relationship appeared stronger in male than in female participants, at both study time-points.

Table 6.
Prevalence of CKD Stage 3 or greater according to age sub-group and hypertension status. The estimates are based on Wave 3 of TILDA.

	N TOTAL*	N CASES	PREVALENCE %	WEIGHTED PREVALENCE % (95% CI)
NO HT				
50-59	691	12	1.73	1.62 (0.67, 2.55)*
60-69	1048	39	3.72	4.28 (2.81, 5.76)
70-79	519	92	17.72	19.59 (15.41, 23.78)
80+	151	71	47.01	51.41 (42.19, 60.64)
TOTAL	2409	214	8.89	10.64 (9.07, 12.21)
WITH HT				
50-59	231	12	5.19	4.80 (1.76; 7.85)*
60-69	548	62	11.31	10.88 (8.14; 13.62)
70-79	339	115	33.92	30.07 (24.92, 35.23)
80+	184	102	55.43	57.46 (49.31, 65.60)
TOTAL	1362	291	21.36	24.16 (21.34, 26.95)

Abbreviations: CI; 95% Confidence Interval.

*The estimate has wide confidence intervals and may be less accurate.

^The weighted prevalence estimates have been calculated for 3,771 out of 3,774 participants in the final dataset, 3 individuals were excluded due to missing cluster/weights data.

5.5.3. Other CKD-related risk factors

In all individuals aged 50+ with eGFR available, the risk of being diagnosed with CKD did not increase with smoking (OR at Wave 3 = 1.12, 95%CI: 0.89; 1.39) and was not significantly different according to the localization of residency in Ireland (Rural vs Dublin or rural vs another city). Among other putative risk factors, higher body weight, defined as BMI >30 kg/m2, was associated with higher odds of CKD prevalence at both Waves in the univariable model; the association persisted (statistically significant) after adjusting for age and sex. Among other socio-economic factors, lower education was strongly associated with greater CKD prevalence, however; this association was attenuated in the multivariable model.

5.6 Prevalence of eGFR stages/CKD grades at TILDA Wave 1 and TILDA Wave 3

CKD and its severity identifies individuals who are at increased risk of future adverse health outcomes and premature mortality. We evaluated the risk profile/eGFR grading of the participants with eGFR diagnosed CKD. The distribution of eGFR CKD stages at TILDA Wave 3 is illustrated in Table 8 and plotted in Figure 2. The same is presented for Wave 1 in Table 7. To allow comparison with previously published data we additionally present the results based on different cystatin C and creatinine based CKD-EPI eGFR formulae.

The national prevalence of mildly decreased to severe renal impairment based on Wave 3 of TILDA was 15.63% (95% CI 20.4-23.5%) using the race-adjusted CKD-EPI eGFRcys-cre thresholds; most cases of CKD were mild-to-moderate (i.e., CKD3a). Based on the subdivision of stage 3 CKD, the prevalence of Stage 3a (eGFR > 45–59 ml/min/1.73 m2) was 9.87% (95% CI: 8.72-11.02) and the prevalence of Stage 3b was 4.42% (95% CI: 3.65, 5.28) (see Table 7). Of all participants, 166 had advanced CKD (i.e., CKD Stage 3b or 4), which translated to a national estimate of 5.70% (95%: 4.69, 6.71) of the Irish population aged 50+ years; only two individuals presented with End Stage Kidney Disease (ESKD) at TILDA Wave 3, these participants were not included in the main analyses. Among adults aged 70+ years, 14.11% (95% CI: 11.50, 16.73) had advanced CKD, compared with 1.26% (95% CI: 0.82, 1.71) among younger individuals.

The standardized prevalence of CKD stage 3 at study Wave 1 was 11.73% (95% CI: 10.41, 13.05), based on race-adjusted creatinine/cystatin C-assessment with the CKD-EPI equation; 3.42 % (95% CI: 2.60, 4.24) of the entire Irish population aged 50+ years had advanced CKD. Of all, 33.14% had normal to increased eGFR, 55.11% had normal to mildly reduced eGFR, 8.31% had CKD stage 3a, 3.00% had CKD stage 3b, 0.42% had CKD stage 4, and 0% developed CKD stage 5 (see Table 8). Among Irish adults aged 70 yrs or older, 12.01% (95%: 8.81, 15.20) had advanced CKD.

The characteristics of TILDA participants by eGFR based CKD stage at Wave 1 of TILDA is shown in the Appendix Section (Table 24). Older age, higher haemoglobin A1c (HbA1c) concentration, systolic blood pressure, and hypertension were significantly associated with CKD presence and also increased severity of CKD.

Table 7.
Cross-sectional prevalence of eGFR categories in Irish adults 50+ by different CKD-EPI equations. Data are based on Wave 1 of TILDA

		eGFR stage % (SE) weighted prevalence estimate 2009-2011		
	eGFRcys-cre	**eGFRcre**	**eGFRcys-cre***	**eGFRcys**
CKD STAGE 1	33.1% (0.88)	32.7% (0.88)	42.6% (0.92)	33.5% (0.86)
CKD STAGE 2	55.1% (0.92)	55.6% (0.93)	48.3% (0.93)	51.8% (0.92)
CKD STAGE 3A	8.3 % (0.56)	8.6% (0.55)	6.2% (0.48)	9.93% (0.61)
CKD STAGE 3B	3.0 % (0.39)	2.6% (0.36)	2.5% (0.37)	3.89% (0.43)
CKD STAGE 4	0.4 % (0.14)	0.41% (0.13)	0.4% (0.13)	0.79% (0.19)
CKD STAGE 5	0 %	0%	0.0%	0.0%
TOTAL CKD ≥ STAGE 3	11.7% (0.67)	11.6% (0.66)	9.1% (0.61)	13.1% (0.70)
TOTAL 3B-4	3.42% (0.41)	3.06% (0.39)	2.85% (0.39)	4.69% (0.47)

*Indicates the new eGFR formula refitted to remove the race adjustment from the regression equation. Abbreviations: cys; cystatin C, cre; creatinine, eGFR; estimated Glomerular Filtration Rate, SE; standard error

Table 8.
Cross-sectional prevalence of eGFR categories in Irish adults 50+ by different CKD-EPI equations. Data are based on Wave 3 of TILDA

		eGFR stage % (SE) weighted prevalence estimate 2013-2015		
	eGFRcys-cre	**eGFRcre**	**eGFRcys-cre***	**eGFRcys**
CKD STAGE 1	29.3% (0.83)	34.6% (0.88)	38.7% (0.90)	25.4% (0.78)
CKD STAGE 2	54.9% (0.93)	52.2% (0.92)	47.9% (0.91)	52.4% (0.92)
CKD STAGE 3A	9.8% (0.58)	9.0% (0.56)	8.56% (0.55)	13.34% (0.65)
CKD STAGE 3B	4.4% (0.43)	3.2% (0.38)	3.46% (0.33)	6.49% (0.51)
CKD STAGE 4	1.3% (0.25)	0.92% (0.24)	1.23% (0.25)	2.19% (0.33)
CKD STAGE 5	0.05% (0.03)	0.03% (0.03)	0.03% (0.03)	0.07% (0.04)
TOTAL CKD ≥ STAGE 3	15.6% (0.75)	13.1% (0.70)	13.3% (0.71)	22.1% (0.84)
TOTAL 3B-4	5.70% (0.51)	4.14% (0.45)	4.70% (0.47)	8.69% (0.60)

*Indicates the eGFR formula refitted to remove the race adjustment from the regression equation. Abbreviations: cys; cystatin C, cre; creatinine, eGFR; estimated Glomerular Filtration Rate, SE; standard error.

5.6.2 Age-specific prevalence of eGFR stages at TILDA Wave 1 & TILDA Wave 3

The prevalence of eGFR grades by age sub-categories at Wave 1 is summarized in Table 9, the same is shown for Wave 3 (see Table 10). At both study waves, we observed, respectively a reduced and increased prevalence of normal to increased eGFR, and mildly to severely reduced eGFR with increasing age category. Particularly, the proportion of individuals with CKD stage 3b–4 in the entire population increased exponentially with age. Similar patterns were obtained for CKD defined with the race-neutral eGFR CKD-EPI formula; the estimated prevalence of GFR Stages with the refitted equation by four age subgroups is summarised in Table 11 and Table 12 and the number of TILDA participants at each eGFR stage by age category is shown in the Appendix section.

Table 9.
eGFRcys-cre (CKD-EPI combination equation) estimated prevalence of eGFR stages in Irish adults aged 50+ years by age group. Data are based on TILDA Wave 1.

% (SE)	Age sub-group at Wave 1 50-59 N=1670*	60-69 N=1343	70-79 N=644	80+ N=117
All				
CKD GFR1	52.46% (1.37)	25.59% (1.34)	8.71% (1.21)	0.27% (0.27)
CKD GFR2	45.49% (1.37)	65.66% (1.46)	64.63% (2.14)	40.71% (5.14)
CKD GFR3a	1.71% (0.33)	7.10% (0.82)	19.54% (1.80)	32.44% (4.90)
CKD GFR3b	0.31% (0.15)	1.58% (0.38)	6.26% (1.19)	22.05% (4.76)
CKD GFR4	0.0%	0.04% (0.04)	0.84% (0.45)	4.49% (2.01)
CKD GFR5	0.0%	0.0%	0.0%	0.0%
CKD3b-4	0.31% (0.15)	1.63% (0.39)	7.10% (1.26)	26.55% (4.92)

Abbreviations: GFR; Glomerular Filtration Rate, SE; standard error. * the weighted estimates were derived for 1667 out of 1670 individuals due to missing cluster/weight data.

Table 10.
eGFRcys-cre (CKD-EPI combination equation) category estimated prevalence of CKD in Irish population aged 50+ years by age group. Data are based on TILDA Wave 3.

% (SE)	Age sub-group at Wave 3 50-59 N=925	60-69 N=1596	70-79 N=918	80+ N=335
All				
CKD GFR1	53.55% (1.81)	32.75% (1.29)	10.71% (1.06)	2.51% (0.97)
CKD GFR2	44.04% (1.82)	60.66% (1.34)	65.15% (1.77)	42.62% (3.09)
CKD GFR3a	1.52% (0.44)	4.99% (0.62)	16.93% (1.41)	29.40% (2.81)
CKD GFR3b	0.66% (0.25)	1.34% (0.31)	5.40% (0.98)	19.41% (2.45)
CKD GFR4	0.09% (0.09)	0.24% (0.11)	1.80% (0.60)	5.91% (1.57)
CKD GFR5	0.11% (0.11)	0.0%	0.0%	0.13% (0.13)
CKD3b-4	0.76% (0.27)	1.59% (0.32)	7.20% (1.13)	25.32% (2.81)

Abbreviations: GFR; Glomerular Filtration Rate, SE; standard error. * The weighted estimates were derived for 922 out of 925 individuals due to missing cluster/weight data.

Table 11.
eGFRcys-cre (CKD-EPI combination equation) category prevalence of CKD in the Irish population aged 50+ years using the race-neutral equation. The estimates are based on TILDA Wave 1 data.

	Age sub-group at Wave 1			
% (SE)	50-59	60-69	70-79	80+
All	N=1670	N=1343	N=644	N=117
CKD GFR1	61.18% (1.33)	38.52% (1.49)	15.72% (1.62)	3.16% (1.80)
CKD GFR2	37.53% (1.33)	55.03% (1.53)	62.84% (2.20)	49.77% (5.28)
CKD GFR3a	1.01% (0.24)	5.50% (0.76)	15.16% (1.67)	23.70% (4.36)
CKD GFR3b	0.27% (0.14)	0.89% (0.27)	5.42% (1.13)	19.66% (4.59)
CKD GFR4	0.0%	0.04% (0.04)	0.83% (0.45)	3.69% (1.85)
CKD GFR5	0.0%	0.0%	0.0%	0.0%
CKD GFR3b-4	0.27% (0.14)	0.93% (0.28)	6.26% (1.21)	23.35% (4.77)

Abbreviations: GFR; Glomerular Filtration Rate, SE; standard error. * the weighted estimates were derived for 1667 out of 1670 individuals due to missing cluster/weight data.

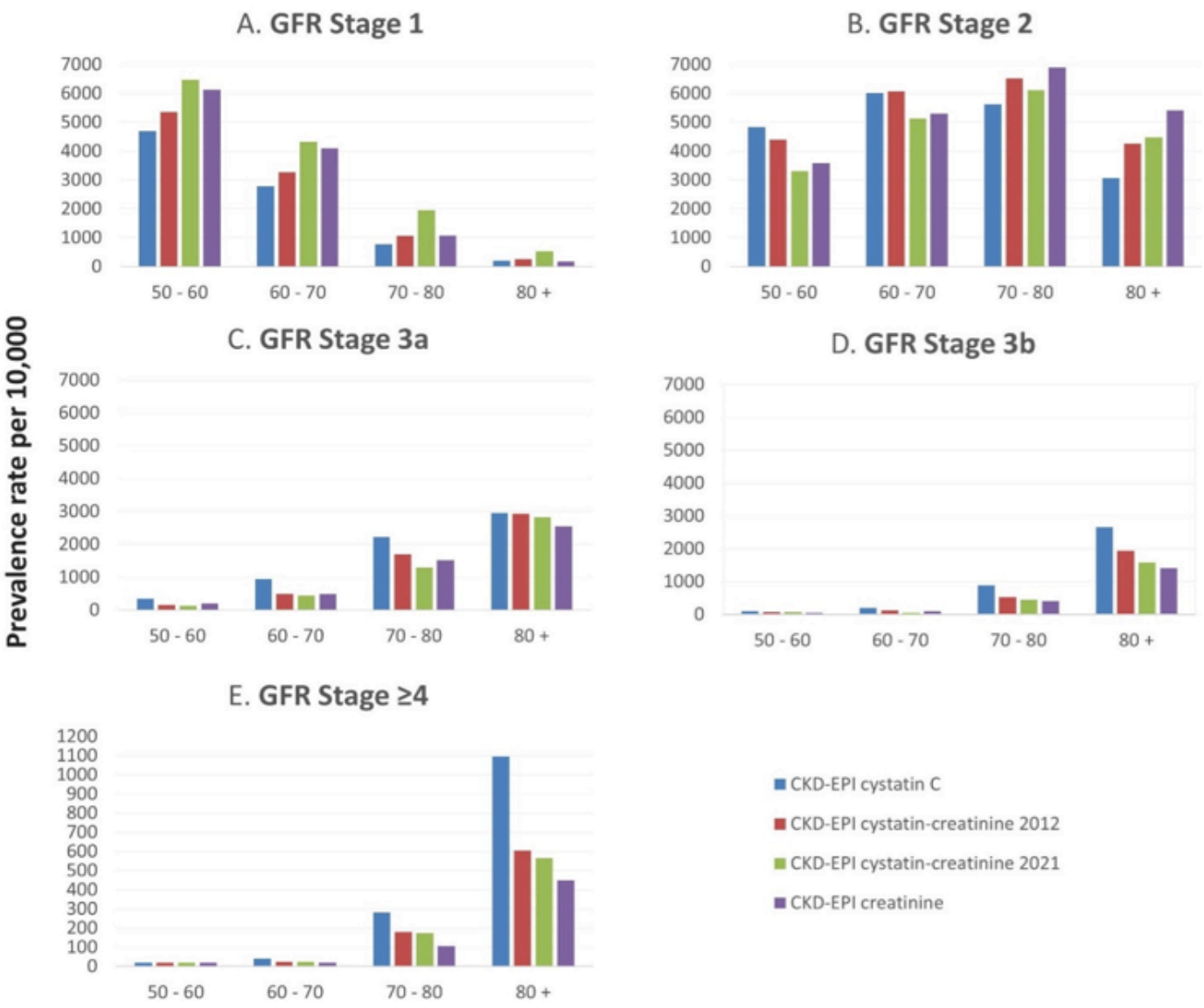
Supplementary Table 12.
eGFRcys-cre (CKD-EPI combination equation) category prevalence of CKD in the Irish population aged 50+ years, using the race-neutral equation. The estimates are based on TILDA Wave 3 data.

	Age sub-group at Wave 3			
% (SE)	50-59	60-69	70-79	80+
All	N=925	N=1596	N=918	N=335
CKD GFR1	64.82% (1.77)	43.30% (1.37)	19.63% (1.44)	5.34% (1.28)
CKD GFR2	33.07% (1.75)	51.44% (1.38)	61.18% (1.81)	44.85% (3.09)
CKD GFR3a	1.22% (0.40)	4.42% (0.59)	12.92% (1.23)	28.23% (2.80)
CKD GFR3b	0.66% (0.25)	0.58% (0.18)	4.50% (0.91)	15.91% (2.31)
CKD GFR4	0.09% (0.09)	0.24% (0.11)	1.75% (0.60)	5.65% (1.53)
CKD GFR5	0.11 (0.11)	0.0%	0.0%	0.0%
CKD GFR3b-4	0.75% (0.27)	0.82% (0.21)	6.25% (1.08)	21.57% (2.70)

Abbreviations: GFR; Glomerular Filtration Rate, SE; standard error. * The weighted estimates were derived for 922 out of 925 individuals due to missing cluster/weight data.

Figure 2.
Age-dependent proportion of Irish adults aged 50+ years at each eGFR stage, based on various CKD-EPI eGFR formulae. The prevalence estimates are based on data from Wave 3 of TILDA.

The respective CKD eGFR Stages 4 and 5 were pooled together. The CKD-EPI cystatin-creatinine 2012 indicates the equation including the race-coefficient. The estimates are weighted prevalence rates expressed per 10,000 individuals. Abbreviations: GFR; glomerular filtration rate. The detailed results for the specific eGFR equations are shown in the Appendix section.



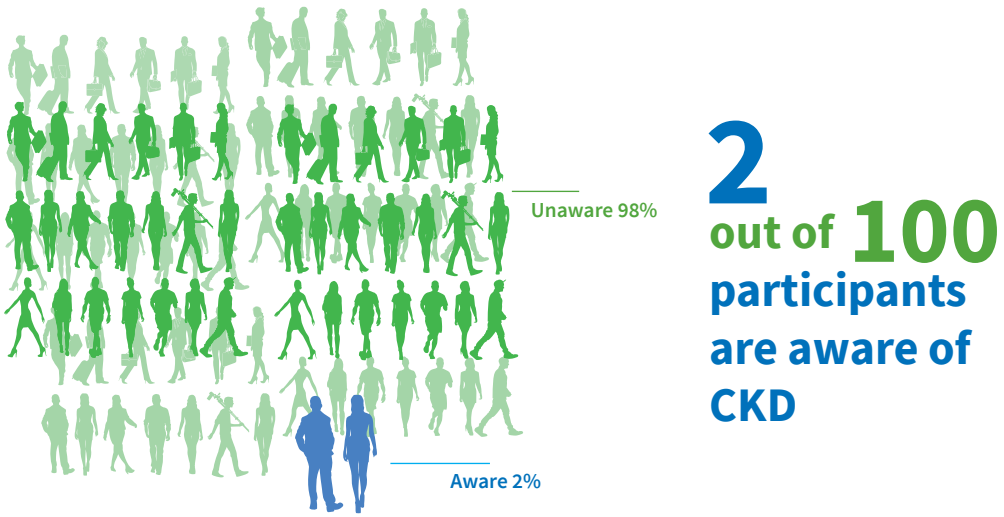
5.7 Characteristics of TILDA participants with prevalent CKD at TILDA Wave 3

Next, we have characterised the sub-group of 505 TILDA participants who had laboratory-diagnosed CKD Stage 3 or greater at TILDA Wave 3 (based on eGFRcre-cys combination equation and including the race coefficient). In particular, we were interested in their awareness of kidney function impairment, their blood pressure control, and anti-hypertensive medication prescription.

5.7.1 Disease Awareness Among TILDA participants with CKD

The prevention of complications of CKD is limited by its silent nature along with the lack of awareness. According to an analysis of the National Health and Nutrition Examination Survey (NHANES), more than 90% of United States Residents aged 20 years or above, who had CKD by current definitions were unaware. In our analysis we found that amongst TILDA participants who fulfilled the diagnostic criteria for CKD Stage 3 or greater, 2% were routinely diagnosed with CKD based on the self-reported disease diagnosis (see Figure 3).

Figure 3.
Percentage of TILDA participants 50 years or older with CKD who were aware of the disease. Data are based on TILDA study Wave 3 data



5.7.2. Blood pressure control amongst TILDA participants with prevalent CKD

The presence of hypertension is an important determinant of CKD progression and the predominant risk factor for future cardiovascular events. In our analyses, we observed, that in most TILDA participants with identified CKD, blood pressure control was less than optimal with 30-55% reaching the recommended target values, depending on the blood pressure management criteria (see Figure 4 Panel A and B). Of note, 412 participants (i.e., 81% of all CKD cases) had uncontrolled blood pressure according to the newly proposed KDIGO guidelines (i.e., systolic and diastolic BP < 120/80 mmHg).[5]

Figure 5 panel A shows the distribution of the participants with uncontrolled blood pressure (defined by the 2012 KDIGO cut-offs) across age and sex categories, panel B shows the prescription of anti-hypertensive medications (AHT). A total of 384 CKD participants (76.04%) have been prescribed at least one blood pressure-lowering medication. Among all CKD participants, the prevalence of antihypertensive medication use was slightly higher among men than women (78.9% vs. 72.9%) and increased monotonically across age categories. Specifically, the prescription of blood pressure–lowering medications was higher in people with CKD aged 60 years or older (about 76%) than in those with CKD aged 50–59 years (62.5%) with highest prevalence in CKD participants aged 80+ (80%). Amongst the participants with CKD and self-reported diabetes 89.7% were Prescribed Blood Pressure–Lowering Medications.

Figure 4.
Blood pressure (BP) control amongst TILDA participants diagnosed with CKD: A) based on 130/90 mmHg and B) based on 140/90 cut-offs for well-controlled systolic and diastolic BP. Estimates are based on Wave 3 data.

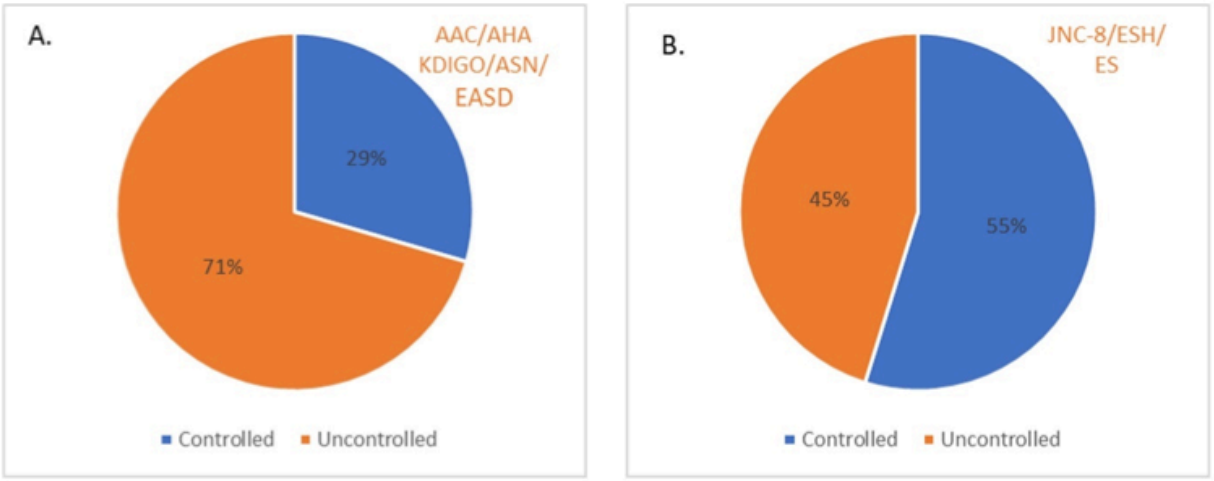
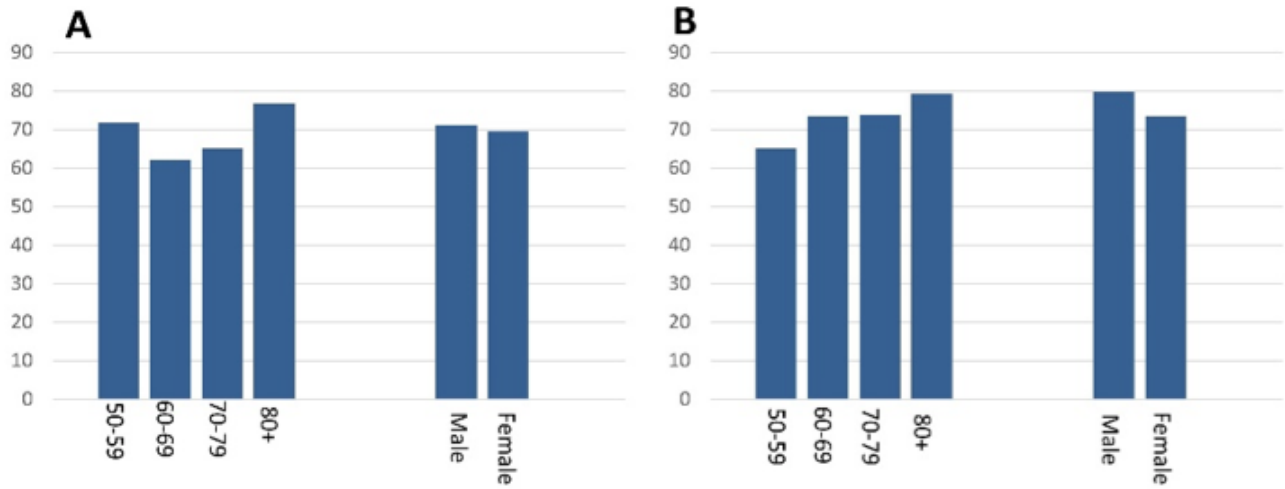


Figure 5.
Blood pressure (BP) control amongst participants diagnosed with CKD: **A.** Prevalence of uncontrolled BP based on KDIGO criteria (systolic or diastolic BP above 130/80 mmHg) by age, and sex distribution. **B.** Prescription of blood pressure–lowering medications amongst participants with CKD by age, and sex distribution. The estimates are based on Wave 3 data of TILDA. The prevalence of uncontrolled BP based on the ESH criteria was 34.9% in participants aged 50-59, 40.2% in participants aged 60-69, 40.9% in participants aged 70-79, and 55.8% in participants aged 80+.



5.8 National estimates in the Irish population

5.8.1 National estimates of CKD at TILDA Wave 3 according to the CKD-EPI eGFR cre-cys equation including the race coefficient

To derive the estimates of the number of people with CKD in Ireland in 2016, we have extrapolated our weighted estimates of CKD to the Central Statistics Office (CSO) of Ireland population data. The sample demographics are presented in Table 14. All estimates are based on data from Wave 3 (2014-2015) of TILDA and most recent population estimates are based on figures collected from the 2016 census (CSO) data, which has reported a total of 1,446,460 people aged over 50 years living in Ireland at that time point. Overall, 15.6% of individuals aged 50 years and older in Ireland have CKD, which equates to 225,937 people living with CKD (See Table 14).

The estimated national prevalence of CKD Stage 3 or greater (defined by eGFR calculated with the CKD-EPI cys-cre combination equation and including the race-coefficient) was 4.95% in individuals aged 50-69 and it was 35.86% in adults aged 70+, that has translated to 50,496 people aged 50-69, and 152,882 people 70+ residing in Ireland. The detailed estimates of the national prevalence of CKD Stage ≥ 3 in Ireland, split across age and sex sub-groups, are shown in Table 14.

As reported in the previous sections, the estimated national prevalence of severe CKD (defined as CKD 3b-4) was 5.70% at TILDA Wave 3. The estimated national prevalence was 1.25% in people 50-70 years old and 14.1% in people 70+, equating to 12,241 and 60,112 people in Ireland in these age categories (see Table 13). Of note, the TILDA sampling excluded people with dementia and people living in nursing homes and as such this data may slightly underestimate the CKD prevalence in the total population in Ireland. In addition, to date TILDA has not assessed urinary albumin excretion and thus we cannot discern CKD in participants with albuminuria but with a normal eGFR.

Table 13.
Percent prevalence of **advanced CKD (i.e., CKD3b-4)** at TILDA Wave 3 extrapolated to CSO population estimate data from 2016. CKD was defined by eGFR estimated with the CKD-EPI cys-cre combination equation and including the race coefficient

Age category (yrs)	Estimated Prevalence	2016 CSO TOTAL	Estimated number of CKD 3b-4 cases in Ireland
50-69	1.2%	1,020,129	12,241
70+	14.1%	426,331	60,112
Total*	5.7%	1,446,460	82,448

*The numbers refer to a number of cases in the community dwelling population aged 50+. The sum over age ranges may not equal the total which is due to slight inaccuracies in age estimates and rounding errors within age each age range.

Table 14.
Percentage prevalence of CKD Stage ≥ 3 at TILDA (Wave 3) extrapolated to central statistics office (CSO) population estimate data from 2016. CKD was defined by eGFR threshold estimated with the race-adjusted CKD-EPI cys-cre combination formula

Age category	Estimated Prevalence	2016 Census Total	Estimated number of CKD ≥ 3 cases in Ireland
Male			
50+ years	**13.06% (0.91)**	697,605	**91,107**
55+ years	**13.40% (0.94)**	**549,393**	**73,619**
55-59 years	2.19% (0.69)	133,858	**2,931**
60-64 years	3.34% (1.00)	118,698	3,965
65-69 years	6.42% (1.34)	104,961	6,738
70-74 years	17.64% (2.90)	79,501	14,024
75-79 years	31.63% (3.92)	54,117	17,117
80-84 years	44.83% (5.25)	35,196	15,866
85+ years	60.82% (8.21)	23,062	14,012
50-69 years	**3.87% (0.57)**	505,729	19,572
70+ years	**32.05% (2.21)**	191,876	61,496
Female			
50+ years	**18.05% (1.11)**	748,855	135,168
55+ years	**18.50% (1.14)**	**597,132**	**110,469**
55-59 years	2.65% (0.87)	136,244	3,610
60-64 years	6.09% (1.32)	120,158	7,318
65-69 years	10.79% (1.78)	106,275	11,467
70-74 years	16.24% (2.32)	82,771	13,442
75-79 years	39.44% (4.42)	61,350	24,196
80-84 years	51.72% (5.02)	45,841	23,709
85+ years	**67.02% (7.06)**	44,493	29,819
50-69 years	**6.03% (0.74)**	514,400	31,018
70+ years	**39.09% (2.38)**	234,455	91,648
All			
50+ years	**15.62% (0.75)**	1,446,460	225,937
55+ years	**16.02% (0.77)**	1,146,525	183,673
55-59 years	2.42% (0.55)	270,102	6,536
60-64 years	4.74% (0.83)	238,856	11,322
65-69 years	8.60% (1.12)	211,236	18,166
70-74 years	16.93% (1.86)	162,272	27,473
75-79 years	35.51% (2.93)	115,467	41,002
80-84 years	48.96% (3.67)	81,037	39,676
85+ years	**64.77% (5.45)**	67,555	43,755
50-69 years	**4.95% (0.47)**	1,020,129	50,496
70+ years	**35.86% (1.68)**	426,331	152,882

*The sum over age ranges may not equal total, due to slight inaccuracies in age estimates and rounding within age each age range.
*In some instances, the number of CKD cases in the TILDA dataset for each of the following categories is limited, and the estimates have wide confidence intervals and therefore may not be less reliable. The estimates for the 50-55 year old subgroup had very wide confidence intervals and were excluded from data presentation.

5.8.2 National prevalence of CKD at TILDA Wave 3 according to the race-neutral eGFR formula

To derive the estimates of CKD in Ireland with the most contemporary eGFR formula, we have replicated our analyses incorporating CSO data, using the CKD estimates based on the refitted eGFR CKD-EPI eGFRcys-cre combination equation (i.e., the race-free eGFRcys-cre).

When using the race-adjusted eGFRcys-cre CKD threshold, 13.29 % of individuals aged 50 or older had CKD (eGFR < 60 ml/min/1.73m2). The estimated national prevalence of CKD Stage 3 or greater was 4.95% in adults 50-69 years old, and it was 35.86% in adults aged 70+; this has translated to 50,496 people aged 50-69, and 152,882 people over 70 year old residing in Ireland. The detailed estimates of the national prevalence of CKD Stage ≥ 3 split across age and sex sub-groups are shown in Table 16. All the estimates are based on data from Wave 3 (2014-2015) of TILDA and the population estimates are based on figures collected from the 2016 Census of Ireland. Using the race free equation the overall prevalence of CKD in those aged 50 years and older was 13.29%, equating to 192234 individuals in Ireland living with CKD.

The estimated national prevalence of severe CKD (CKD ≥ 3b) was 4.70%. The estimated national prevalence was 0.80 % in people aged 50-70 years old and 12.09% in people aged 70+ years, equalizing to 8,161 and 51,586 people living in Ireland, respectively (see Table 15).

Table 15.
Percent prevalence of **advanced CKD** (i.e., CKD3b-4) at TILDA Wave 3 extrapolated to Central Statistics Office (CSO) population estimate data from 2016. CKD was defined by eGFR estimated with the CKD-EPI cys-cre combination equation refitted to remove the race coefficient from the regression equation

Age category (yrs)	Estimated Prevalence	2016 CSO TOTAL	Estimated number of CKD 3b-4 cases in Ireland
50-70	0.80 %	1,020,129	8,161
70+	12.09 %	426,331	51,586
Total	4.70%	1,446,460	67,983

*The numbers refer to a number of cases in the community-dwelling general population aged 50+. The sum over age ranges may not equal the total which is due to slight inaccuracies in age estimates and rounding errors within age each age range.

Table 16.

Percent prevalence of CKD Stage ≥ 3 at TILDA Wave 3 extrapolated to Central Statistics Office (CSO) population estimate data from 2016. CKD was defined by eGFR estimated with the CKD-EPI cystatin C-creatinine combination formula refitted to remove the race coefficient from the regression equation

Age category	Estimated Prevalence	2016 Census Total	Estimated number of CKD ≥ 3 cases in Ireland
Male			
50+ years	**10.93% (0.84)**	697,605	**76,248**
55+ years	**11.18% (0.87)**	**549,393**	**61,422**
55-59 years	2.09% (0.67)	133,858	2,677
60-64 years	2.57% (0.90)	118,698	3,050
65-69 years	4.96% (1.20)	104,961	5,206
70-74 years	13.67% (2.43)	79,501	10,868
75-79 years	25.45% (3.77)	54,117	13,773
80-84 years	39.37% (5.20)	35,196	13,857
85+ years	55.93% (8.31)	23,062	12,899
50-69 years	**3.14% (0.53)**	505,729	**13,880**
70+ years	**27.03% (2.11)**	191,876	**51,864**
Female			
50+ years	**15.53% (1.07)**	748,855	**116,297**
55+ years	**15.92% (1.09)**	597,132	**95,063**
55-59 years	2.17% (0.80)	136,244	2,956
60-64 years	4.84% (1.18)	120,158	5,815
65-69 years	8.91% (1.63)	106,275	10,426
70-74 years	13.14% (2.13)	82,771	10,876
75-79 years	31.20% (4.29)	61,350	19,141
80-84 years	43.73% (5.04)	45,841	20,046
85+ years	67.02% (7.06)	44,493	29,819
50-69 years	**4.91% (0.68)**	514,400	**25,257**
70+ years	**34.12% (2.35)**	234,455	**79,996**
All			
50+ years	**13.29% (0.71)**	1,446,460	**192,234**
55+ years	**13.62% (0.73)**	1,146,525	**156,156**
55-59 years	2.10% (0.52)	270,102	5,672
60-64 years	3.72% (0.75)	238,856	8,885
65-69 years	6.93% (1.02)	211,236	14,639
70-74 years	13.40% (1.61)	162,272	21,744
75-79 years	28.31% (2.84)	115,467	32,689
80-84 years	41.92% (3.65)	81,037	33,971
85+ years	63.03% (5.51)	67,555	42,580
50-69 years	**4.02% (0.43)**	1,020,129	**41,009**
70+ years	**30.88% (1.65)**	426,331	**131,651**

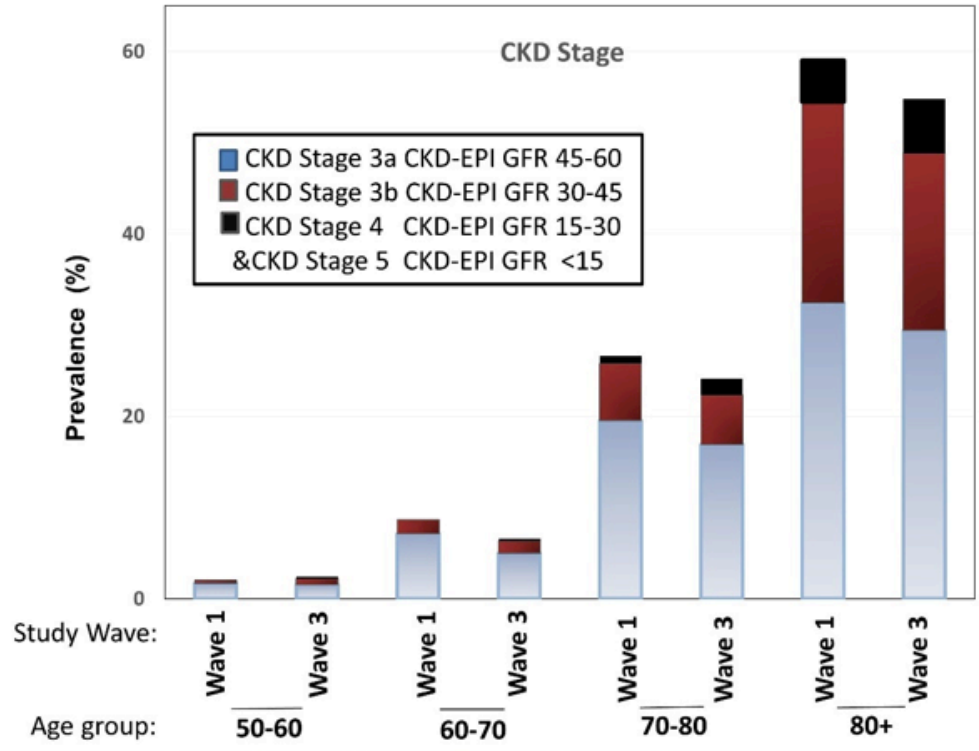
** The sum over age ranges may not equal the total, due to slight inaccuracies in age estimates and rounding within age each age range.
*In some instances, the number of CKD cases in the TILDA dataset for each of the following age categories is quite limited, and the estimates have wide confidence intervals and therefore may be less reliable. The estimates for the 50-55 age subgroup had very wide confidence intervals and were excluded from data presentation

5.8.3 Trends in CKD prevalence in the TILDA dataset from Wave 1 (2009-2011) to Wave 3 (2015-2016):

As reported in previous sections, the overall prevalence of CKD in the Irish population aged 50+ years was 13.1 % in 2009-2011 and increased to 15.6% in 2014-2015 (the prevalence in the TILDA dataset was 9.6% and 13.3%, by CKD-EPI eGFRcre-cys, respectively) (p for the difference <0.001). The prevalence estimate for each stage of CKD was higher in 2014-2015 than in 2009-2011 with the difference seen in CKD stages 2 through 4 and overall. Moderately reduced eGFR (i.e., Stage 3a) increased in prevalence from 8.3% to 9.8% and the prevalence of severely reduced eGFR (3b-4) increased from 3.4% to 5.7%. The analyses stratified by sex showed similar trends.

Figure 6 compares the CKD trends by four age subgroups at Wave 1 of TILDA, and Wave 3 of TILDA. When compared within age sub-groups at each wave, the CKD trends over time were not increasing within age categories, indicating that the increasing trends were primarily due to age differences in the study population (however, slightly more adults were diagnosed with CKD below the threshold for CKD4 at TILDA Wave 3) (see figure 6).

Figure 6.
Estimated prevalence of Chronic Kidney Disease (CKD) Stages by Age Group at TILDA 2009-2011 (Wave 1) and 2013-2015 (Wave 3). The age sub-groups are calculated separately for Wave 1 and Wave 3



CKD 3a (%)	1.72	1.52	7.10	4.99	19.54	16.93	32.44	29.41
CKD 3b (%)	0.32	0.66	1.58	1.34	6.26	5.40	22.05	19.42
CKD 4&5 (%)	0	0.20	0.04	0.24	0.84	1.79	4.50	6.01
Total (%)	2.04	2.38	8.73	6.57	26.64	24.12	59.00	54.85

5.9 Incidence rate of CKD Stage 3 or greater in Ireland.

During the 13851 person-years of follow up, we determined that 218 individuals developed CKD Stage ≥3 using the race-adjusted cystatin-creatinine combination equation eGFR threshold. Accordingly, 208 new CKD cases were estimated using the race-neutral GFR equation. The age standardised estimates of CKD incidence by both GFR formulas are presented in Tables 18 and 19.

The overall CKD incidence rate was 16 per 1000 person-years, (95% CI: 13; 18) utilising race-adjusted GFR equation (Table 18). The incidence increased gradually with increasing age category from 5 per 1000 person-years in participants aged 50-59 years old to 87 per 1000 person years in participants 80 years or older (Table 18). Additionally, the incidence rates for CKD were 16 (96% CI: 13; 19) per 1000 person years in male and 15 (13, 18) per 1000 person years in female participants and were more than two-times higher in those with prevalent comorbidities (i.e., self-reported diabetes or hypertension). Of note, when comparing the plasma cystatin C and plasma creatinine -based eGFR estimates the number with new onset CKD was considerably higher while utilising the plasma cystatin C eGFR threshold.

Table 19.
The age-standardized incidence rate of CKD Stage ≥ 3 defined using race-adjusted cystatin C-creatinine CKD-EPI combination eGFR equation

AGE GROUP AT TILDA WAVE 1	NUMBER OF NEW CASES	TILDA POPULATION COUNT*	TILDA AGE-SPECIFIC RATE	IRISH STANDARD POPULATION COUNT^
50-59	34	1,670	0.51	518,908
60-69	69	1,343	1.36	392,424
70-79	97	644	4.85	233,226
80+	18	117	8.70	128,529
TOTAL	218	3,774**	15.6	1,273,087

**The population count excluding CKD cases at baseline was 3,411.
*The TILDA population count at baseline (2009-2011).
^ the Irish population count was imported from the 2011 Central Statistics Office at EY007.20230404160032.xlsx (live.com)

Finally, we have determined the incidence of the new onset CKD cases in each CKD category (i.e., CKD 3a, CKD 3b, and CKD 4-5). Figure 7 shows the number of new CKD cases split into specific KDIGO stages. The majority of new-onset new CKD were Stage 3a (86.2%). Age stratification across CKD grades demonstrated that younger age groups (i.e., 50-59, and 60-69 years old) were more likely to become incident at later eGFR stage.

Table 20.
Age-stratification of incident CKD stages.

Age at Wave1 (n cases/%)	50-59	60-69	70-79	80-89	Total CKD
CKD Stage 3a	25 (11.47%)	60 (27.52%)	88 (40.33%)	15 (6.88%)	188 (86.24 %)
CKD Stage 3b	7 (3.21%)	6 (2.75%)	8 (3.69%)	2 (0.92%)	23 (10.55 %)
CKD Stage 4 & 5	2 (0.92%)	3 (1.38%)	1 (0.46%)	1 (0.46%)	7 (3.21 %)
Total CKD	34	69	97	18	218 (100 %)

CKD Stages were defined based on race-adjusted CKD-EPI cystatin-creatinine combination eGFR formula.

6 Discussion:

In this prospective nationally representative cohort study, including approximately 8,000 participants, the prevalence of CKD in community dwelling residents of Ireland aged 50 years or older was 11.7% in 2009-2011 and rose to 15.6% in 2014-2015. This translated to more than 200,000 people living in Ireland with moderately to severely impaired kidney function in 2015. CKD was closely aligned with hypertension and diabetes, and prevalence increased with age, particularly in participants aged 70-79 and 80+ years. The estimated incidence of CKD in Ireland between 2009 and 2015 was 16 per 1000 person-years, which along with rising prevalence will likely contribute to considerable future demand on renal services in Ireland.

Kidney Research UK recently reported CKD to be a public health emergency in the UK, [1] affecting approximately 10% of the population with an estimated cost of 7 billion pounds a year to the UK economy, rising to 13 billion pounds in 10 years.[1] The authors also call for significant government action to implement interventions to save 10,000 lives in the UK by 2033.[1]

While the prevalence of 15.6% in Ireland contrasts the estimated global prevalence of 9%,2 perhaps changing demographics in Ireland contributes to this contrast. According to the Department of Health, the number of individuals aged 65 years and over in Ireland has been increasing at a faster rate than other EU neighbours, in fact it has increased by 36% since 2012, and is projected to double by 2042, with the largest proportional increases in those aged over 85 years and older.[12] There is also a rising prevalence of risk factors for CKD in the population including hypertension, obesity and diabetes contributing further to a high burden of CKD. This change in demographics will have significant implications for healthcare utilisation in general and particularly for chronic kidney disease which rises in prevalence with age. Significant efforts at healthcare resource allocation planning for the future are needed in order to optimise chronic kidney disease care in Ireland.[12] This report is the initial step towards recognizing the scale of CKD across the ageing population of Ireland and identifying groups at high risk. Key strategies to identify CKD and prevent its complications should include greater public awareness and education; earlier identification of high-risk individuals; detection of CKD in a broader setting; earlier use of new, available treatment strategies as indicated; and timely referral to specialist nephrology clinics where necessary. In addition, strategies such as the inclusion of CKD in the primary care Chronic Disease Management Program in Ireland, and funding proven interventions such as SGLT2 inhibitors and GLP-1 agonists use in patients both with and without diabetes and non-steroidal mineralocorticoid antagonists in diabetic patients where indicated will contribute to improved care for people with CKD in Ireland.

The strengths of our study include its population-based design with high participation and a low attrition rate; in fact the TILDA cohort represents 1 in 156 people aged 50 years and over in Ireland.[17] Based on established clinical CKD criteria, 11-15% of the entire population of Ireland had CKD Stage 3 or worse and around one-third of those individuals with CKD had severe kidney function impairment and are at elevated risk of adverse outcomes as a result. Advanced CKD (eGFR Stage ≥ 3b) was more than ten times more prevalent in people aged 70 years or older than in younger individuals, with considerable implications for healthcare utilisation in Ireland. We found that only 2% of individuals who fulfilled the diagnostic laboratory criteria for CKD were aware that they had CKD . While population screening for CKD is not currently undertaken in Ireland, this report underlines the need for rising awareness around CKD nationally. With recent developments in the treatment of CKD, particularly the introduction of agents with specific benefits for CKD such as the SGLT2 inhibitors [7-10] , GLP-1 agonists and non-steroidal mineralocorticoid antagonists[24-28] perhaps screening programs in high-risk subgroups could indeed be warranted, which is a matter of debate internationally. Another important strength of this study is our use of the most accurate indirect estimate of renal function available, one based on determinations of a combination of serum creatinine and cystatin C to estimate eGFR rather than either marker alone and using the most contemporary eGFR equations.[18,20] The combined measurements of these markers helps to assure a good representation of renal function in older individuals and particularly those with normal or mildly decreased renal function.[18] This fact provides assurances that our study optimised the identification of CKD in Ireland, a portion of which may have been unrecognized by previous studies in Ireland.[13,14] There is considerable discussion internationally on the impact of the inclusion of race as a parameter in eGFR formulae.[29] In this study, we observed that the removal of race from the CKD-EPI equation would decrease the number of adults aged 50 yrs. and over fulfilling the diagnostic criteria for advanced CKD. Therefore the adoption of race-free creatinine equation in healthcare institutions for estimating GFR on a nationwide scale will significantly impact the estimates for CKD and subsequent care for patients with CKD in Ireland. Importantly, the implications for a diagnosis of CKD in older individuals merits particular focus in future clinical research programs in order to more fully understand and characterise the significance of the contribution of age to eGFR formula.

We acknowledge the limitations of our study. The determination of the presence of kidney disease based on eGFR thresholds was made on a single random sample of the laboratory values at both wave 1 and wave 3 TILDA, so the presence of CKD on multiple repeated testing in the same individual could not be verified. Furthermore, variability in eGFR estimates in the same individual on serial measurements is acknowledged which can lead to a diagnosis of CKD on one occasion and not another, however this is a limitation of all general population cohort studies.[30] Also, the level of albuminuria, or individual cause of CKD in each participant was not available as part of TILDA.

In conclusion, based on a large, prospective, nationally representative cohort study we characterised the population with CKD in Ireland, and show that the prevalence of CKD is 15% in adults 50 years or older in the general population as of 2016. Furthermore, according to clinical CKD grading, around one-third of those individuals with CKD in Ireland had moderate to severe CKD, with an intermediate or, high risk of associated complications including cardiovascular disease, premature mortality and the potential to progress to ESKD. The increasing prevalence of CKD has implications for future treatment policies in nephrology in Ireland, including healthcare resource allocation planning as part of Sláintecare as well as the implications of new treatment options for CKD on the Chronic Disease Management Programs in Ireland.

7. Appendix

Supplementary Table 1.
Number of individuals by CKD classification and age categories. Data are based on TILDA Wave 1

Age at Wave 1 Creatinine- Cystatin C CKD-EPI, 2012	50-59	60-69	70-79	>=80	Total
G1	877 (53.1%)	342 (25.4%)	61 (9.5%)	1 (0.8%)	1,291 (34.5%)
G2	748 (44.8%)	894 (66.5%)	428 (66.4%)	50 (42.7%)	2,120 (56.2%)
G3a	30 (1.1%)	84 (6.3%)	115 (17.8%)	38 (32.4%)	267 (7.1%)
G3b	5 (0.3%)	22 (1.6%)	36 (5.5%)	22 (18.8%)	85 (2.3%)
G4	0 (0%)	1 (0.1%)	4 (0.6%)	6 (5.1%)	11 (0.3%)
G5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	n=1,670	n=1,343	n=644	n=117	n=3,774

Supplementary Table 2.
Number of individuals by CKD classification and age categories. Data are based on TILDA Wave 3

Age at Wave 3 Creatinine- Cystatin C CKD-EPI, 2012	50-59	60-69	70-79	>=80	Total
G1	507(54.8%)	530 (33.2%)	104 (11.3%)	9 (2.7%)	1,150 (30.5%)
G2	349 (42.6%)	965 (60.5%)	607 (66.1%)	153 (45.7%)	2,119 (56.1%)
G3a	15 (1.6%)	73 (4.6%)	154 (16.8%)	96 (28.7%)	338 (9.0%)
G3b	7 (0.8%)	23 (1.4%)	41 (4.5%)	60 (17.9%)	131 (3.4%)
G4	1 (0.1%)	5 (0.3%)	12 (1.3%)	16 (4.8%)	34 (0.9%)
G5	1 (0.1%)	0 (0%)	0 (0%)	1 (0.3%)	2 (0.1%)
Total	n=925	n=1,596	n=918	n=335	n= 3,774

Supplementary Table 3.
Number of individuals by CKD classification and age categories, using race adjusted CKD-EPI combination equation. Data are based on TILDA Wave 1

Age at Wave 1 Creatinine-Cystatin C CKD-EPI, 2021	50-59	60-69	70-79	>=80	Total
G1	1,044 (62.5%)	516 (38.4%)	105 (16.3%)	5 (4.3%)	1,670 (44.2%)
G2	603 (36.1%)	750 (55.8%)	421 (65.4%)	60 (51.3%)	1,834 (48.6%)
G3a	19 (1.1%)	63 (4.7%)	83 (12.9%)	28 (23.9%)	193 (5.1%)
G3b	4 (0.2%) 1	3 (1%)	31 (4.8%)	19 (16.2%)	67 (1.8%)
G4	0 (0%)	1 (0.2%)	4 (0.6%)	5 (4.3%)	10 (0.3%)
G5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	n=1,670	n=1,343	n=644	n=117	n=3,774

Supplementary Table 4.
Number of individuals by CKD classification and age categories, using race adjusted CKD-EPI combination equation. Data are based on TILDA Wave 3

Age at Wave 3 Creatinine- Cystatin C CKD-EPI, 2021	50-59	60-69	70-79	>=80	Total
G1	616 (66.6%)	706 (44.2%)	181 (19.8%)	21 (6.3%)	1,524 (40.4%)
G2	288 (31.1%)	810 (50.8%)	575 (62.6%)	160 (47.7%)	1,833 (48.6%)
G3a	12 (1.3%)	63 (3.9%)	117 (12.7%)	91 (27.2%)	283 (7.5%)
G3b	7 (0.8%)	12 (0.8%)	34 (3.7%)	47 (14.1%)	100 (2.6%)
G4	1 (0.1%)	5 (0.3%)	11 (1.2%)	16 (4.8%)	33 (0.9%)
G5	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	1 (0.03%)
Total	n=925	n=1,596	n=918	n=335	n= 3,77

Supplementary Table 5.
Number of individuals by CKD classification and age categories, using cystatin C CKD-EPI equation. Data are based on TILDA Wave 1

AGE AT WAVE 1 CYSTATIN C eGFR	50-59	60-69	70-79	>=80	TOTAL
G1	911 (54.6%)	355 (26.4%)	70 (10.9%)	1 (0.4%)	1,337 (33.7%)
G2	719 (43.1%)	855 (63.6%)	383 (59.4%)	36 (30.8%)	1,993 (52.8%)
G3A	31 (1.9%)	107 (7.9%)	129 (20.0%)	48 (41.0%)	315 (8.3%)
G3B	8 (0.5%)	25 (1.9%)	51 (7.9%)	22 (18.8%)	106 (2.8%)
G4	1 (0.1%)	1 (0.1%)	11 (1.7%)	10 (8.5%)	23 (0.1%)
G5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0.0%)
TOTAL	n=1,670	n=1,343	n=644	n=117	3,774

Supplementary Table 6.
Number of individuals by CKD classification and age categories, using cystatin C CKD-EPI equation. Data are based on TILDA Wave 3

AGE AT WAVE 3 CYSTATIN C eGFR	50-59	60-69	70-79	>=80	TOTAL
G1	459 (49.6%)	463 (29.0%)	98 (10.7%)	10 (3.0%)	1,030 (27.3%)
G2	425 (45.9%)	960 (60.2%)	533 (58.1%)	105 (31.3%)	2,023 (53.6%)
G3A	28 (3.0%)	136 (8.5%)	194 (21.1%)	107 (31.9%)	465 (12.3%)
G3B	11 (1.2%)	29 (1.8%)	70 (7.6%)	85 (25.4%)	195 (5.2%)
G4	2 (0.2%)	7 (0.4%)	23 (2.5%)	26 (7.8%)	58 (1.5%)
G5	0 (0%)	1 (0.1%)	0 (0%)	2 (0.6%)	3 (0.01%*)
TOTAL	n=925	n=1,596	n=918	n=335	3,774

Supplementary Table 7.
Baseline characteristic of TILDA participants by eGFR stage

GFR Stage	G1 N=1291	G2 N=2120	G3a N=267	G3b N=85	G4 – G5 N=11	P-value*
Characteristics at Wave 1						
Age [yrs]	61.7; 5.9	67.6; 7.8	74.8; 8.5	78.2; 8.1	84.0; 6.4	<0.001
BMI [kg/m2]	27.6; 4.5	28.7; 4.8	29.7; 6.1	30.1; 4.9	31.1; 8.7	<0.001
HbA1c [mmol/mol]	32.6; 32.0; 5.4	33.1;32.0; 5.1	34.1; 33.0; 4.8	35.0; 34.0; 5.4	36.4; 34; 8.14	0.001
Female gender [%]	51.5	53.2	64.0	55.2	45.5	0.01
Diabetes mellitus [%]	5.5	5.5	11.2	18.8	18.2	<0.001
Hypertension [%], self-report	26.3	34.0	60.7	76.5	72.7	<0.001
Hypertension [%], objective	39.2	41.5	50.2	50	50	<0.001
Systolic BP [mmHg]	133; 131; 19	135; 134; 20	139; 139; 21	140; 139; 23	149; 143; 34	<0.001
Smoking [Yes/No]	615/676	968/1152	113/154	39/46	4/7	0.1

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