Australian Government
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Diabetes and chronic kidney disease as risks for other diseases

Australian Burden of Disease Study 2011

AUSTRALIAN BURDEN OF DISEASE STUDY SERIES NO. 8

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Authoritative information and statistics to promote better health and wellbeing

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Cat. no. BOD 9

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This publication is part of the Australian Institute of Health and Welfare's Australian Burden of Disease Study series. A complete list of the Institute's publications is available from the Institute's website <www.aihw.gov.au>.

ISSN 2204-4108 (PDF)
ISSN 2006-4508 (Print)
ISBN 978-1-76054-045-6 (PDF)
ISBN 978-1-76054-047-0 (Print)

Suggested citation

Australian Institute of Health and Welfare 2016. Diabetes and chronic kidney disease as risks for other diseases. Australian Burden of Disease Study 2011. Australian Burden of Disease Study series no. 8. Cat. no. BOD 9. Canberra: AIHW.

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Published by the Australian Institute of Health and Welfare

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Contents

Acknowledgments

This report was prepared by staff in the Australian Burden of Disease Unit and the Cardiovascular, Diabetes and Kidney Unit of the Australian Institute of Health and Welfare (AIHW). The main authors were Wendy Ho, Melanie Dunford and Vanessa Prescott, under the guidance of Michelle Gourley, Sushma Mathur and Lynelle Moon. Other AIHW staff who made a substantial contribution were Michael DeLooper and Roslyn Seselja.

Melissa Goodwin and David Whitelaw from the AIHW provided valuable input and statistical advice, while Geoff Neideck, Fadwa Al-Yaman and Justin Harvey provided constructive comments and review. Their contributions are gratefully acknowledged.

The authors would also like to acknowledge the comments received from the Epidemiology Branch of the Public Health Division from the Western Australian Department of Health.

The report was prepared under the guidance of the **National Vascular Diseases Monitoring Advisory Group** (NVDMAG). Members are: Erin Lalor (Chair), Elizabeth Flynn and Bernie Towler. The NVDMAG includes the following expert advisory groups and their members:

Cardiovascular Disease Expert Advisory Group: Andrew Tonkin (Chair), Tom Briffa, Derek Chew, Annette Dobson, Mandy Thrift and Mark Nelson

Diabetes Expert Advisory Group: Jonathan Shaw (Chair), Stephen Colagiuri, Maria Craig, Wendy Davis, Mark Harris, Greg Johnson, Glynis Ross and Sophia Zoungas

Chronic Kidney Disease Expert Advisory Group: Steven Chadban (Chair), Alan Cass, Jeremy Chapman, Joan Cunningham, Bettina Douglas, Stephen McDonald and David Parker.

The Australian Government Department of Health funded this report. The authors acknowledge the valuable comments from individual staff members.

Abbreviations

AB	attributable burden
ABDS	Australian Burden of Disease Study
ABS	Australian Bureau of Statistics
AHS	Australian Health Survey
AIHW	Australian Institute of Health and Welfare
ANZDATA	the Australia and New Zealand Dialysis and Transplant Registry
CHD	coronary heart disease
CI	confidence interval
CKD	chronic kidney disease
DALY	disability-adjusted life years
e.g.	for example
eGFR	estimated glomerular filtration rate
ESKD	end-stage kidney disease
GBD	Global Burden of Disease (study)
HR	hazard ratio
OR	odds ratio
PAF	population attributable fraction
RR	relative risk
WHO	World Health Organization
YLD	years lived with disability
YLL	years of life lost

Symbols

mg/dL	milligrams per decilitre
mmol/L	millimoles per litre
mL/min	millilitres per minute
1.73m^2	a standard body surface area (measure for eGFR)
>	greater than
≥	greater than or equal to
<	less than
≤	less than or equal to
%	per cent
—	nil or rounded to zero
+	plus
–	minus
±	plus minus

Summary

Diabetes (type 1 and type 2) and chronic kidney disease (CKD) can act as risk factors for other diseases such as coronary heart disease, stroke and dementia. The Australian Burden of Disease Study (ABDS) 2011 only reported on the direct burden of diseases. To fully account for the health loss attributable to a specific disease, a diseases-as-risks approach (linked disease) can be used to estimate their 'indirect' or additional burden. The direct and indirect burden can be added to estimate their collective burden.

Diabetes and CKD burden doubled when taking into account indirect burden

The ABDS 2011 reported that diabetes and CKD were responsible for 2.3% and 0.9% respectively of the total burden of disease and injury in Australia in 2011 (the direct burden). When the indirect burden due to linked diseases was taken into account:

- the collective burden due to diabetes was 1.9 times as high, and CKD was 2.1 times as high, as their direct burden
- the indirect diabetes burden varied by sex, with males experiencing 31% more burden than females
- the indirect burden due to diabetes and CKD occurred at a later age than direct burden, being responsible for over 50% of the collective diabetes burden and 65% of the collective CKD burden from age 75 onwards.

Of the 12 linked diseases examined for diabetes:

- the burden attributable to diabetes was highest for coronary heart disease, stroke and CKD—together accounting for 75% of the indirect diabetes burden measured
- diabetes was responsible for 21% of the CKD burden, 14% of the stroke burden, 12% of the liver cancer burden and 11% of the coronary heart disease burden.

Of the 4 linked diseases examined for CKD:

- the burden attributable to CKD was highest for coronary heart disease—accounting for almost half (48%) of the indirect CKD burden measured
- CKD was responsible for 19% of peripheral vascular disease burden, 8% of dementia burden and 7% of stroke burden.

Around one-fifth of future diabetes burden could be avoided if the current rise in diabetes is halted

If the current trends in diabetes and CKD prevalence and mortality continued to 2020, the estimated collective diabetes burden is projected to be 1.6 times as high as in 2011, and the estimated collective CKD burden is projected to be 1.4 times as high. This compares to rate ratios of 1.3 if prevalence and mortality rates are maintained at 2011 levels to 2020, (which reflects population growth and ageing). Put differently, if the current rise in these diseases is halted, 21% of future diabetes burden and 5% of future CKD burden could be avoided.

In terms of indirect burden, the greatest gains are expected to be made in those aged 65–94 for diabetes, and 65–84 for CKD, where around 36% of diabetes attributable burden and 15% of CKD attributable burden could be avoided by 2020 if the prevalence of these diseases is maintained at 2011 levels. Results from this study could be used to inform population health monitoring and may assist in the development of chronic disease policy.

1 Introduction

Diabetes mellitus (diabetes) and chronic kidney disease (CKD) are increasingly common in Australia, partly related to changing lifestyle factors and ageing population factors. These chronic diseases have major impacts on health and other support services. It is well known that they have common modifiable risk factors—such as smoking, obesity, physical inactivity and poor nutrition—that can often be prevented or effectively controlled through behavioural change, medications and health-care interventions (AIHW 2015).

Some diseases can also act as risk factors for other diseases (referred to as 'linked' diseases in this report). Evidence suggests people with diabetes or CKD are at higher risk for other chronic diseases (Liao et al. 2015; Tonelli et al. 2012). For example, diabetes can increase the risk of coronary heart disease, stroke, peripheral vascular disease, CKD, certain cancers and dementia (Cheng et al. 2014; Emerging Risk Factors Collaboration 2010; Prince et al. 2014; Vigneri et al. 2009). CKD is associated with the development of cardiovascular diseases such as coronary heart disease, stroke and peripheral vascular disease (Tong & Stevenson 2007), as well as dementia.

The burden of each disease as calculated in the Australian Burden of Disease Study (ABDS) 2011 only captured the 'direct' disease burden. For example, the direct burden of diabetes is the burden directly related to diabetes, such as diagnosed diabetes, diabetic neuropathy and retinopathy. To fully account for the health loss attributable to diabetes, the 'indirect' or additional burden from diseases linked to diabetes must also be calculated, including the proportion of burden of linked diseases caused by diabetes complications (for example coronary heart disease and stroke). The direct and indirect burden are added together to estimate the collective burden (Figure 1.1). To date, the indirect burden of diabetes and CKD is unknown in Australia.

Examples of direct burden

- Diagnosed diabetes
- Diabetic neuropathy
- Diabetic foot ulcer
- Amputation due to diabetes
- Vision impairment due to diabetes

Examples of indirect burden

- Coronary heart disease
- Stroke
- Peripheral vascular disease
- Dementia
- Chronic kidney disease
- Some cancers

Figure 1.1: Examples of direct and indirect burden of diabetes

1.1 This report, its aims and analytical approach

This study aims to provide a more comprehensive picture of the full health loss attributable to diabetes and CKD. It quantifies the impact of diabetes and CKD on the additional burden of linked diseases as they act as risk factors. This effect is termed 'disease-as-risks', and presents estimates of the collective burden of diabetes and CKD in Australia in 2011. It uses estimates of disease burden from the ABDS 2011 (AIHW 2016a) and extends the standard approach for analysis of risk factors for diseases to assess the impact of diabetes and CKD as risk factors for other diseases.

The aims of this report are to:

- assess the indirect disease burden (DALY) attributable to diabetes and CKD
- determine the collective burden (indirect and direct) of diabetes and CKD
- explore the effect of reducing diabetes or CKD prevalence on the burden of various linked diseases as well as on the collective burden due to diabetes and CKD.

The analyses in this report are innovative for Australia. Previously, the Global Burden of Disease (GBD) 2013 study reported high fasting plasma glucose levels and low glomerular filtration rate—biomedical indicators of diabetes and CKD—as risk factors for diseases (GBD 2013 Risk Factors Collaborators 2015). The New Zealand burden of disease study also undertook diseases-as-risks analysis for some conditions, including diabetes and CKD (MOH 2012).

Results from this report provide estimates of the collective burden of diabetes and CKD, which can give a more comprehensive picture on the health loss attributable to these conditions. These results could be used to inform population health monitoring and may assist in the development of chronic disease policy.

Another report in this series looks at a range of modifiable vascular risk factors for dementia, including vascular diseases that act as risk factors for dementia—diabetes, stroke, atrial fibrillation and CKD, and estimates their individual and combined contribution to the burden of dementia in Australia (AIHW 2016d).

This first chapter provides background information on diabetes and CKD and their impact on other diseases. It then describes the 'burden of disease' approach used in the subsequent analysis and finally summarises the content of the following chapters.

1.2 Background

More about diabetes and CKD

Definitions of diabetes and CKD for the purposes of analyses in this report are provided in Box 1.1.

A range of behavioural and metabolic risk factors increase the risk of a person developing type 2 diabetes and CKD, such as tobacco smoking, overweight and obesity and high blood pressure. Similarly, diabetes and CKD increase the risk of developing other chronic diseases. There is evidence to suggest that diabetes can increase the risk of coronary heart disease, stroke, kidney disease, cancer and dementia (Cheng et al. 2014; Emerging Risk Factors Collaboration 2010; Prince et al. 2014 Vigneri et al. 2009). For example, diabetes is now the leading cause of treated end-stage kidney disease (ESKD) in Australia, accounting for 1 in 3

new cases in 2011 (ANZDATA 2013). ESKD is associated with large excesses of cardiovascular and all-cause mortality (Afkarian et al. 2013), and development of cardiovascular diseases such as coronary heart disease and heart failure (Tong & Stevenson 2007).

Box 1.1: Diabetes and chronic kidney disease

Diabetes

Diabetes is a chronic disease marked by high levels of glucose in the blood. It is caused either by the inability to produce insulin, or by the body not being able to use insulin effectively, or both. Diabetes manifests as a high level of sugar in the blood. The main types of diabetes are:

- type 1 diabetes—an autoimmune disease that usually has onset in childhood or early adulthood
- type 2 diabetes—largely preventable, usually associated with lifestyle factors and with later onset
- gestational diabetes—when higher than normal blood glucose is diagnosed during pregnancy (AIHW 2014).

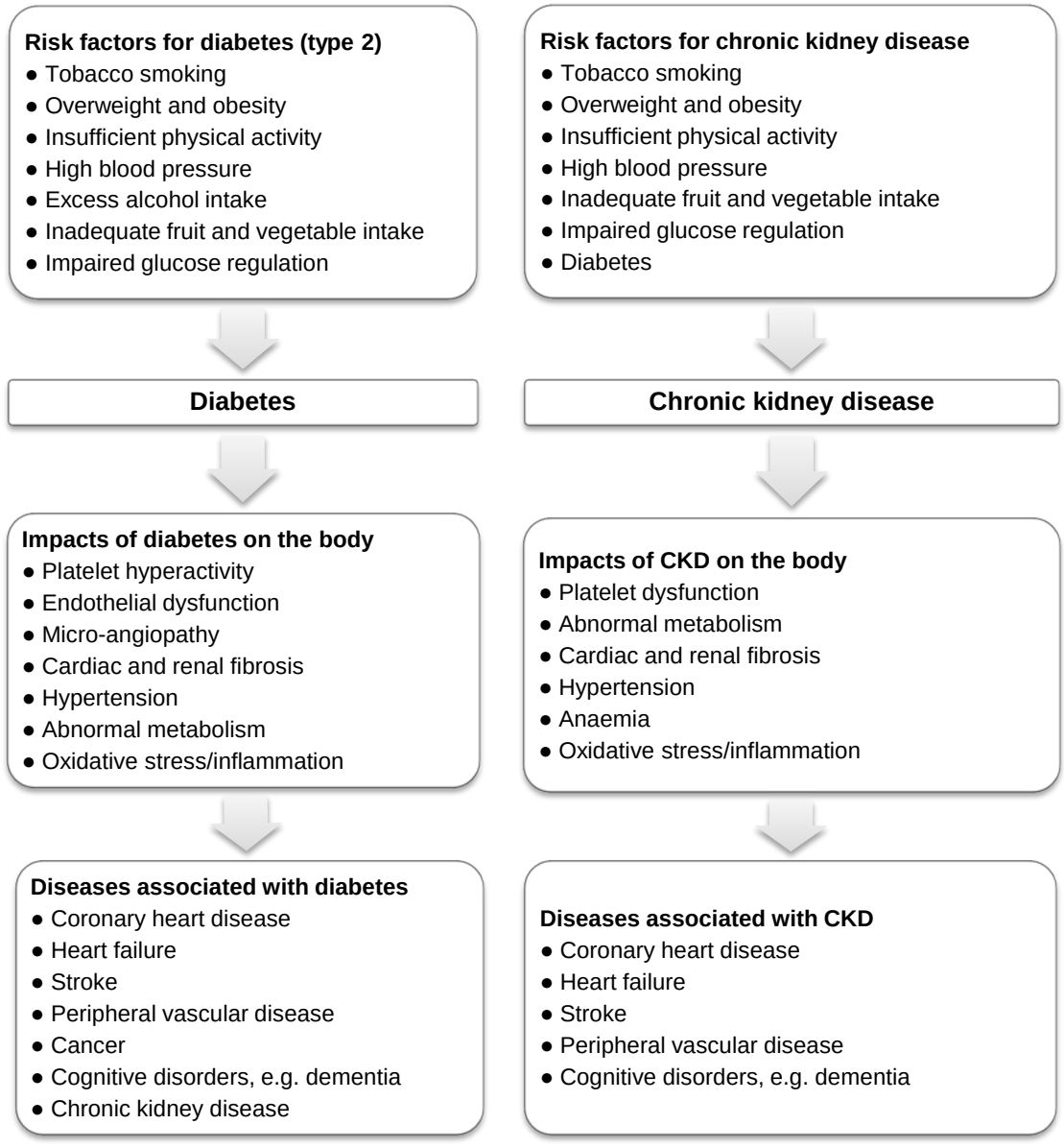
In this report, gestational diabetes was not considered as a risk factor for other linked diseases; diabetes includes type 1 and type 2 but not gestational diabetes. This is consistent with the ABDS 2011, where gestational diabetes was not included under diabetes.

Chronic kidney disease (CKD)

CKD refers to all conditions of the kidney, lasting at least 3 months, where a person has had evidence of kidney damage and/or reduced kidney function. Evidence of kidney damage manifests as either urinary protein or albumin (a type of protein that is a more sensitive and specific marker of kidney disease), blood in the urine, or scarring detected by imaging tests.

CKD is usually categorised into 5 stages (1 to 5, where stage 1 is least kidney damage and stage 5 is most kidney damage) according to the level of kidney function and evidence of kidney damage, indicated by biological markers such as blood or protein in the urine. In the ABDS 2011, CKD stages were defined using eGFR (estimated glomerular filtration rate) results for kidney function. In this study, CKD as a risk factor included stage 3 to 5, consistent with the ABDS 2011.

Figure 1.2 illustrates possible causal pathways of the development of diabetes and CKD and associated diseases.



Sources: AIHW 2014, Montemarano et al. 2013, Vulesevic et al. 2014.

Figure 1.2: An example of possible causal pathways of diabetes and CKD to associated diseases

What is burden of disease?

Burden of disease analyses assesses and compares the health impact of different diseases, conditions or injuries (referred to as 'diseases' for simplicity) and risk factors on a population. It captures the impact of both living with the disease and dying prematurely.

The ABDS 2011 quantified the fatal and non-fatal effects of these diseases in a consistent manner so that they can then be combined into a summary measure of health called the DALY—disability-adjusted life years. The DALY combines the estimates of years of life lost due to premature death (YLL) and years lived in ill health or with disability (YLD) to count

the total years of healthy life lost from disease and injury. These and other key terms relating to burden of disease analyses are defined in Box 1.2.

Taking all diseases into account, this health loss represents the difference between the current health status of the population and the ideal situation where everyone lives a long life, free of disease. Burden of disease estimates capture both the quantity and quality of life, and reflect the magnitude, severity and impact of disease and injury within a population in the given year. The analysis also estimates the contribution of various risk factors to health loss, known as the attributable burden.

Attributable burden reflects the direct relationship between a risk factor (diabetes or CKD in this report) and a disease outcome (linked disease). It is the amount by which disease burden would be reduced if exposure to the risk factor (including diseases as risks) had been avoided or reduced to the lowest possible exposure.

For detailed information about the most recent ABDS, and further information on the methods used to calculated disease burden, please refer to *Australian Burden of Disease Study: impact and causes of illness and death in Australia 2011* (AIHW 2016a) and *Australian Burden of Disease Study 2011: methods and supplementary material* (AIHW 2016b).

1.3 Structure of this report

This report provides a comprehensive analysis of the direct and indirect burden of diabetes and CKD using a 'diseases-as-risks' approach. The structure of this report is:

- Chapter 2 describes the methods used in this report to estimate the direct and indirect burden of diabetes and CKD.
- Chapter 3 summarises the results of analyses to estimate the impact of diabetes on the burden of linked diseases.
- Chapter 4 summarises the results of analyses to estimate the impact of CKD on the burden of linked diseases.
- Chapter 5 provides commentary on the implications of the findings, strengths and limitations of the study and concluding remarks.
- Appendixes A and B provide information on the selection of effect sizes used in this report for the association between diabetes and linked diseases, and CKD and linked diseases, respectively.
- Appendix C describes the methods used in scenario modelling where the direct and indirect burden due to diabetes and CKD were extrapolated to 2020 under 2 different scenarios.
- Appendix D provides information on the data sources used for the diabetes and CKD estimates presented in this report.

Box 1.2: Key terms used in this report

attributable burden: The disease burden attributed with a particular risk factor. It is the reduction in fatal and non-fatal burden that would have occurred if exposure to the risk factor had been avoided (or, more precisely, had been at its theoretical minimum).

collective burden: The sum of the direct and indirect burden**.**

comparative risk assessment: The process for estimating the burden of disease attributable to selected risk factors. It involves 5 key steps: selection of risk–outcome pairs; estimation of exposure distribution; estimation of effect sizes; choice of theoretical minimum risk exposure level; and finally the calculation of attributable burden.

DALY (disability-adjusted life years): Measure (in years) of healthy life lost, either through premature death defined as dying before the expected life span (YLL) or, equivalently, through living with ill health due to illness or injury (YLD).

direct burden: In burden of disease analysis, it is the burden calculated to capture the main disabling consequences of the disease. For example, the direct diabetes burden includes diabetic nephropathy, neuropathy and retinopathy.

diseases-as-risks: Diseases act as risk factors for other diseases. To fully account for the health loss attributable to diseases-as-risks requires that their 'indirect' burdens be calculated and then added to their 'direct' burdens in order to estimate their collective burdens.

effect size: A statistical measure of the strength of the relationship between 2 variables (in this context, between a risk exposure and a disease outcome), expressed, for example, as a relative risk.

hazard ratio (HR): Hazard ratio has similar interpretation to relative risk. It is the ratio of the probability of an event (e.g. disease outcome) in the exposed group to the probability in the control group. Hazard ratios differ from relative risks in that the latter are cumulative over an entire study, using a defined endpoint, while the former represent instantaneous risk at some particular time period during the study.

indirect burden: In burden of disease analysis, where the disease of interest is considered to be a risk factor (that is, disease-as-risk) for linked diseases, it is the burden attributable to the disease-as-risk for linked diseases. For example, diabetes is considered to be a risk factor for coronary heart disease, stroke, dementia and other diseases, so the indirect burden is the burden attributable to diabetes for these linked diseases.

linked disease: Many diseases can act as risk factors for developing certain diseases; for example, diabetes is associated with increased risk of developing coronary heart disease. The disease in association is a linked disease to the risk factor.

meta-analysis: A statistical technique for combining findings from previous independent studies. It provides a quantitative estimate of the overall effect of an intervention or variable on a defined outcome, giving due weight to the size of the different studies included.

population attributable fraction (PAF): The proportion (fraction) of a disease, illness, disability or death in a population that can be attributed to a particular risk factor or combination of risk factors.

(continued)

Box 1.2 (continued): Key terms used in this report

odds ratio (OR): Odds ratio is a measure of association which compares the odds of disease in those exposed to the odds of disease in those unexposed.

relative risk (RR): The risk of an event relative to exposure, calculated as the ratio of the probability of the event occurring in the exposed group to the probability of it occurring in the non-exposed group. A relative risk of 1 implies no difference in risk; a RR <1 implies the event is less likely to occur in the exposed group; and a RR >1 implies the event is more likely to occur in the exposed group.

risk factor (for health): Any factor that causes or increases the likelihood of a health disorder or other unwanted condition or event.

YLD (years lived with disability): A measure of the years of what could have been a healthy life but were instead spent in states of less than full health. YLD represent non-fatal burden.

YLL (years of life lost): Years of life lost due to premature death defined as dying before the ideal life span. YLL represent fatal burden.

(See Glossary for a full list of definitions used in the report.)

2 Methods

The disease burden attributable to diabetes or CKD was estimated using the comparative risk assessment methodology (see Box 1.2 for definition). This is the standard approach for burden of disease risk factor analysis globally (GBD 2013 Risk Factors Collaborators 2015). In this study, diabetes and CKD are the risk factors of interest.

To measure the contribution of diabetes or CKD, the calculations use high-quality information on evidence of a causal association between diabetes or CKD and other diseases. The amount of extra risk of developing or dying from that disease caused by exposure to diabetes or CKD (that is, effect size) and the number of people in the population exposed to diabetes or CKD are also included in the calculation. Exposure to the risk factor disease is measured as the disease prevalence in the population.

In this study, the steps followed were:

- select linked diseases and the effect size of risk factors on linked disease
- estimate the risk factor (diabetes or CKD) exposure and define the theoretical minimum risk exposure distribution
- calculate the population attributable fraction
- quantify the indirect diabetes or CKD burden.

These steps are further explored in this chapter and form the structure of this chapter.

2.1 Defining linked diseases

Diseases linked to diabetes or CKD were chosen for analysis if they met the following criteria:

- sufficient evidence for a causal association between exposure and linked disease outcome based on high quality epidemiological studies
- sufficient data to estimate population exposure to the risk factor
- a plausible biological mechanism linking risk factor and linked disease
- modifiable or preventable.

For diabetes-as-risk, most literature pertained to type 2 diabetes. In this study, calculation of diabetes burden included type 1 and type 2, consistent with the ABDS 2011 which did not calculate direct burden by diabetes type. Further, this diseases-as-risk study included: diagnosed diabetes, where diabetes prevalence was obtained from self-reported data or measured biomedical data; and undiagnosed diabetes, where diabetes has not been diagnosed by a doctor, but an individual has plasma glucose levels that satisfy established criteria for diabetes.

Twelve linked diseases to diabetes-as-risk were included: 3 cardiovascular diseases (coronary heart disease, stroke and peripheral vascular disease), 7 types of cancer (liver, pancreatic, bowel, breast, uterine, kidney and bladder), chronic kidney disease and dementia. See Appendix A for a detailed description of the selection of linked diseases for diabetes.

For CKD-as-risk, most literature defined CKD by eGFR of less than 60 mL/min/1.73 m^2 or by the levels of urinary protein or albumin. This definition of a reduced eGFR is consistent

with stages 3 to 5 of CKD used in the ABDS 2011. Four linked diseases were included: coronary heart disease, stroke, peripheral vascular disease and dementia. See Appendix B for a detailed description of the selection of linked diseases for CKD.

Criteria for inclusion of linked diseases

For a linked disease outcome to be included, there must be convincing or probable evidence of a causal association following exposure (to diabetes or CKD), preferably from a meta-analysis or cohort study. This aligns with the World Cancer Research Fund criteria of convincing or probable evidence for a causal association (see Box 2.1).

Box 2.1: World Cancer Research Fund criteria for level of evidence

The World Cancer Research Fund used a criterion for grading evidence to support a judgement of a relationship with cancer. Its grading system breaks down data sources into 'convincing', 'probable', 'possible' and 'insufficient' evidence (WCRF & AICR 2007). Convincing evidence describes a causal relationship that is 'robust enough to be highly unlikely to be modified in the foreseeable future as new evidence accumulates'. Probable evidence suggests a causal relationship is often described and is unlikely to change with increased knowledge.

Evidence for inclusion of linked disease was categorised as convincing or probable based on the robustness and volume of studies demonstrating a relationship. Convincing evidence included linked diseases with a well-known causal relationship, or where numerous high-quality studies applicable to Australia demonstrated a causal relationship after adjusting for confounders.

A probable level of evidence included linked diseases where a causal relationship had been identified by high-quality studies, but supporting evidence was not as robust as those categorised as convincing. The main reason for classifying as probable evidence was that a meta-analysis had not been conducted, or only a few high-quality studies were available for selection. Pancreatic cancer was an exception, with a strong causal relationship to diabetes demonstrated by a number of studies; however, there is uncertainty on the direction of the relationship suggested by 1 study, depending on the time period of developing both conditions. The association between diabetes and pancreatic cancer was therefore classified as probable level of evidence.

The levels of evidence are further explained in Appendix A for diabetes as a risk and Appendix B for CKD as a risk.

Diseases excluded

A linked disease was included in this study if it met the criteria of inclusion as mentioned above and if it was a specific disease captured in the ABDS 2011.

Heart failure as a linked disease for diabetes and CKD is supported by a substantial body of research. However, it was not considered a separate disease in the ABDS 2011; instead the effects of heart failure were included as a consequence of a number of underlying cardiovascular diseases (such as coronary heart disease and rheumatic heart disease). As such, its burden was not estimated separately in the ABDS 2011, and therefore, it was not possible to include a separate calculation of heart failure burden in this study.

Some other conditions, such as sleep apnoea and thyroid disease, may also be associated with diabetes (Baronea & Menna-Barretob 2011; Kadiyala et al. 2010). The burden of these linked diseases were not able to be included in this study because they were not captured as separate diseases in the ABDS 2011.

While there is some evidence of a possible association between CKD and some cancers, cancer was not included as a linked disease for CKD in this study. This was because the literature suggests these associations can be bi-directional dependent on therapies used to treat CKD, and there was not enough convincing evidence for specific cancers to enable its inclusion (Stengel 2010).

2.2 Selection of effect size

Burden of disease studies use effect size to measure the association between risk factors and disease outcomes. For the linked diseases included in this study, except for diabetes and its association with CKD, effect sizes were selected from published meta-analyses or applicable prospective studies (see tables A1 and B1). In this study, meaures of effect include relative risk (RR), odds ratio (OR) and hazard ratio (HR).

For the association between diabetes and CKD, direct evidence from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) was used to ascertain the proportion of people who have CKD due to diabetes (the population attributable fraction). The registry captures data for virtually all cases of treated ESKD in Australia and provides evidence to attribute CKD to diabetes. The proportions were modelled for people aged 90 and over due to limited data on the registry for these ages.

Each effect size was applied to both fatal and non-fatal burden. Depending on the method used in the primary analysis, effect sizes may have been adjusted for confounders as well as other diseases included in this study as described in appendix tables A2 and B2. The selection of effect sizes for diabetes or CKD and its linked disease is described in detail in Appendixes A and B.

2.3 Population exposure: prevalence of diabetes or CKD

Definitions used to calculate exposure to the risk factors diabetes and CKD are described in Table 2.1. Further details on exposure data sources are in Appendix D. Exposure was aligned as best as possible with the evidence of causal association in the studies where effect sizes were sourced.

For this study, exposure was treated as a dichotomous categorical variable: that is, the prevalence of those who have diabetes or CKD compared with the prevalence of those who do not have diabetes or CKD. The proportion of those who do not have diabetes or CKD is referred to as the theoretical minimum risk exposure level or the proportion ‘not exposed’. Those who have diabetes or CKD are the ‘exposed’ population and at risk of linked diseases.

Table 2.1: Risk factor population exposure definition, 2011

Risk factor	Definition of exposure
Diabetes	Prevalence of diagnosed and undiagnosed diabetes but with established high plasma glucose level (type 1 and type 2).
Chronic kidney disease	Prevalence of persons with CKD, stages 3 to 5.

Australian population distributions of diabetes and CKD by age and sex were sourced directly from the ABDS 2011 (AIHW 2016b). Diabetes and CKD definitions (Table 2.1) were used to guide data extraction. The ABDS 2011 derived the proportions of people who have and do not have diabetes or CKD using the finest possible increments from the original data source. To reduce the impact of survey error, the data were extracted at a level where the relative standard error was 25% or less. For further information on the methods used to derive disease prevalence, please refer to the *Australian Burden of Disease Study 2011: methods and supplementary material* (AIHW 2016b).

The prevalence of a risk factor influences the attributable burden. That is, the attributable burden may be greater for a risk factor with a small effect size and high prevalence compared with a risk factor with a large effect size and low prevalence. Therefore, this analysis is dependent on accurate prevalence estimates for diabetes or CKD.

2.4 Calculation of population attributable fractions

Population attributable fractions (PAFs) determine the proportion of a particular disease that could have potentially been avoided if the population had never been exposed to a risk factor (Box 2.2).

The calculation of PAFs requires the input of:

- the effect size, that is the RR, OR or HR, of the risk factor on the outcome of interest, and
- the prevalence of exposure in the population (P).

The PAF is calculated as:

$$PAF = \frac{P(effect\ size - 1)}{P(effect\ size - 1) + 1}$$

Attributable burden (AB) is calculated as:

$$AB = PAF \times C$$

Where, *C = the direct burden (DALY) of a specific outcome, such as stroke.*

Box 2.2: Example of how a population attributable fraction is applied to the population

In the population, a proportion of all liver cancer is due to diabetes. This proportion is estimated using a population attributable fraction (PAF) which takes into account the number of people in each age group, say for males aged 50–54. It uses the number of males in this age range who have diabetes (for example 9%) and the size of the association between the risk factor and the linked disease (liver cancer). In this case, the relative risk is 2.31 (selected from published meta-analyses). This is calculated using the following formula:

$$PAF = \frac{P(RR-1)}{P(RR-1)+1}$$

Using this formula for diabetes and liver cancer, we get:

$$PAF = \frac{0.09(2.31-1)}{0.09(2.31-1)+1}$$

$$PAF = 0.105$$

In 2011, 2,840 DALY were estimated for liver cancer in Australian men aged 50–54. Attributable burden is an estimate of the amount of this liver cancer burden that is due to diabetes. This is calculated by multiplying the population attributable fraction and the linked disease burden.

AB = PAF x DALY

AB = 0.105 x 2,840

AB = 298

Therefore, 298 DALY from liver cancer in males aged 50–54 were attributable to diabetes. Note that this is an example and the calculations are done separately for each age group and sex.

2.5 Disease-as-risks analysis: calculating indirect burden

In burden of disease analysis, each disease is defined to be mutually exclusive to every other disease in the study. This enables the burden from all diseases to be summed to estimate the total burden in the population. As a result, the burden calculated in the ABDS 2011 only captured the direct burden of each disease. However, some diseases act as risk factors for other diseases and to fully account for the health loss attributable to diseases-as-risks requires that their 'indirect' or additional burden be calculated. Their direct and indirect burden can then be added to estimate their collective burden.

For example, in the ABDS 2011, microvascular complications of diabetes (such as diabetic nephropathy, neuropathy and retinopathy) are considered a main disabling consequence of diabetes and captured in the direct diabetes burden, but the macrovascular complications of diabetes (such as coronary heart disease, peripheral vascular disease and stroke) are captured under the more direct cardiovascular condition, not included under diabetes. Diabetes is considered to be a risk factor for coronary heart disease, stroke, dementia and other diseases, so the burden from these linked diseases due to diabetes (the 'indirect'

diabetes burden) can be added to the direct diabetes burden to estimate the collective diabetes burden without any overlap.

When interpreting the results, it is important to note that collective burden of diabetes and CKD were calculated independently and it is not possible to add them together due to overlaps between these risk factors.

2.6 Scenario modelling

Scenario modelling was used to explore the impact of changes in the prevalence of diabetes and CKD on the burden of linked diseases, as well as the collective burden for these 2 diseases under 2 scenarios: if the prevalence rate of diabetes or CKD continues its increasing trend, or if it remains steady to 2020. These scenarios provide an indication of the amount of burden that may be avoided if the current rise of diabetes or CKD prevalence is halted, compared with the amount of burden if the current trends continue.

The year 2020 was chosen because it aligns with the National Strategic Framework for Chronic Conditions and the World Health Organization's Global Action Plan for the Prevention and Control of Non-communicable Diseases 2013–2020 (WHO 2013).

Results from both methods were compared with 2011 burden to estimate the difference in the impact between the 2 scenarios. Detailed information on the methods used for scenario modelling is in Appendix C.

3 Diabetes estimates

This chapter describes the diabetes burden estimates as reported in the ABDS 2011 (referred to as the 'direct burden') and the burden from linked diseases due to diabetes (referred to as the 'indirect burden'). The list of diseases included is outlined in Table A1.

3.1 Diabetes burden in the ABDS 2011

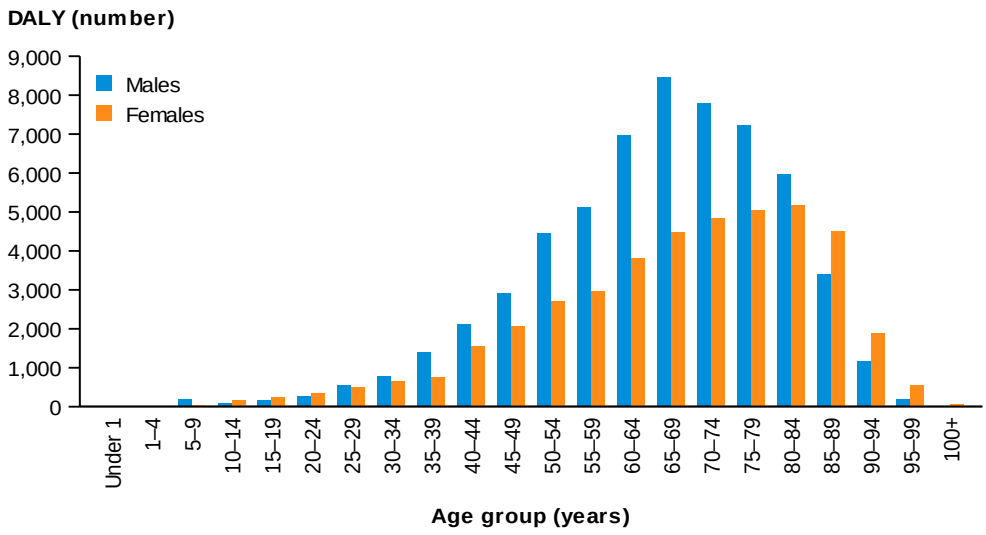
In 2011, diabetes accounted for 2.3% of the total burden of diseases and injuries in Australia (AIHW 2016a). Overall, diabetes was the 12th leading cause of burden, equating to 101,653 DALY. A higher proportion of diabetes burden was evident in males (58%) compared with females (42%) (Table 3.1). The diabetes burden had a similar proportion of fatal and non-fatal burden (53% fatal; 47% non-fatal).

Table 3.1: Diabetes direct burden, by sex, 2011

	DALY		YLL		YLD	
	Number	%	Number	%	Number	%
Males	59,298	58.3	31,114	57.5	28,183	59.3
Females	42,356	41.7	22,996	42.5	19,360	40.7
Persons	**101,653**	**100.0**	**54,110**	**100.0**	**47,543**	**100.0**

Source: AIHW burden of disease database, 2011.

In both males and females, diabetes burden varied by age (Figure 3.1). Males experienced a greater amount of burden in most age groups. In males, burden increased steadily to age 69, reaching a peak of 8,461 DALY, and then decreased rapidly after age 84. Females experienced more burden than males from age 85 onwards, probably influenced by the relative longevity in females. In females, the number of DALY increased with age—but not as steeply as seen in males—peaking at age 80–84 (5,169 DALY).



Source: AIHW burden of disease database, 2011.

Figure 3.1: Diabetes direct burden, by age and sex, 2011

3.2 What is the collective burden of diabetes?

The diabetes burden reported in the ABDS 2011 is referred to as the direct burden. The burden of other diseases attributable to diabetes is referred to as the indirect burden. The sum of the direct and indirect burden is the collective diabetes burden.

Table 3.2 shows the number of DALY for diabetes due to direct and indirect burden, and its total collective burden. There were 101,653 DALY estimated due to the direct impact of diabetes in 2011. Additional 88,332 DALY were estimated due to the indirect burden of diabetes on linked diseases.

Collectively, diabetes was responsible for 189,985 DALY. The collective burden due to diabetes was almost twice (1.9 times) the direct diabetes burden reported in the ABDS 2011. By including indirect diabetes burden, the burden of diabetes for males increased by 84% and for females it increased by 90%.

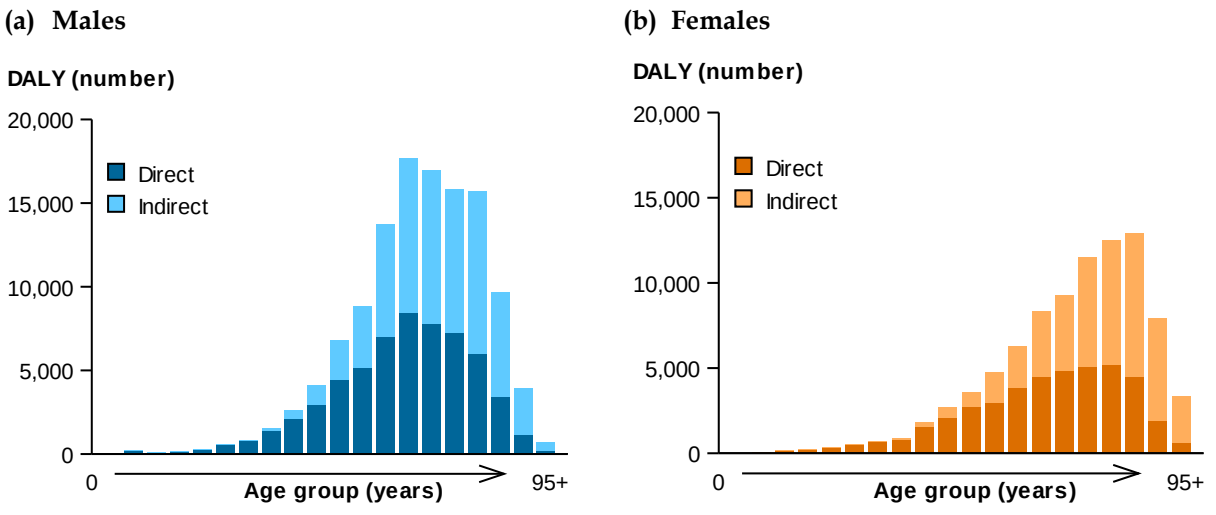
Table 3.2: Collective burden (DALY) of diabetes, by direct and indirect burden and sex, 2011

	Direct	Indirect	Collective
Males	59,298	50,045	109,343
Females	42,356	38,288	80,644
Persons	**101,653**	**88,332**	**189,985**

Note: Numbers may not sum to the total due to rounding.

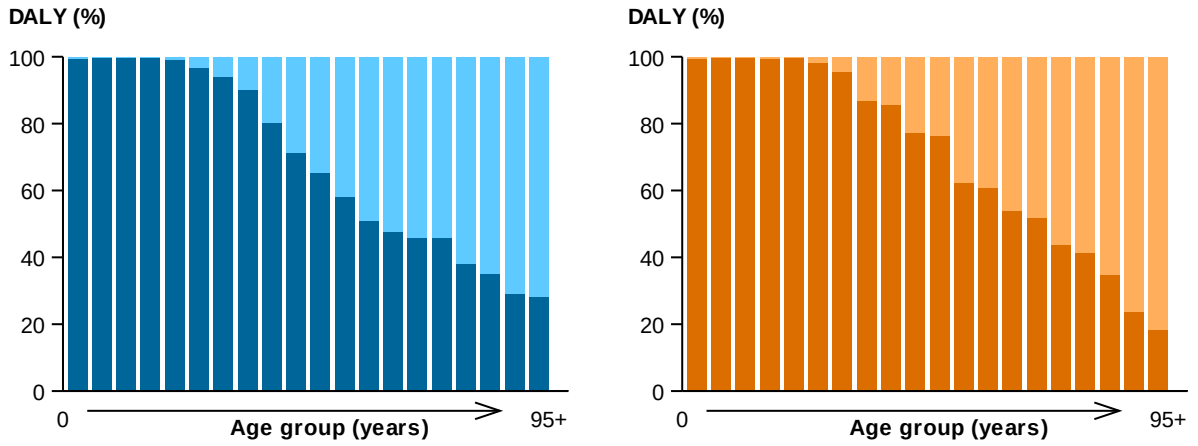
Source: AIHW analysis of burden of disease database, 2011.

The indirect and direct diabetes burden differed by age (Figure 3.2). The indirect burden occurred at a later age than direct burden, because the linked diseases are generally conditions that progress over an extended period and predominantly affect older people. In both males and females, the indirect burden was responsible for over 50% of the collective diabetes burden from age 75 onwards.



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.2: Collective burden (DALY) of diabetes, by direct and indirect burden, by age and sex, 2011



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.2 (continued): Collective burden (DALY) of diabetes, by direct and indirect burden, by age and sex, 2011

3.3 How much burden from linked diseases is due to diabetes?

The indirect diabetes burden was estimated as the number of DALY due to linked diseases. Overall, the indirect diabetes burden was responsible for 88,332 DALY (Table 3.3).

The burden attributable to diabetes was highest in coronary heart disease (38,852 DALY), followed by stroke (18,730 DALY) and CKD (8,945 DALY). These 3 diseases were responsible for 75% of the indirect diabetes burden, with almost half (44%) of the total indirect diabetes burden from coronary heart disease.

The indirect diabetes burden varied by sex, with males experiencing 31% more burden than females (50,045 DALY compared with 38,288 DALY). This is due to both overall diabetes prevalence and the burden of some linked diseases such as coronary heart disease, being higher among males.

Table 3.3: Attributable burden due to diabetes, by linked disease and sex, 2011

Linked disease	Males		Females		Persons	
	Attributable DALY	Proportion of linked disease (%)[a]	Attributable DALY	Proportion of linked disease (%)[a]	Attributable DALY	Proportion of linked disease (%)[a]
Cardiovascular diseases						
Coronary heart disease	23,539	10.4	15,313	12.7	38,852	11.2
Stroke	8,864	13.5	9,866	13.9	18,730	13.7
Peripheral vascular disease	509	10.9	262	7.0	771	9.2
Chronic kidney disease	5,164	24.0	3,781	17.9	8,945	21.0
Dementia[b]	3,597	6.5	4,421	4.6	8,018	5.3
Cancer						
Liver cancer	2,926	13.5	729	9.6	3,655	12.4
Pancreatic cancer	2,397	9.7	1,258	6.4	3,655	8.2
Bowel cancer	2,078	3.9	915	2.3	2,993	3.2
Breast cancer	—	—	875	1.4	875	1.4
Kidney cancer	570	4.6	170	3.1	739	4.2
Uterine cancer	—	—	610	8.0	610	8.0
Bladder cancer	401	3.4	88	2.1	489	3.1
Total	**50,045**		**38,288**		**88,332**	

(a) The 'Proportion of linked disease (%)' column is the attributable DALY due to diabetes divided by the total direct linked disease burden estimated in the ABDS of that row. Numbers may not sum to the total due to rounding.

(b) The burden of dementia due to diabetes was estimated only in people aged 65 and over, because the association is in late life dementia only.

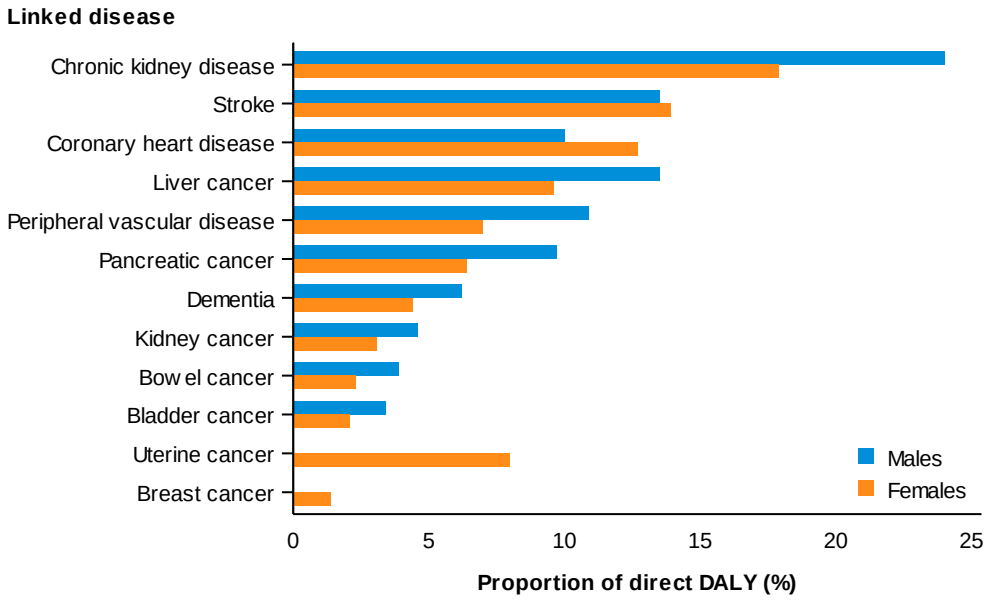
Source: AIHW analysis of burden of disease database, 2011.

The proportion of disease burden that is attributable to diabetes was estimated for each linked disease (Table 3.3 and Figure 3.3). This is derived from the number of DALY attributable to diabetes divided by the direct burden of each linked disease. For example, we estimated 38,852 DALY of coronary heart disease can be attributable to diabetes; this is 11% of the direct burden of coronary heart disease (346,651 DALY).

In males, 24% of the chronic kidney disease burden, 13% of the liver cancer burden and 13% of the stroke burden was due to diabetes. Diabetes was also responsible for 11% of the peripheral vascular disease burden and 10% of the coronary heart disease burden. In females, diabetes was responsible for 18% of the chronic kidney disease burden, 14% of the stroke burden and 13% of coronary heart disease burden (Table 3.3, Figure 3.3).

Comparing male and female proportions of attributable DALY by disease, males had a larger proportion of underlying disease burden attributable to diabetes, with the exception of coronary heart disease and stroke. The largest absolute difference was seen in CKD, liver cancer, peripheral vascular disease and pancreatic cancer.

Uterine and breast cancer were estimated for the female population only. Diabetes was attributable to 8.0% and 1.4% of the uterine and breast cancer burden, respectively.



Source: AIHW analysis of burden of disease database, 2011.

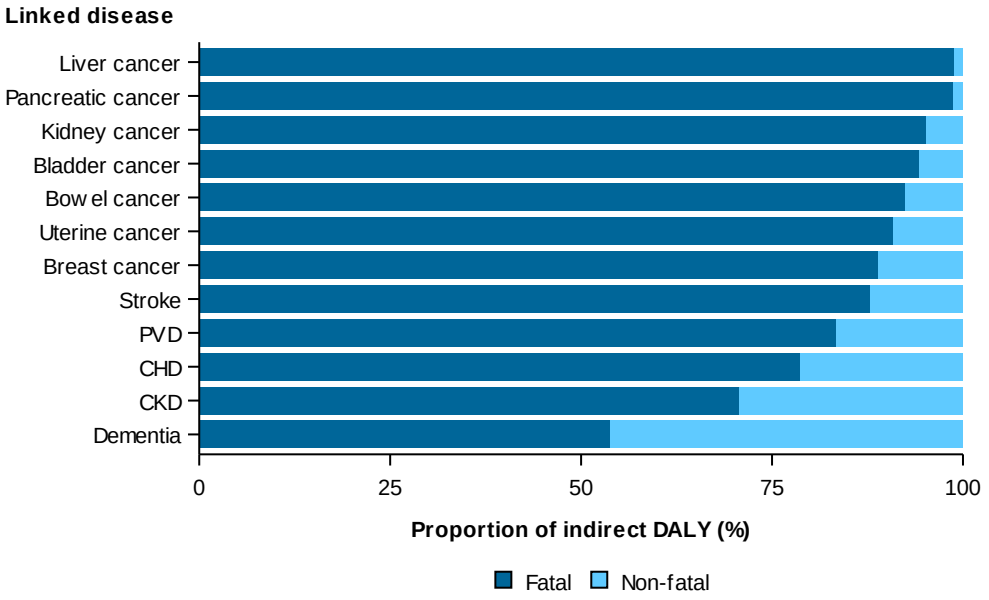
Figure 3.3: Proportion of burden attributable to diabetes, by linked disease and sex, 2011

Was the indirect burden due to fatal or non-fatal outcomes?

In the ABDS 2011, the direct burden of diseases associated with diabetes was predominantly fatal, with the exception of dementia burden, where it was mainly non-fatal. This influenced the proportion of fatal and non-fatal outcomes for the indirect diabetes burden.

The indirect diabetes burden was mostly due to fatal burden, with the exception of dementia attributable to diabetes (54% fatal; 46% non-fatal).

The proportion of indirect diabetes burden that was fatal differed by linked disease (Figure 3.4). The proportion of fatal burden for linked cancers ranged between 89% of the breast cancer burden attributable to diabetes to 99% of the liver cancer burden attributable to diabetes. The proportion of fatal burden for linked cardiovascular diseases ranged from 79% of the coronary heart disease burden attributable to diabetes to 88% of the stroke burden attributable to diabetes. Similarly, 71% of the burden of CKD attributable to diabetes was due to fatal outcomes.

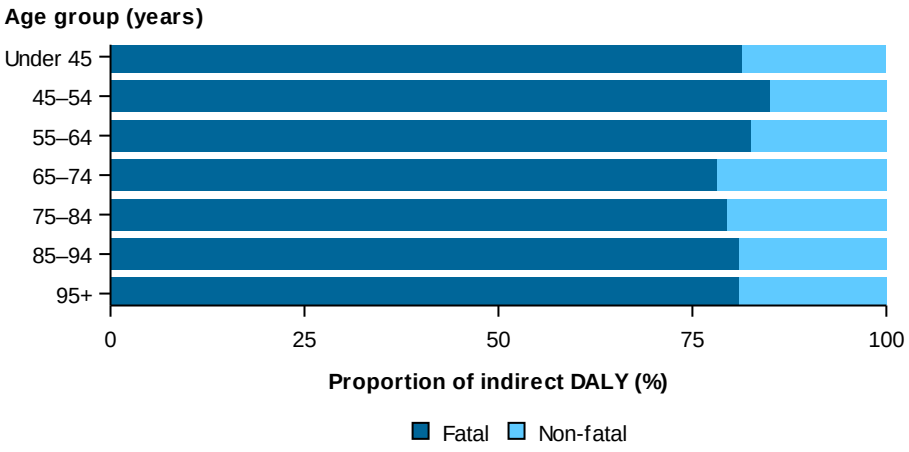


Note: PVD = Peripheral vascular disease; CHD = Coronary heart disease; CKD = Chronic kidney disease.

Source: AIHW analysis of burden of disease database, 2011.

Figure 3.4: Proportion of indirect diabetes burden, by linked disease due to fatal and non-fatal outcomes, 2011

The proportion of indirect diabetes burden that was fatal differed by age (Figure 3.5). The proportion of fatal outcomes was higher for younger age groups—responsible for 81–85% of the indirect diabetes burden under age 55. This decreased to 79% between ages 65 and 74 and increased slightly to 81% for age 85 and over.



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.5: Proportion of indirect diabetes burden due to fatal and non-fatal outcomes, by age, 2011

3.4 Indirect diabetes burden by linked disease

This section looks at the impact of diabetes on individual linked diseases by age and sex.

The indirect burden was measured by the number and proportion of DALY from the disease that was caused by the risk factor—in this case diabetes. Where possible, similar scales have

been used for graphs across linked diseases to depict the relative size of the burden estimates reported and to aid interpretation.

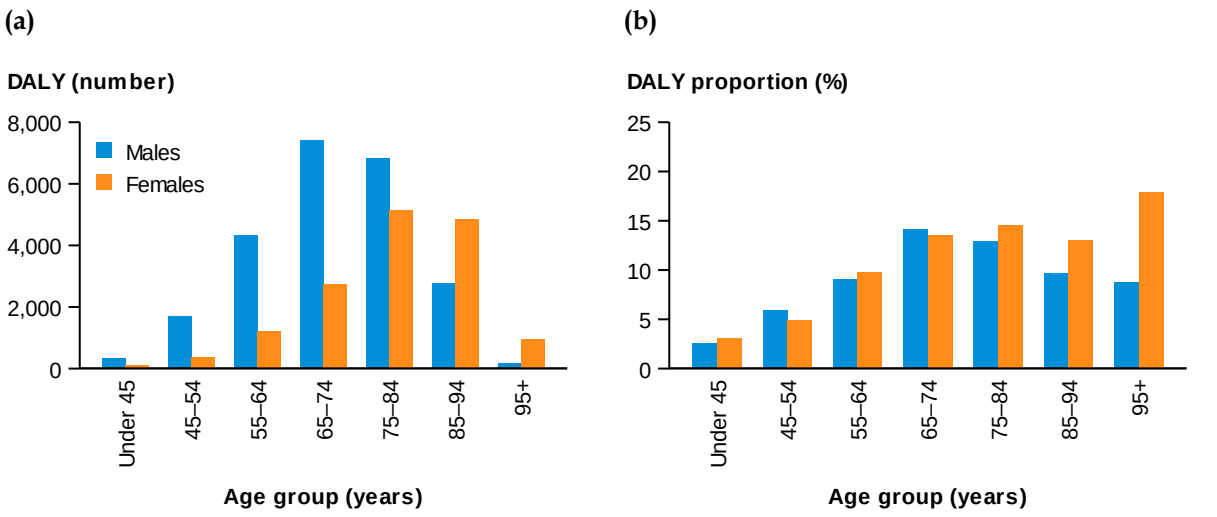
Cardiovascular disease estimates

Coronary heart disease

Diabetes contributed to 11% of the coronary heart disease burden in 2011, equating to 38,852 DALY (Table 3.3). Males experienced a greater number of DALY (23,539), compared with females (15,313).

Males experienced most of the coronary heart disease DALY due to diabetes between ages 65 and 84 (Figure 3.6a). Females experienced most of the attributable burden at a later age, with the majority occurring between ages 75 and 94.

Overall, the proportion of coronary heart disease burden due to diabetes increased with age (Figure 3.6b). The proportion of attributable burden peaked at 14% in males at ages 65–74 and decreased to 8.7% at age 95 and over. In females the attributable burden gradually increased with age, and was higher than males from ages 75 onwards, peaking at 18% at age 95 and over.



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.6: Burden (DALY) of coronary heart disease attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

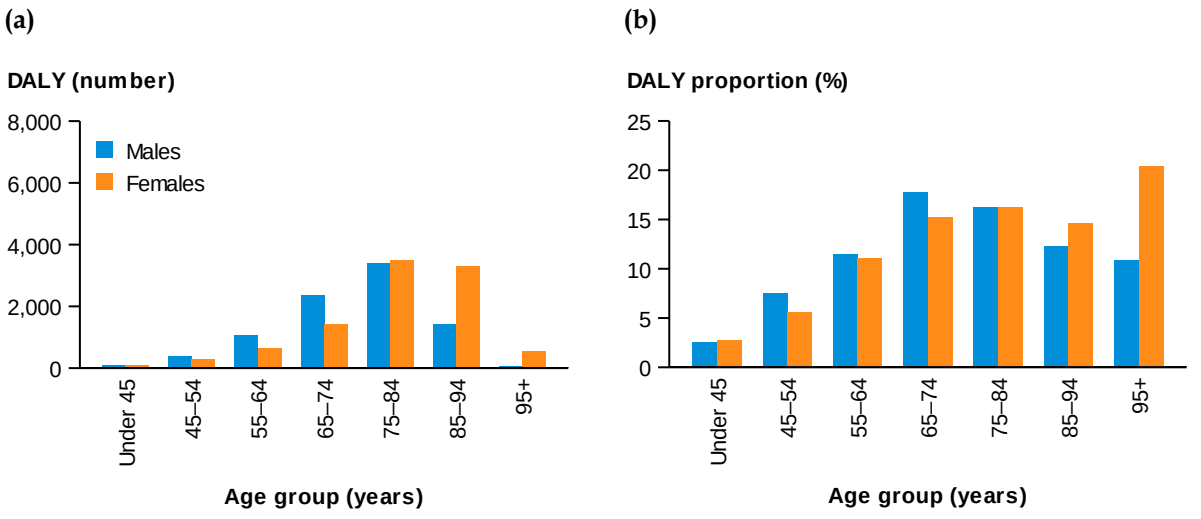
Stroke

In total, 14% of the stroke burden was attributable to diabetes or 18,730 DALY (Table 3.3). Males experienced a slightly lower number of DALY (8,864), compared with females (9,866), but a similar proportion of the burden was evident in both sexes (13.5% males; 13.9% females).

The stroke burden due to diabetes increased steeply with increasing age in males, peaking at 3,411 DALY between ages 75 and 84 (Figure 3.7a). From age 85, the number of attributable DALY decreased dramatically. Females also experienced an increase in DALY with increasing age, but a lower number of DALY compared with males before age 75. Unlike

males, the number of DALY in females remained high and was similar between ages 75–84 and 85–94.

In males and females from age 55 onwards, between 10 and 20% of the stoke burden was attributable to diabetes (Figure 3.7b). In males, the proportion was highest at ages 65–74, where 18% of stroke burden was due to diabetes. In females, this proportion was highest at age 95 and over (20%).



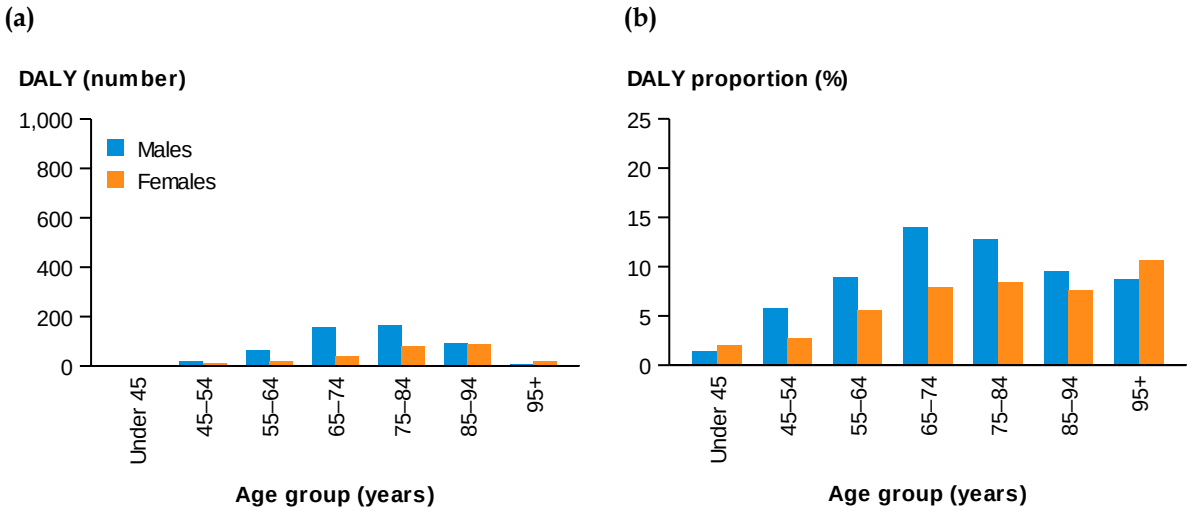
Source: AIHW analysis of burden of disease database, 2011.

Figure 3.7: Burden (DALY) of stroke attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

Peripheral vascular disease

Diabetes contributed to 9.2% of the peripheral vascular disease burden in 2011 (771 DALY; Table 3.3). Males experienced two-thirds of the attributable burden (509 DALY), with 11% of the peripheral vascular disease burden in males due to diabetes. This proportion was lower in females (7.0%).

Similar to coronary heart disease, the attributable burden increased with age and was higher in males in all ages, compared with females, except at age 95 and over (Figure 3.8a). The proportion of attributable burden peaked at 14% in males at ages 65–74 and decreased to 8.7% at age 95 and over (Figure 3.8b). In females, the attributable burden gradually increased with age, but was much lower in all ages, with the exception of those aged 95 and over.



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.8: Burden (DALY) of peripheral vascular disease attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

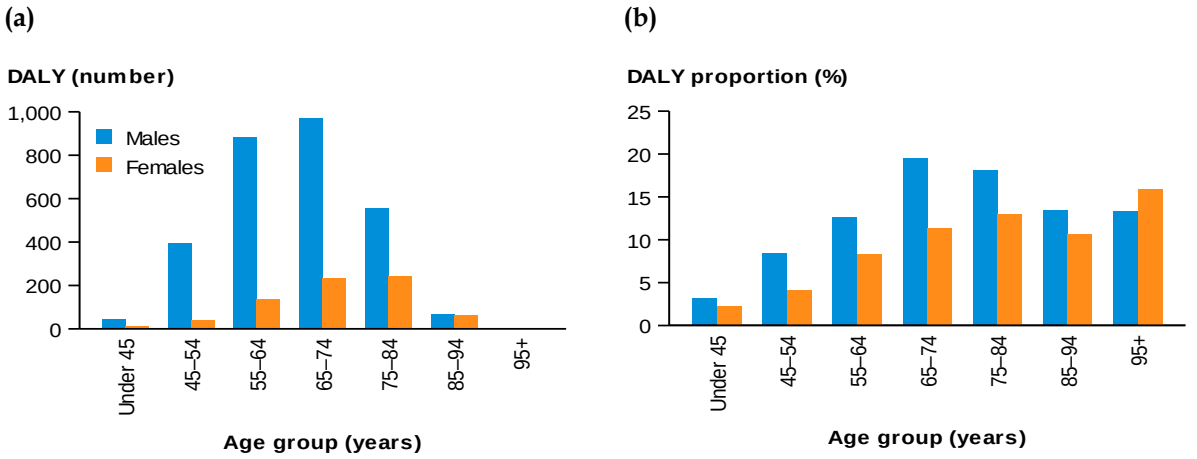
Cancer estimates

Liver cancer

In total, 12% of the liver cancer burden was attributable to diabetes (3,655 DALY; Table 3.3), most of which (2,926 DALY; 80%) was experienced by males. This is influenced by the higher prevalence of both diabetes and liver cancer in males compared with females.

The proportion of liver cancer burden attributable to diabetes was higher in males (13%) compared with females (9.6%). Males experienced most of the liver cancer attributable burden between ages 55 and 74, peaking at 972 DALY between ages 65 and 74 (Figure 3.9a). Females experienced attributable burden at a later age, with the majority occurring between ages 65 and 84.

Between 10 and 20% of the liver cancer burden after age 65 was attributable to diabetes (Figure 3.9b). In males, the proportion was highest at ages 65–74, where 20% of liver cancer burden was due to diabetes. In females, this proportion was highest at age 95 and over (16%).



Note: For age group 95+, liver cancer attributable to diabetes was <10 DALY.

Source: AIHW analysis of burden of disease database, 2011.

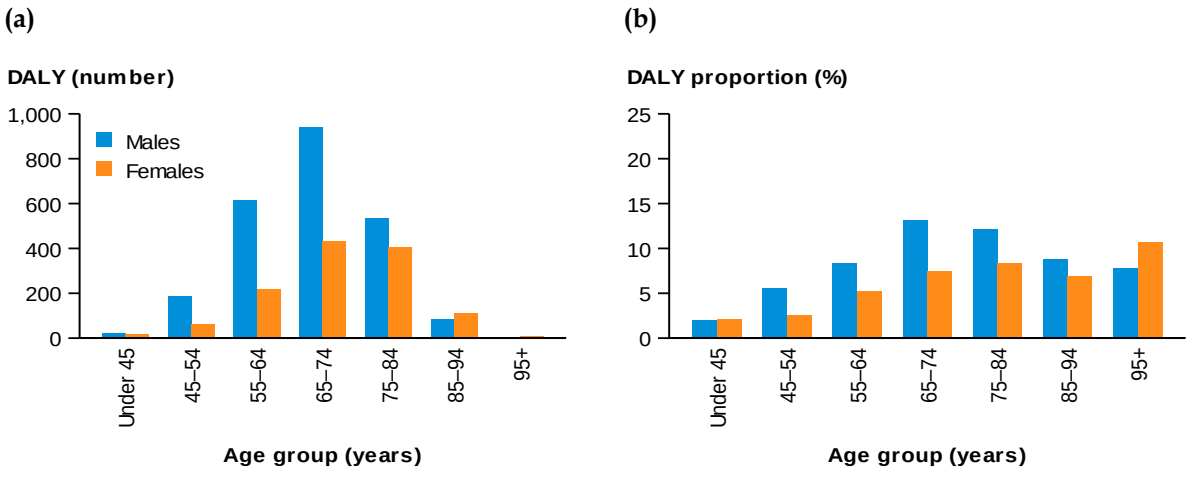
Figure 3.9: Burden (DALY) of liver cancer attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

Pancreatic cancer

In 2011, 8.2% of the pancreatic cancer burden was attributable to diabetes, equating to 3,655 DALY (Table 3.3). Males experienced almost two-thirds (66%) of the pancreatic cancer burden due to diabetes. The proportion of pancreatic cancer burden attributable to diabetes was also higher in males (9.7%), compared with females (6.4%).

In males, the number of attributable DALY increased steeply with age, peaking at 942 DALY between ages 65 and 74 (Figure 3.10a). From age 75 onwards, this decreased dramatically. In females, the burden increased gradually and was experienced at a later age compared with males. The majority of the burden in females occurred between ages 65 and 84.

The proportion of pancreatic cancer burden due to diabetes also increased with age and peaked at 13% in males aged 65–74 and 11% in females aged 95 and over (Figure 3.10b).



Note: For age group 95+, pancreatic cancer attributable to diabetes was <10 DALY.

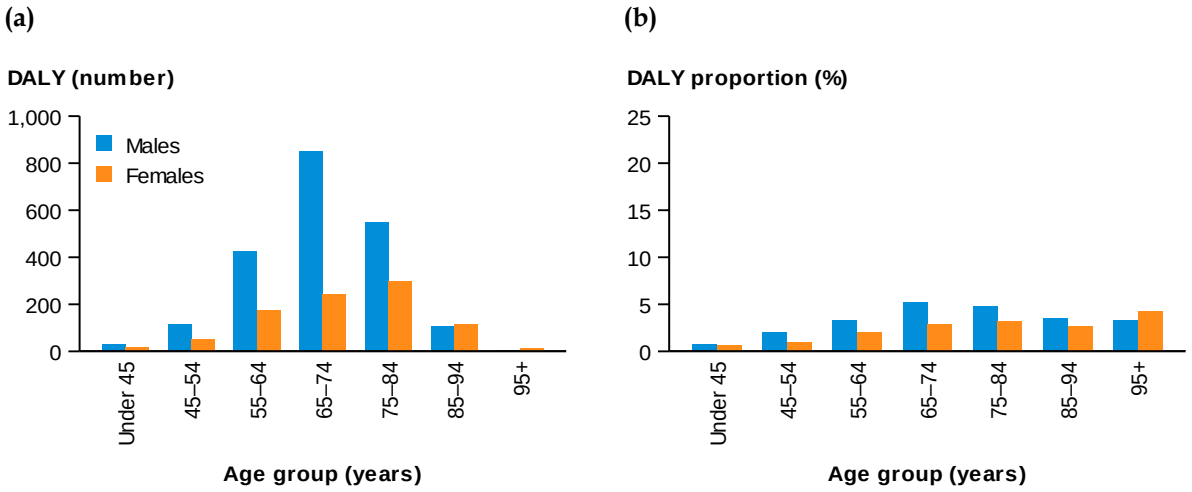
Source: AIHW analysis of burden of disease database, 2011.

Figure 3.10: Burden (DALY) of pancreatic cancer attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

Bowel cancer

In 2011, 3.2% of the bowel cancer burden was attributable to diabetes, equating to 2,993 DALY (Table 3.3). Males experienced 69% of the bowel cancer attributable burden due to diabetes. The proportion of bowel cancer burden attributable to diabetes was less than 5% in both males (3.9%) and females (2.3%).

In males, bowel cancer burden due to diabetes increased steeply with age, peaking at 849 DALY between ages 65 and 74 (Figure 3.11a). In females, the number of attributable DALY increased slightly with age, peaking at ages 75–84. The proportion of attributable burden peaked at 5.3% in males aged 65–74 and 4.3% in females aged 95 and over (Figure 3.11b).



Note: For age group 95+, bowel cancer attributable to diabetes was <20 DALY.

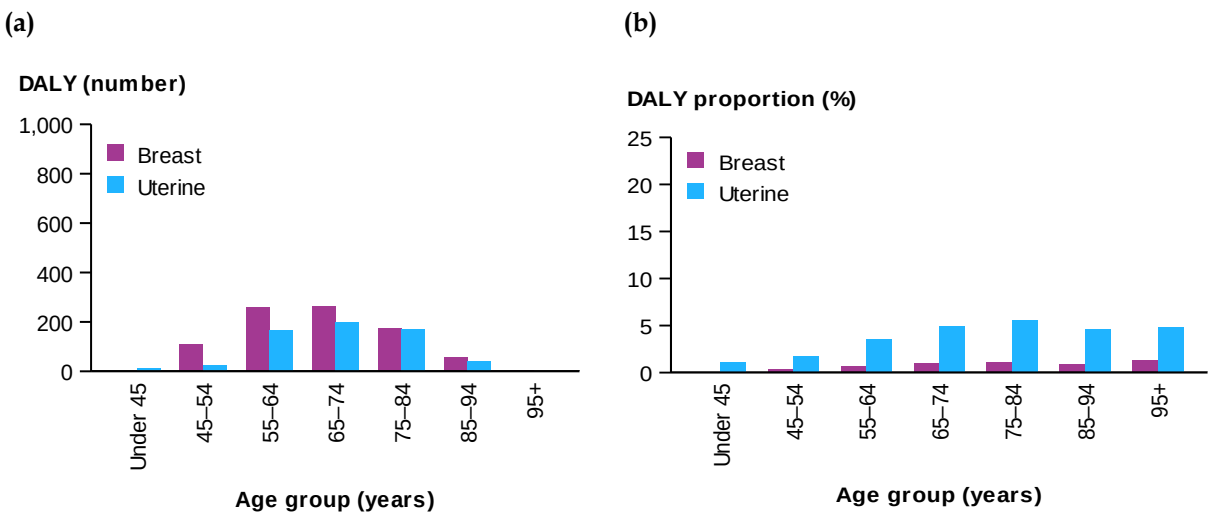
Source: AIHW analysis of burden of disease database, 2011.

Figure 3.11: Burden (DALY) of bowel cancer attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

Uterine and breast cancer in females

In 2011, 8.0% of the uterine cancer burden and 1.4% of the breast cancer burden in females was attributable to diabetes, equating to 610 and 875 DALY, respectively (Table 3.3). The burden of breast cancer due to diabetes was estimated only in women aged 45 and over, because studies found its association with diabetes was mainly in post-menopausal women (Boyle et al. 2012; Larsson et al. 2007).

In females, the number of attributable DALY for uterine and breast cancer mostly occurred between ages 55 and 84 (Figure 3.12a). Between 9 and 11% of uterine cancer over age 65 was attributable to diabetes (Figure 3.12b). The proportion of attributable burden of breast cancer due to diabetes peaked at 2.6% in women aged 95 and over (Figure 3.12b).



Source: AIHW analysis of burden of disease database, 2011.

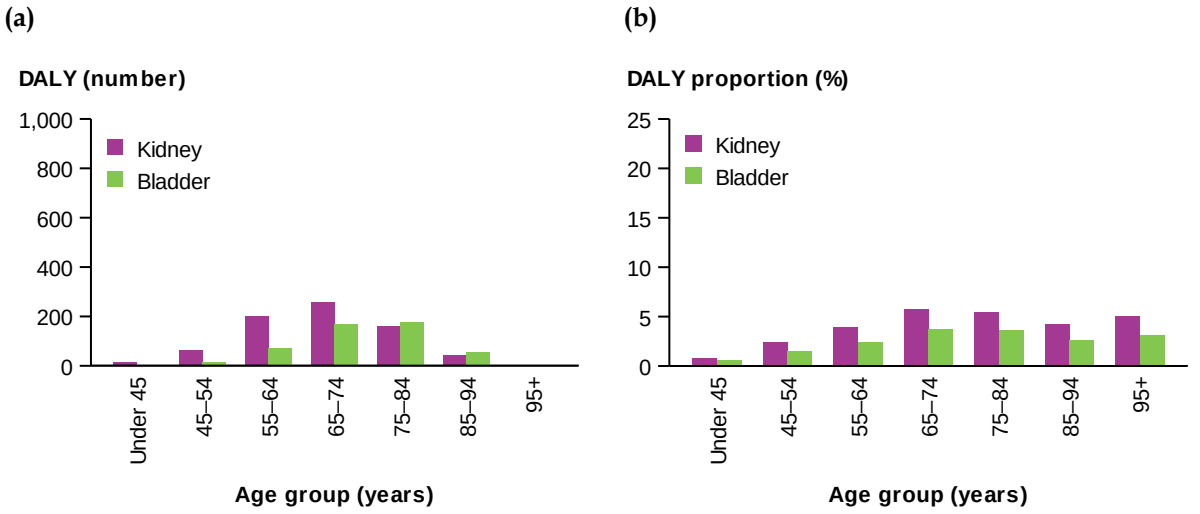
Figure 3.12: Burden (DALY) of breast and uterine cancers attributable to diabetes, by (a) number and (b) proportion of burden, by age and cancer type, 2011

Kidney and bladder cancer

Diabetes contributed to 4.2% of kidney and 3.1% of the bladder cancer burden in 2011 (Table 3.3). This equated to 739 and 489 DALY, respectively.

Males experienced 77% of the attributable diabetes burden from kidney cancer and 82% from bladder cancer. This compares with 23% and 18%, respectively, for females. This is influenced by higher direct burden of both kidney and bladder cancer in males compared with females.

Attributable burden increased with age for kidney cancer, peaking between ages 65 and 74 (258 DALY). The attributable burden in bladder cancer increased at a later age, with both linked cancers showing a similar number of DALY between ages 75 and 84 (Figure 3.13a). The proportion of attributable burden peaked at ages 65–74 for kidney cancer (5.8%) and bladder cancer (3.7%) (Figure 3.13b).



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.13: Burden (DALY) of kidney and bladder cancer attributable to diabetes, by (a) number and (b) proportion of burden, by age and cancer type, 2011

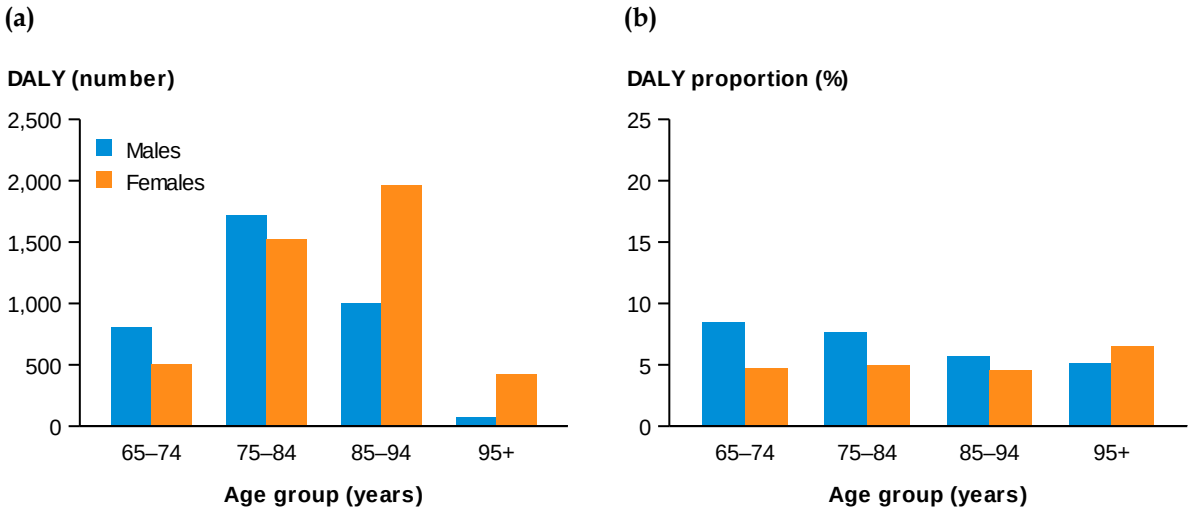
Dementia estimates

Diabetes contributed to 5.3% of the dementia burden at age 65 and over, equating to 8,018 DALY (Table 3.3). The burden of dementia due to diabetes was estimated only in people aged 65 and over, because the association is in late life dementia only.

Males experienced a slightly lower number of DALY (3,597) compared with females (4,421), but the proportion of dementia burden attributable to diabetes was higher in males (6.5% compared with 4.6% in females).

Males experienced most of the attributable burden between ages 75 and 84, peaking at 1,719 DALY (Figure 3.14a). Females experienced attributable burden at a later age, peaking between ages 85 and 94 (1,964 DALY).

The proportion of dementia burden attributable to diabetes decreased with age in males, from 8.5% at ages 65–74 to 5.1% at age 95 and over (Figure 3.14b). In females, this increased with age, from 4.7% at ages 65–74 to 6.5% at age 95 and over.



Note: Attributable burden was not calculated for ages under 65, because the association is with dementia in late-life (age 65 and over).

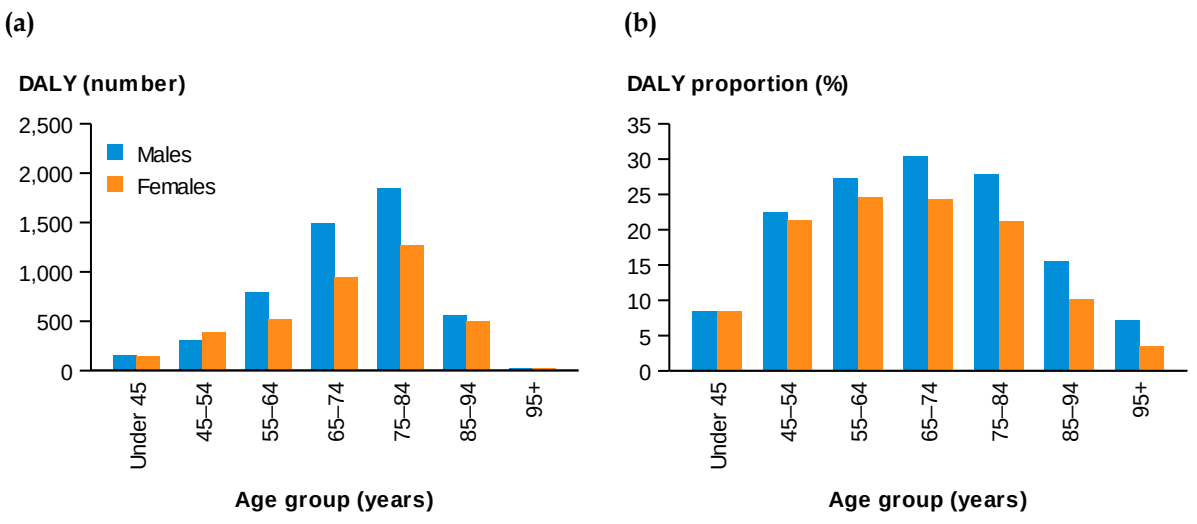
Source: AIHW analysis of burden of disease database, 2011.

Figure 3.14: Burden (DALY) of dementia attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

Chronic kidney disease estimates

Diabetes contributed to 21% of the CKD burden, equating to 8,945 DALY (Table 3.3). Males experienced 57% of the attributable burden (5,164 DALY), and the proportion of CKD burden attributable to diabetes was higher in males (24% compared with 18% in females).

Males and females experienced most of the attributable burden between ages 75 and 84 (1,492 DALY and 947 DALY, respectively) (Figure 3.15a), and 21–30% of CKD between ages 45–74 was due to diabetes (Figure 3.15b).



Source: AIHW analysis of burden of disease database, 2011.

Figure 3.15: Burden (DALY) of chronic kidney disease attributable to diabetes, by (a) number and (b) proportion of burden, by age and sex, 2011

3.5 Estimated diabetes burden in 2020 under 2 different scenarios

Table 3.4 presents the indirect and direct diabetes burden in 2011, compared with the diabetes burden in 2020 under 2 different scenarios. These scenarios provide an indication of the amount of burden that may be avoided if the current rise of diabetes is halted, compared with the amount of burden if the current trend continues (see Appendix D for detailed methods used).

For the direct burden, Scenario A describes the impact of the annual rate of change in fatal and non-fatal burden rates between 2003 and 2011 continued to 2020. Scenario B describes the impact of population growth and ageing, where the diabetes fatal and non-fatal burden rates remain stable to 2020.

For the indirect burden, Scenario A describes the impact of the annual rate of change in diabetes prevalence between 2003 and 2011 continued to 2020. Scenario B describes the impact of the diabetes prevalence rate remaining stable to 2020. The 2011 burden rates for each linked disease were assumed to remain the same to 2020 for ease of calculation.

The annual rate of change in prevalence and fatal burden between 2003 and 2011 was derived for each sex and age group (see tables C1 and C2). The annual rate of change in non-fatal burden between 2003 and 2011 was calculated at the sequela level for each sex and age group. Sequelae are consequences associated with the disease, that is undiagnosed and diagnosed diabetes (see Appendix D).

The results of the scenario analyses are presented below.

If the rate of change observed between 2003 and 2011 in diabetes prevalence, fatal and non-fatal burden continued to 2020:

- The estimated indirect diabetes burden is projected to be 180,000 DALY in 2020, which is twice as high as the indirect burden in 2011 (Table 3.4).
- The estimated direct diabetes burden is projected to be 130,000 DALY in 2020, fatal burden is expected to be 6% higher, and non-fatal burden 52% higher, than the direct burden in 2011 (Table 3.4).
- The estimated collective diabetes burden is projected to be 310,000 DALY in 2020, which 1.6 times as high as the collective burden in 2011 (Table 3.4).

If the current rise in diabetes is halted (that is, the prevalence, fatal and non-fatal burden rates remain stable from 2011 to 2020), then by 2020:

- the estimated collective diabetes burden is projected to be 244,000 DALY, which is 1.3 times as high as the collective burden in 2011 (and reflects population increase and ageing alone) (Table 3.4).

In comparing the 2 scenarios, if the current rise in diabetes is halted compared with if the current trend continues, then by 2020:

- 21% of future collective diabetes burden could be avoided (Table 3.4)
- 36% of future indirect diabetes burden could be avoided, with reductions ranging from 32% for CKD to 40% for bladder cancer and dementia (Table C5).

Table 3.4: Estimated diabetes burden in 2020 under different exposure scenarios

		Scenario A		Scenario B		Scenario B compared with Scenario A	
		Continued trend in diabetes prevalence rate to 2020		Stable diabetes prevalence rate to 2020		DALY that would be avoided in 2020	
	DALY in 2011	DALY in 2020	Percentage change from 2011 DALY[(a)]	DALY in 2020	Percentage change from 2011 DALY[(a)]	DALY number	DALY (%)[(b)]
Indirect burden total	**88,332**	**180,084**	**103.9**	**115,788**	**31.1**	**64,297**	**35.7**
Direct diabetes burden							
Fatal (YLL)	54,110	57,382	6.0	69,315	28.1	–11,933	–20.8
Non-fatal (YLD)	47,543	72,431	52.3	59,233	24.6	13,197	18.2
Total (DALY)[(c)]	**101,653**	**129,812**	**27.7**	**128,548**	**26.5**	**1,264**	**1.0**
Collective diabetes burden[(d)]	**189,985**	**309,896**	**63.1**	**244,337**	**28.6**	**65,561**	**21.2**

(a) Percentage change is the change in burden between 2020 and 2011 divided by the burden in 2011 for each scenario.

(b) Percentage difference is the difference in attributable DALY in 2020 between Scenario A and B divided by the attributable DALY in 2020 for Scenario A.

(c) Numbers may not sum to the total due to rounding.

(d) Collective diabetes burden is the sum of indirect diabetes burden and the total (DALY) for each scenario.

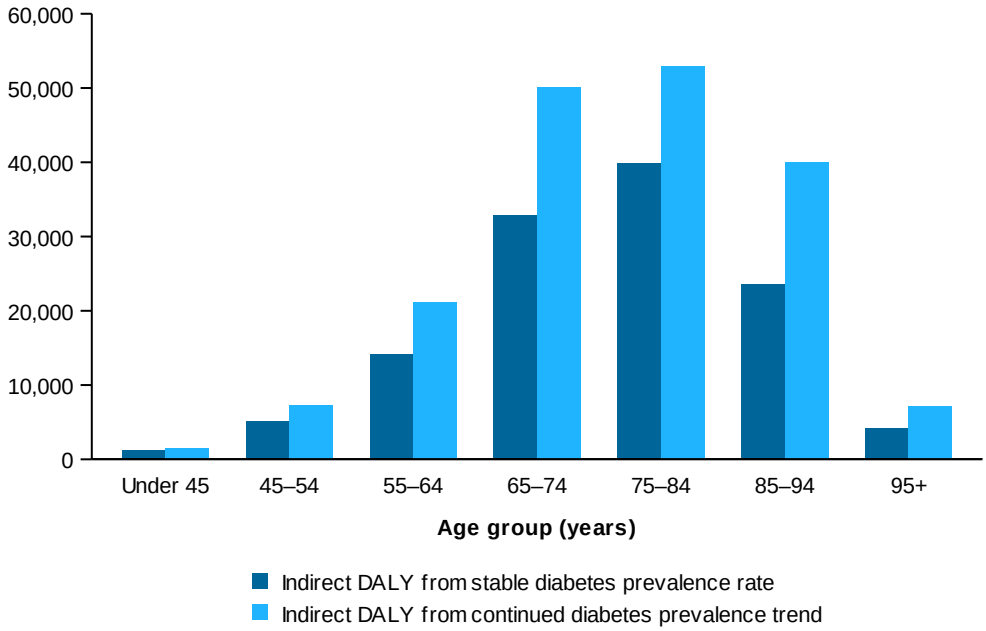
Source: AIHW analysis of burden of disease database, 2011.

3.6 Scenario differences by age

Indirect diabetes burden

The indirect diabetes burden in 2011 occurred mainly in older ages, because the linked diseases progress over an extended period of time and become more prevalent with age.

Figure 3.16 shows the indirect diabetes burden by age in 2020 under the 2 different scenarios. In both scenarios, the indirect burden estimated for 2020 was highest in people aged 75–84. Under both scenarios, the indirect DALY due to diabetes was relatively similar in those aged under 45 and 95 and over. If the current rise in diabetes is halted, 34% of the future indirect burden due to diabetes in people aged 45–64, and 36% in those aged 65–94, could be avoided in 2020.



Note: 'Stable diabetes' is the scenario where the rise of diabetes prevalence is halted; 'continued diabetes' is the scenario where the current prevalence trends continue to rise. The stable diabetes prevalence rate is based on 2011 prevalence rate.

Source: AIHW analysis of burden of disease database, 2011.

Figure 3.16: Estimated indirect diabetes burden (DALY) in 2020 under different exposure scenarios, by age

4 Chronic kidney disease estimates

This chapter examines the CKD estimates as reported in the ABDS 2011 (direct burden) and the burden in linked diseases due to CKD (indirect burden). The linked diseases include coronary heart disease, stroke, dementia and peripheral vascular disease.

4.1 Chronic kidney disease burden in the ABDS 2011

In 2011, CKD accounted for 0.9% of the total burden of diseases and injuries in Australia, equating to 42,574 DALY (AIHW 2016a). The number of DALY was similar by sex (Table 4.1). Nearly three-quarters (72%) of CKD burden was due to fatal outcomes.

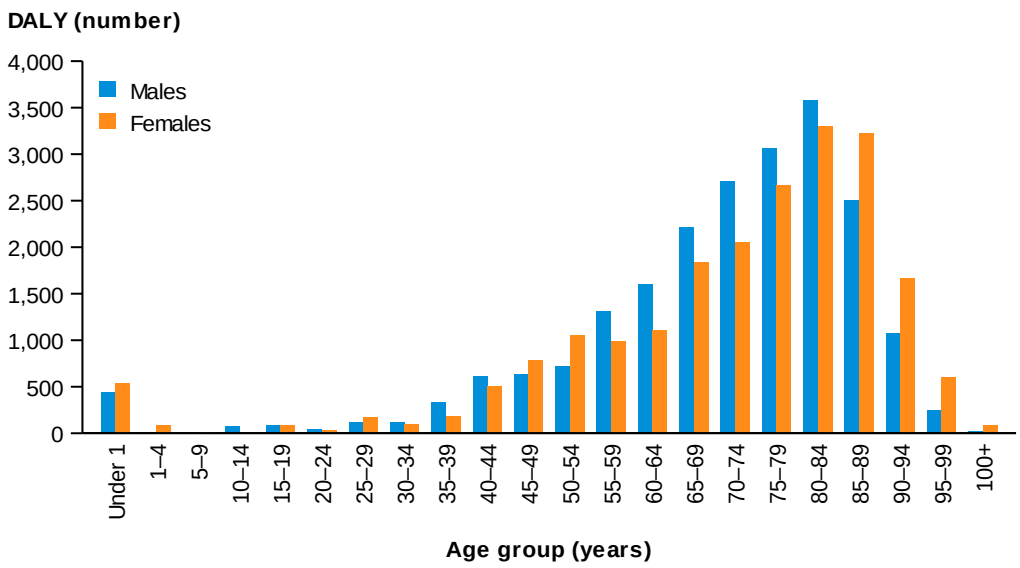
Table 4.1: Chronic kidney disease direct burden, by sex, 2011

	DALY		YLL		YLD	
	Number	%	Number	%	Number	%
Males	21,490	50.5	15,680	51.2	5,810	48.7
Females	21,084	49.5	14,965	48.8	6,119	51.3
Persons	**42,574**	**100.0**	**30,645**	**100.0**	**11,929**	**100.0**

Note: Numbers may not sum to the total due to rounding.

Source: AIHW burden of disease database, 2011.

CKD burden increased with age, with the exception of burden in infants (Figure 4.1). Males experienced a greater amount of burden, before age 85. In males, burden increased steadily to age 84, reaching a peak of 3,575 DALY. Females experienced more burden than males from age 85 onwards, peaking at 80–84 (3,300 DALY).



Source: AIHW burden of disease database, 2011.

Figure 4.1: Chronic kidney disease direct burden, by age and sex, 2011

4.2 What is the collective burden of chronic kidney disease?

Table 4.2 shows the number of DALY for CKD due to direct and indirect burden, and its total collective burden. There were 42,574 DALY estimated due to the direct impact of CKD in 2011. Additional 46,866 DALY were estimated due to the indirect burden of CKD on linked diseases.

Collectively, CKD was responsible for 89,460 DALY. The collective burden due to CKD was twice (2.1 times) the direct CKD burden reported in the ABDS 2011. By including the indirect CKD burden, the burden of CKD for males doubled, and for females it more than doubled (ratio of 2.2).

Table 4.2: Collective burden (DALY) of chronic kidney disease, by direct and indirect burden and sex, 2011

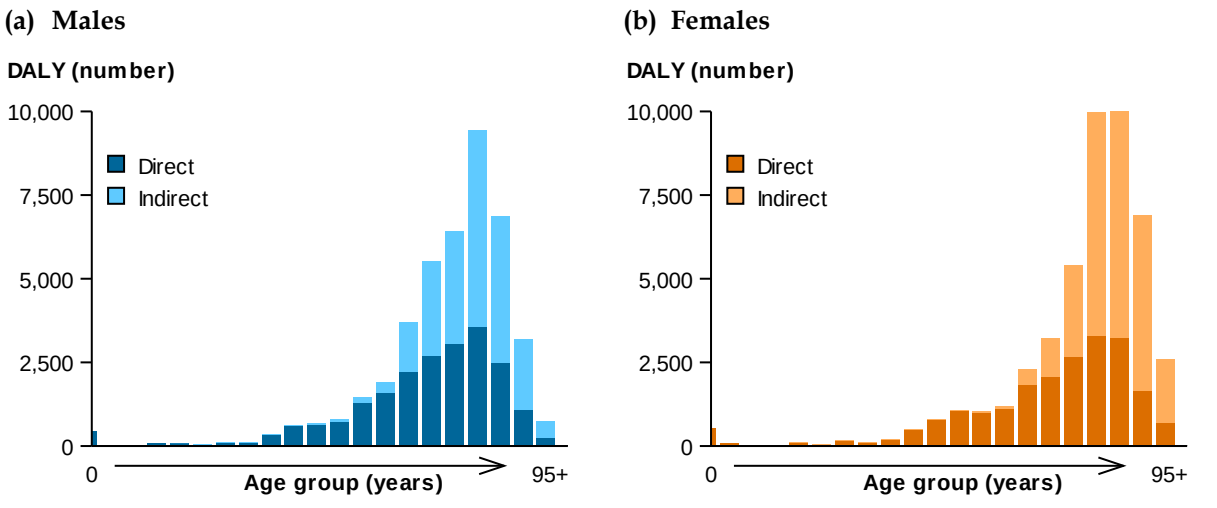
	Direct	Indirect	Collective
Males	21,490	21,152	42,642
Females	21,084	25,732	46,816
Persons	**42,574**	**46,886**	**89,460**

Note: Numbers may not sum to the total due to rounding.

Source: AIHW analysis of burden of disease database, 2011.

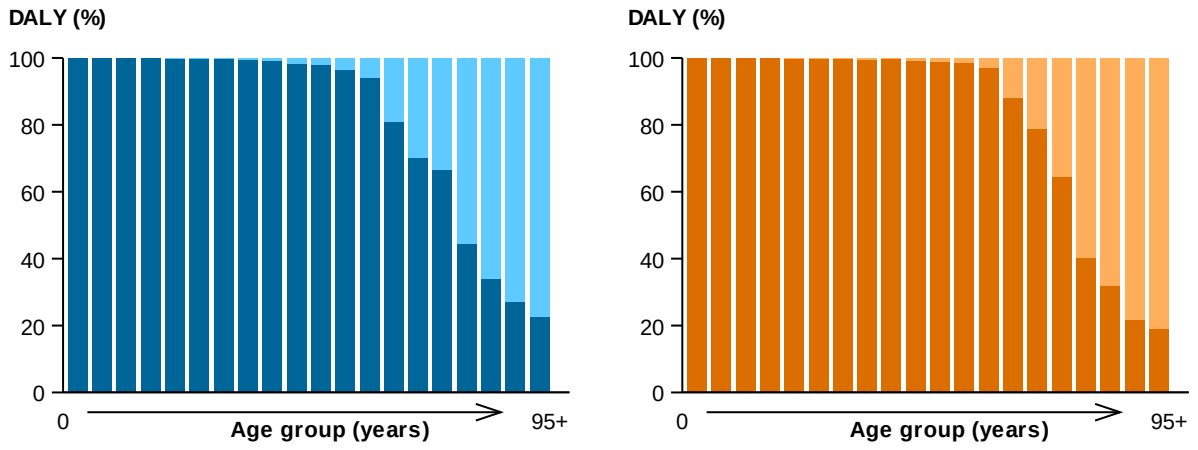
The age disparity between indirect and direct burden in both sexes is shown in Figure 4.2. Males experienced most of the collective burden between ages 75 and 89. The proportion of indirect burden increased with age, with 10% of the collective burden between ages 50 and 59 being indirect burden, compared with 60–65% after age 75, reflecting the onset of cardiovascular diseases and dementia in late life.

Females experienced most of the collective burden in later life due to linked diseases—primarily because females live longer than males. Indirect CKD burden was responsible for less than 10% of the collective CKD burden up to age 65. From age 80 onwards, this proportion increased to 68–73% of the collective burden.



Source: AIHW analysis of burden of disease database, 2011.

Figure 4.2: Collective burden (DALY) of chronic kidney disease, by direct and indirect burden, by age and sex, 2011



Source: AIHW analysis of burden of disease database, 2011.

Figure 4.2 (continued): Collective burden (DALY) of chronic kidney disease, by direct and indirect burden, by age and sex, 2011

4.3 How much burden from other diseases is due to chronic kidney disease?

The indirect disease burden due to CKD was responsible for 46,886 DALY (Table 4.3). This is slightly more than the direct burden estimated as part of the ABDS 2011 (42,574 DALY).

The attributable burden was highest in coronary heart disease (22,728 DALY)—responsible for almost half (48%) of the total attributable burden—followed by dementia (12,678 DALY; 27%) and stroke (9,859 DALY; 21%). The overall CKD attributable burden varied by sex, with males experiencing a slightly lower number of DALY, compared with females. This was mainly due to females experiencing a greater amount of dementia burden.

Table 4.3: Attributable burden due to chronic kidney disease, by linked disease and sex, 2011

	Males		Females		Persons	
Linked disease	**Attributable DALY**	**Proportion of linked disease (%)[a]**	**Attributable DALY**	**Proportion of linked disease (%)[a]**	**Attributable DALY**	**Proportion of linked disease (%)[a]**
Coronary heart disease	12,186	5.4	10,541	8.7	22,728	6.6
Dementia[b]	4,067	7.3	8,611	9.0	12,678	8.4
Stroke	4,063	6.2	5,796	8.2	9,859	7.2
Peripheral vascular disease	836	17.9	784	21.0	1,621	19.2
Total	**21,152**		**25,732**		**46,886**	

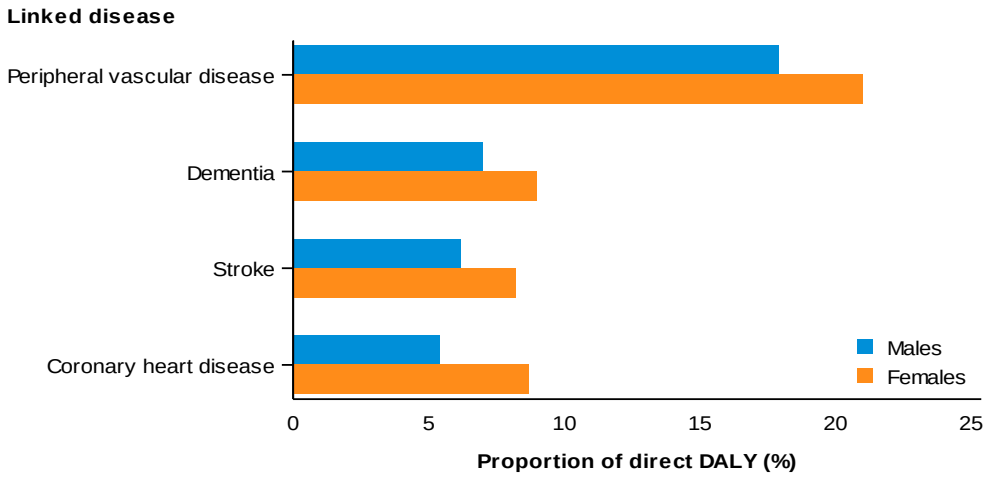
(a) The 'Proportion of linked disease (%)' column is the attributable DALY due to CKD divided by the total direct linked disease burden estimated in the ABDS of that row. Numbers may not sum to the total due to rounding.

(b) The burden of dementia due to CKD was estimated only in people aged 65 and over, because the association is in late life dementia only.

Source: AIHW analysis of burden of disease database, 2011.

The proportion of disease burden that is attributable to CKD was estimated for each linked disease (Table 4.3 and Figure 4.3). This is derived from the number of DALY attributable to CKD divided by the direct burden of each linked disease. For example, we estimated 22,728 DALY of coronary heart disease can be attributable to CKD; this is 6.6% of the direct burden of coronary heart disease (346,651 DALY).

CKD contributed the greatest proportion of attributable burden for peripheral vascular disease: 18% in males and 21% in females. For the remaining linked diseases, CKD attributed 5–7% of the disease burden in males and 8–9% in females. A larger proportion of disease burden was attributable to CKD in females in every linked disease (Table 4.3, Figure 4.3). This is mainly due to an increased amount of burden occurring in older age groups in females, compared with males.

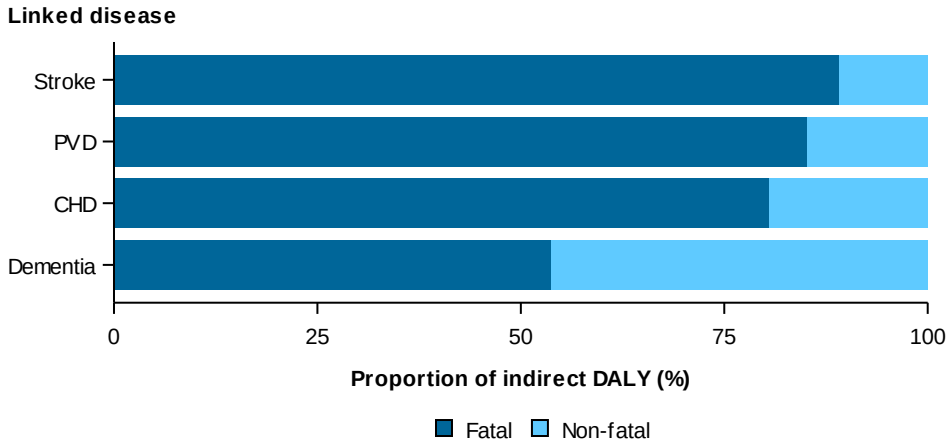


Source: AIHW analysis of burden of disease database, 2011.

Figure 4.3: Proportion of burden attributable to chronic kidney disease, by linked disease and sex, 2011

In the ABDS 2011, the direct burden of diseases associated with CKD was predominantly fatal, with the exception of dementia burden, where it was mainly non-fatal. This influenced the proportion of fatal and non-fatal outcomes for the indirect CKD burden.

The proportion of indirect CKD burden was mostly fatal; however, this varied by linked disease (Figure 4.4). Over 80% of indirect burden from linked cardiovascular disease was due to fatal burden: stroke (89%), peripheral vascular disease (85%) and coronary heart disease (80%) (Figure 4.4). A similar proportion of fatal and non-fatal burden was evident in the dementia burden attributable to CKD (54% fatal; 46% non-fatal).

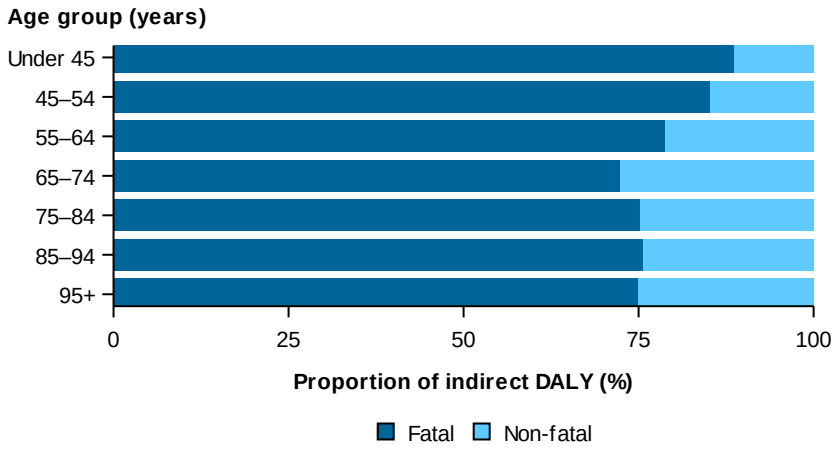


Note: PVD = Peripheral vascular disease; CHD = Coronary heart disease.

Source: AIHW analysis of burden of disease database, 2011.

Figure 4.4: Proportion of indirect chronic kidney disease burden, by linked disease due to fatal and non-fatal outcomes, 2011

The proportion of indirect CKD burden due to fatal and non-fatal outcomes differed by age (Figure 4.5). Fatal outcomes were responsible for 85–88% of the indirect CKD burden under age 55. After this age, fatal outcomes were responsible for around three-quarters of the indirect CKD burden.



Source: AIHW analysis of burden of disease database, 2011.

Figure 4.5: Proportion of indirect chronic kidney disease burden due to fatal and non-fatal outcomes, by age, 2011

4.4 Indirect CKD burden by linked disease

The impact of CKD on linked diseases is discussed individually for each disease: coronary heart disease, stroke, dementia and peripheral vascular disease.

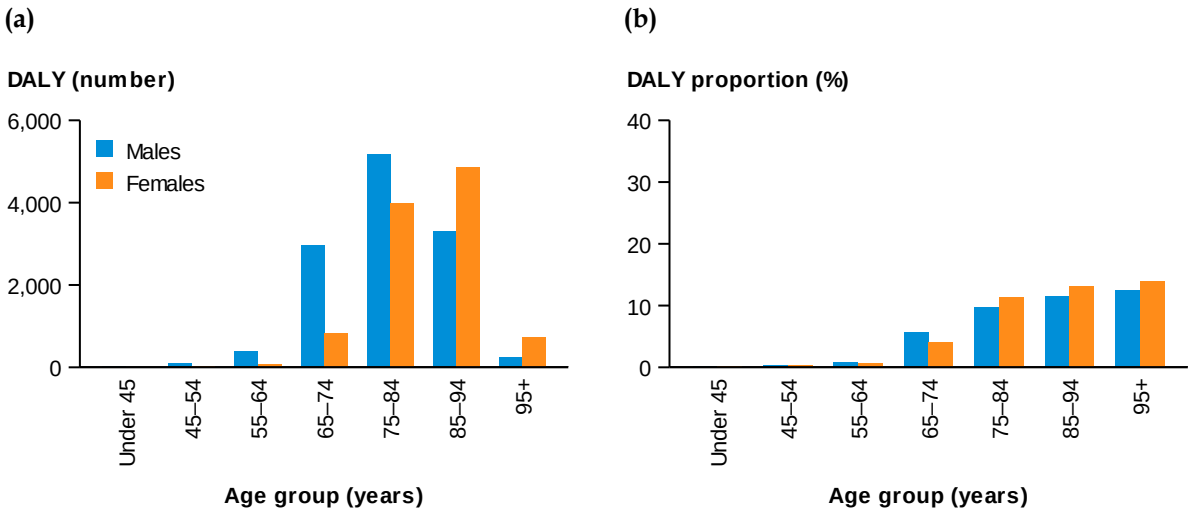
The indirect burden was measured by the number and proportion of DALY from the disease that was caused by the risk factor—in this case CKD. Where possible, similar scales have been used for graphs across linked diseases to depict the relative size of the burden estimates reported and to aid interpretation.

Coronary heart disease

CKD contributed to 6.6% of the coronary heart disease burden in 2011, equating to 22,728 DALY (Table 4.3). Males experienced a slightly greater number of DALY (12,186), compared with females (10,541 DALY).

Males experienced nearly half of the total attributable burden between ages 75 and 84, peaking at 5,181 DALY (Figure 4.6a). Females experienced most of the attributable burden at a later age, peaking at 4,866 DALY between ages 85 and 94.

From age 75 onwards, CKD was responsible for 10–14% of coronary heart disease burden (Figure 4.6b). The proportion of attributable burden increased with age, and peaked at 12% in males aged 95 and over, and 14% in females aged 95 and over.



Source: AIHW analysis of burden of disease database, 2011.

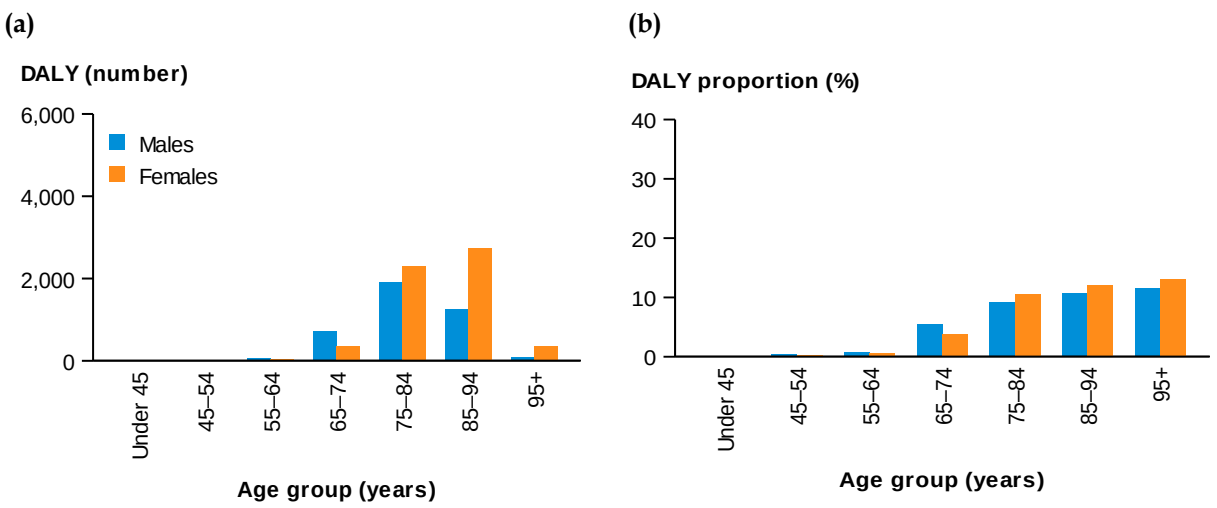
Figure 4.6: Burden (DALY) of coronary heart disease attributable to chronic kidney disease, by (a) number and (b) proportion of burden, by age and sex, 2011

Stroke

CKD contributed to 7.2% of the stroke burden in 2011 (9,859 DALY; Table 4.3). Females experienced 59% of the total attributable burden (5,796 DALY).

Nearly all stroke burden due to CKD occurred after age 65 (Figure 4.7a). Males experienced the majority of the attributable burden between ages 75 and 94. The attributable burden peaked later for females: it was highest in older age groups, peaking at 2,734 DALY between ages 85 and 94, and is considerably higher than males.

From age 75 onwards, CKD was responsible for 10–13% of stroke burden (Figure 4.7b). The proportion of attributable burden increased with age, and peaked at 11% in males aged 95 and over, and 13% in females aged 95 and over.



Source: AIHW analysis of burden of disease database, 2011.

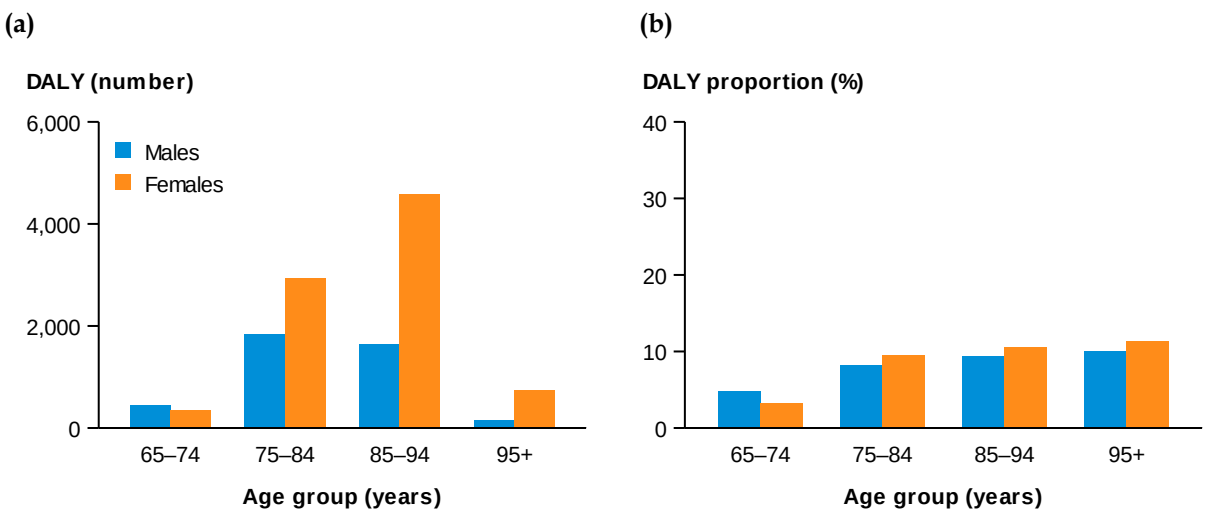
Figure 4.7: Burden (DALY) of stroke attributable to chronic kidney disease, by (a) number and (b) proportion of burden, by age and sex, 2011

Dementia

CKD contributed to 8.4% of the dementia burden age 65 and over, equating to 12,678 DALY (Table 4.3). The burden of dementia due to CKD was estimated only in people aged 65 and over, because the association is with late life dementia only. Females experienced 68% of the total attributable burden.

Nearly all dementia burden due to CKD occurred after age 65, coinciding with dementia increasing with age (Figure 4.8a). Males experienced the majority of their attributable burden between ages 75 and 94. Females experienced most of their attributable burden at a later age, peaking at 4,585 DALY between ages 85 and 94.

CKD contributed to 9–11% of dementia burden after age 75 (Figure 4.8b). The proportion of attributable burden increased with age, and peaked at 10% in males and 11% in females aged 95 and over.



Note: Attributable burden was not calculated in ages under 65, because the association with dementia is with late-life (aged 65 and over).

Source: AIHW analysis of burden of disease database, 2011.

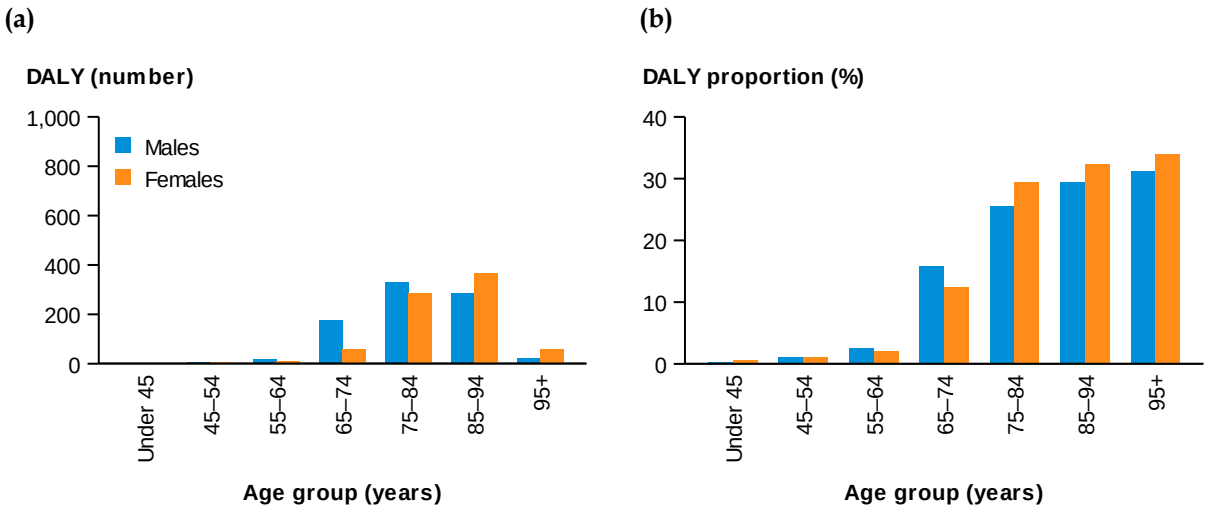
Figure 4.8: Burden (DALY) of dementia attributable to chronic kidney disease, by (a) number and (b) proportion of burden, by age and sex, 2011

Peripheral vascular disease

CKD contributed to 19% of the peripheral vascular disease burden in 2011 (1,621 DALY; Table 4.3).

Males experienced 52% of the attributable burden (836 DALY). In males, the burden occurred at an earlier age than for females, peaking at 330 DALY at ages 75–84 (Figure 4.9a). In females, the attributable burden peaked between ages 85 and 94 (367 DALY).

From age 75 onwards, CKD contributed to 27–33% of the burden from peripheral vascular disease (Figure 4.9b).



Source: AIHW analysis of burden of disease database, 2011.

Figure 4.9: Burden (DALY) of peripheral vascular disease attributable to chronic kidney disease, by (a) number and (b) proportion of burden, by age and sex, 2011

4.5 Estimated CKD burden in 2020 under 2 different scenarios

Table 4.4 presents the indirect and direct CKD burden in 2011, compared with the CKD burden in 2020 under 2 different scenarios. These scenarios provide an indication of the amount of burden that may be avoided if the current rise of CKD is halted, compared with the amount of burden if the current trend continues (see Appendix D for the detailed methods used).

For the direct burden, Scenario A describes the impact of the annual rate of change in fatal and non-fatal burden rates between 2003 and 2011 continued to 2020. Scenario B describes the impact of population growth and ageing, where the CKD fatal and non-fatal burden rates remain stable to 2020.

For the indirect burden, Scenario A describes the impact of the annual rate of change in CKD prevalence between 2003 and 2011 continued to 2020. Scenario B describes the impact of the CKD prevalence rate remaining stable to 2020. The 2011 burden rates for each linked disease were assumed to remain the same to 2020 for ease of calculation.

The annual rate of change in prevalence and fatal burden between 2003 and 2011 was derived for each sex and age group (see tables C3 and C4). The annual rate of change in non-fatal burden between 2003 and 2011 was calculated at the sequela level for each sex and age group. Sequelae are consequences associated with the disease, such as stages 3 to 5 of CKD (see Appendix D).

The results of the scenario analyses are presented below.

If the rate of change observed between 2003 and 2011 in CKD prevalence, fatal and non-fatal burden continued to 2020:

- The estimated indirect CKD burden is projected to be 67,400 DALY in 2020, which is 1.4 times as high as the indirect burden in 2011 (Table 4.4).
- The estimated direct CKD burden is projected to be 55,800 DALY in 2020; fatal burden is expected to be 25% higher, and non-fatal burden 45% higher, than the direct burden in 2011 (Table 4.4).
- The estimated collective CKD burden is projected to be 123,000 DALY in 2020, which is 1.4 times as high as the collective burden in 2011 (Table 4.4).

If the current rise in CKD is halted (that is, the prevalence, fatal and non-fatal burden rates remain stable from 2011 to 2020), then by 2020:

- the estimated collective CKD burden is projected to be 117,000 DALY, which is 1.3 times as high as the collective burden in 2011 (and reflects population increase and ageing alone).

In comparing the 2 scenarios, if the current rise in CKD is halted compared with if the current trend continues, then by 2020:

- 4.8% of future CKD collective burden could be avoided (Table 4.4)
- 7.5% of future indirect CKD burden could be avoided, with reductions ranging between 6.0% for dementia and peripheral vascular disease, to 8.2% for coronary heart disease (Table C6).

Table 4.4: Estimated chronic kidney disease burden in 2020 under different exposure scenarios

		Scenario A		Scenario B		Scenario B compared with Scenario A	
		Continued trend in CKD prevalence rate to 2020		Stable CKD prevalence rate to 2020		DALY that would be avoided in 2020	
	DALY in 2011	DALY in 2020	Percentage change from 2011 DALY[(a)]	DALY in 2020	Percentage change from 2011 DALY[(a)]	DALY number	DALY (%)[(b)]
Indirect CKD burden	**46,886**	**67,410**	**43.8**	**62,342**	**33.0**	**5,068**	**7.5**
Direct CKD burden							
Fatal (YLL)	30,645	38,421	25.4	39,780	29.8	-1,359	-3.5
Non-fatal (YLD)	11,929	17,338	45.3	15,178	27.2	2,160	12.5
Total (DALY)[(c)]	**42,574**	**55,758**	**31.0**	**54,958**	**29.1**	**800**	**1.4**
Collective CKD burden[(d)]	**89,440**	**123,168**	**37.7**	**117,300**	**31.1**	**5,868**	**4.8**

(a) Percentage change is the change in burden between 2020 and 2011 divided by the burden in 2011 for each scenario.

(b) Percentage difference is the difference in attributable DALY in 2020 between Scenario A and B divided by the attributable DALY in 2020 for Scenario A.

(c) Numbers may not sum to the total due to rounding.

(d) Collective CKD burden is the sum of indirect CKD burden and the total (DALY) for each scenario.

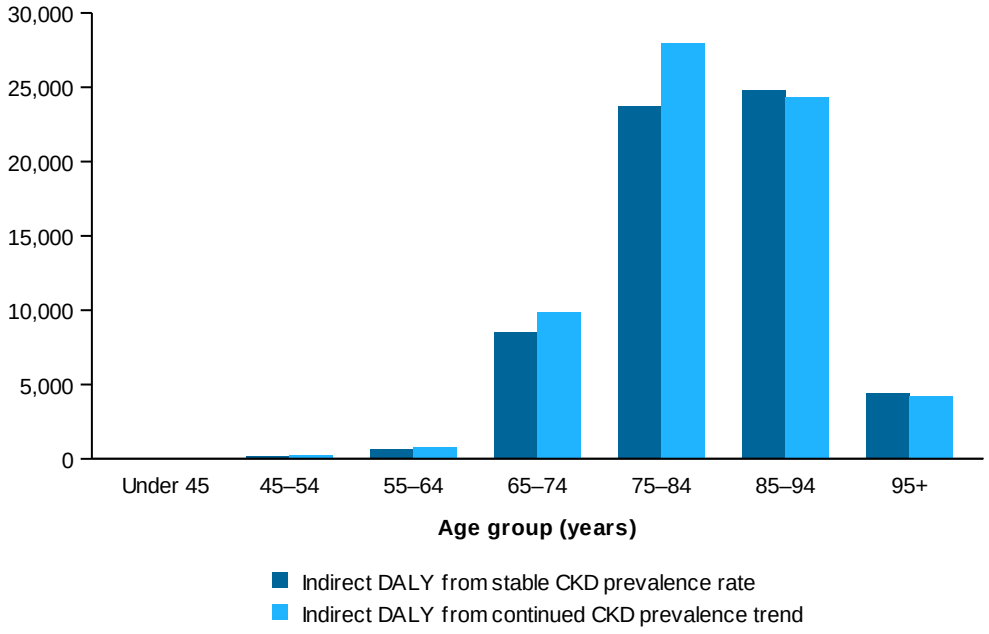
Source: AIHW analysis of burden of disease database, 2011.

4.6 Scenario differences by age

Indirect CKD burden

Figure 4.10 shows the indirect CKD burden in 2020 by age under the 2 different scenarios.

In both scenarios, the indirect burden estimated for 2020 was highest in ages 75–94. Under both scenarios, the indirect DALY due to CKD was similar in all age groups except for ages 75–84. If the increase in the rate of CKD prevalence is halted, 15% of the future indirect burden due to CKD in people aged 65–84 could be avoided in 2020.



Note: 'Stable CKD' is the scenario where the rise of CKD prevalence is halted; 'continued CKD' is the scenario where the current prevalence trends continue to rise. The stable CKD prevalence rate is based on 2011 prevalence rate.

Source: AIHW analysis of burden of disease database, 2011.

Figure 4.10: Estimated indirect chronic kidney disease burden (DALY) in 2020 under different exposure scenarios, by age

5 Discussion

5.1 Key findings

This study found that the burden due to diabetes and CKD is around twice as high when taking into account the indirect burden of their linked diseases. By including the indirect burden due to these diseases with their direct burden, the total burden of disease due to diabetes increased by 84% for males and by 90% for females. For CKD, this increased by 98% for males and by 122% for females.

Scenario analyses suggested that around one-fifth (21%) of future diabetes burden and 5% of future CKD burden could be avoided if the prevalence rate of these 2 diseases is maintained at 2011 levels to 2020. This proportion is higher for diabetes than CKD because: firstly, diabetes was responsible for more direct burden than CKD in 2011 (101,653 DALY compared with 42,574 DALY); and secondly, because the rate of change used to model current and future trends in disease prevalence and burden was greater for diabetes than CKD (see Appendix C).

In terms of indirect burden, the greatest gains are expected to be made in those aged 65–94 for diabetes, and 65–84 for CKD, where around 36% of diabetes attributable burden and 15% of CKD attributable burden could be avoided by 2020 if the prevalence rate of these diseases is maintained at 2011 levels.

5.2 Contribution to evidence base and policy analysis

This study provides insight into the impact of diabetes and CKD on a number of other chronic diseases by looking at them as risk factors for these other diseases. It does this by quantifying the collective burden—the sum of the direct and indirect impact or burden associated with health loss from these conditions.

The impact of diabetes and CKD on population health is emphasised by their collective burden. When the indirect burden of diabetes and CKD was added to their direct burden, the collective burden is 1.9 and 2.1 times, respectively, higher than their direct burden. This highlights the contribution of diabetes and CKD to disease burden, both in their own right and as risk factors for other diseases, such as cardiovascular diseases and dementia.

There is evidence that reducing the prevalence of diabetes or CKD could, at a population level, reduce the prevalence of a broader range of chronic diseases. For example, several studies have shown the observed prevalence of age-specific dementia is decreasing, possibly due to improvements in cardiovascular health, including hypertension and diabetes over past decades (Norton et al. 2014). There is consistent evidence that optimal glycaemic control (along with other modifiable risk factors) could reduce cardiovascular risk in patients with type 2 diabetes (Martín-Timón et al. 2014). Scenario analysis in this study also showed that if the current rise of diabetes or CKD prevalence is halted, chronic disease burden may be reduced across a range of diseases.

Given the age of exposure, duration and association with linked diseases, strategies aimed at preventing or delaying the onset of diabetes and CKD across the life-course have the potential to achieve major health gains. Early detection of risk factors and disease has the

potential to reduce or delay complications and consequently other chronic conditions, which would result in significant health benefits for the population.

Results from this study provide substantial details about the association between diabetes and CKD and their linked diseases. The information about the extent of these relationships across sex, age groups and for different diseases may be used to better target disease prevention and management policies.

5.3 New Zealand comparison

Disease-as-risk analysis was previously undertaken as part of the New Zealand Burden of Disease Study (MOH 2012). The New Zealand study used the same comparative risk assessment methodology as used in the Australian Burden of Disease study and this report, but assumptions for the inclusion of linked diseases and effect sizes differed.

The New Zealand study had a more conservative approach to selecting linked diseases and effect sizes. Effect sizes were only included if they were greater than 1.4, and the linked disease was responsible for greater than 1% of the total burden in at least 1 population group. These criteria were considered to exclude some linked diseases that could be measured based on a convincing or probable level of evidence, and therefore were not applied in this study. As a result, a greater number of linked diseases were included in this Australian analysis.

Despite these differences, the proportion of attributable burden by linked diseases common to both studies can be compared. Coronary heart disease and stroke were identified in both studies as linked diseases for diabetes. Table 5.1 shows the comparison between results in this study and indirect burden estimates from the New Zealand study. Overall, a similar proportion of attributable burden due to diabetes was identified for coronary heart disease and stroke combined, with differences in the contribution of each.

Table 5.1: Comparison of direct and indirect diabetes burden between Australia and New Zealand diseases-as-risks analyses

	ABDS estimates			New Zealand estimates		
	Direct burden	Indirect burden		Direct burden	Indirect burden	
Linked disease		Attributable DALY	Proportion of linked disease(%)[(a)]		Attributable DALY	Proportion of linked disease(%)[(a)]
Coronary heart disease	346,651	38,852	11.2	89,159	12,900	14.5
Stroke	136,771	18,730	13.7	37,688	3,600	9.6
Total	**483,422**	**57,582**	**11.9**	**126,847**	**16,500**	**13.0**

(a) The 'Proportion of linked disease (%)' column is the attributable DALY due to diabetes divided by the total direct linked disease burden estimated in the ABDS of that row. Numbers may not sum to the total due to rounding.

Source: AIHW analysis of burden of disease database, 2011, MOH 2012.

Differences were also evident between studies for the indirect burden of CKD. The New Zealand study reported that one-third of the collective CKD burden was due to indirect burden. Our Australian study found the indirect CKD burden contributes approximately one-half of the collective CKD burden. This could be due to a greater number of linked diseases identified in this study contributing to the collective CKD burden.

5.4 Limitations

Literature review and linked diseases

Data are not available to obtain a complete understanding of the causal pathways and associated probabilities of developing linked diseases due to diabetes and CKD in Australia. The estimates of attributable burden used in this study rely on the best available effect size estimates from recent high-quality studies and meta-analyses. The studies included here as sources of effect sizes were deemed to be relevant for Australia and demonstrated a sufficient association between diabetes or CKD and their linked disease (based on a probable or convincing level of evidence). The exception was for CKD and its association with dementia, which was assessed as a possible/probable level of evidence. Further research is likely to update the effect sizes used for this association and may identify other possible linked diseases for diabetes and CKD.

Meta-analysis was typically chosen over other study designs for effect size estimates to provide greater statistical power and an ability to extrapolate to the affected general Australian population. However, a limitation inherent in meta-analysis of published studies is the possibility of publication bias. Where meta-analyses were based on prospective studies, or case-control studies (which are susceptible to recall and selection bias), there may be issues with confounding factors that may explain the observed associations reported. However, many studies used in this study adjusted for potential confounders and the association was similar for studies that controlled for body mass index, physical inactivity and alcohol consumption, and for studies that did not adjust for these variables.

There are several limitations that should be considered when interpreting results for the burden of diabetes. First, most of the literature used to determine effect sizes pertained to type 2 diabetes, with only limited literature available about type 1 diabetes as a risk factor for other diseases. The effect size was applied to exposure data which included both type 1 and type 2 diabetes. Because type 1 diabetes (which accounts for 5–10% of all diagnosed cases of diabetes) may not be a risk factor for linked diseases, the magnitude of the relationship between diabetes and linked diseases may have been somewhat overestimated. There were also limited studies in which the analysis provided results for type 2 diabetes by insulin status. We therefore could not examine whether attributable burden may differ for those using insulin to manage their type 2 diabetes.

In selecting the literature for effect sizes of linked diseases to diabetes or CKD, where possible, the definitions of disease outcome in studies selected were similar to the definitions used in estimating the disease burden in the ABDS 2011 (tables A2 and B2). This was the case for most linked diseases except for peripheral vascular disease for which the definition used in the studies selected for effect sizes differ to that used in the ABDS 2011. Its effect size was based on an objective measure—Ankle Brachial Index, while the ABDS 2011 defined its disease consequence as intermittent claudication due to peripheral vascular disease. It was not possible to ascertain the relationship between the objective measure and self-reported symptoms. The indirect burden estimates for peripheral vascular disease reported in this study should therefore be interpreted with caution.

Further, the effect size selected for the association between diabetes and stroke from the Emerging Risk Factors Collaboration (2010) referred to ischaemic stroke. Our study inferred this effect size to all stroke subtypes, as the majority of burden estimates in the ABDS 2011 was due to ischaemic stroke. This may have overestimated the indirect burden of stroke due to diabetes.

The proportion of CKD that was attributable to diabetes used in this study was based on data from the ANZDATA. Using direct evidence from an Australian registry was considered to be more appropriate than using effect size from the literature for this linked disease pair. Because the ANZDATA is specific to persons with treated ESKD (stage 5 CKD), one assumption and limitation in using this data was that it was assumed that the proportion of people with stage 5 CKD due to diabetes was the same as for those with stage 3 or stage 4 CKD. Further details are provided in Appendix D.

Common risk factors

It is important to consider common risk factors, such as smoking, obesity, physical inactivity and poor nutrition, are potential confounders to the associations of diabetes or CKD and their linked diseases. For example, for tobacco smoking, being a risk factor for diabetes and cardiovascular diseases, some people may develop both conditions independently due to their individual risk factor profile, rather than developing cardiovascular diseases due to having diabetes (AIHW 2012b).

Scenario analysis was undertaken to estimate the extent of burden that could be reduced if the prevalence rates of diabetes and CKD remain stable compared with an increasing trend to 2020 (Appendix C). This was based on modelling the flow-on effects of controlling the direct burden due to diabetes and CKD, which then have an impact on the indirect burden of the linked diseases. However, it is acknowledged that, in treating or preventing chronic diseases, it is often important to target associated risk factors to limit the diseases' development or progression (AIHW 2012b). Strategies that target common risk factors—such as smoking, obesity, physical inactivity and poor nutrition—are another way that the burden of diabetes and CKD might be reduced.

Estimating trends in diabetes and CKD prevalence for scenario modelling

In order to estimate projected burden due to diabetes and CKD in 2020 used in the scenario analyses, information on current trends in the prevalence of these diseases was required. This was sourced from the ABDS 2011, which included estimates of prevalence for 2003 and 2011. Although biomedical data from the 2011–12 Australian Health Survey (AHS) was used to estimate prevalence of diagnosed diabetes and stage 3 and 4 CKD in 2011, comparable information was not available from earlier health surveys because they did not include biomedical components. As such, the 2003 estimates for diabetes were modelled using trends in self-report data from previous health surveys, which assumes that changes in self-reported diabetes follows a similar rate of change to diagnosed diabetes. For stage 5 CKD, ANZDATA was used to inform trends in prevalence. For stage 3 and 4 CKD, 2003 estimates were modelled using a ratio of the prevalence of treated ESKD sourced from ANZDATA to the prevalence of stage 3 CKD and stage 4 CKD sourced from the 2011–12 AHS. This assumes that this ratio was similar in 2003 as in 2011. These assumptions should be kept in mind when interpreting the results of the scenario modelling presented in this report.

As mentioned earlier in the report, the 2011 burden rates for each linked disease were assumed to remain the same to 2020 for ease of calculation. This does not take into account potential improvements in disease outcomes in the future.

5.5 Future directions

This study presents a more detailed picture of the impact of diabetes and CKD in Australia. The results show that reducing diabetes or CKD could also reduce broader chronic disease burden, resulting in less health loss due to these 2 conditions and their linked diseases.

Diabetes and CKD are also common chronic diseases among Aboriginal and Torres Strait Islander people. At present, published literature on the effect sizes specific to the Indigenous population is limited but effect sizes from this study could be applied as a proxy or re-selected from current literature. Differences in the indirect burden of diabetes and CKD between the Indigenous and total Australian populations would be mostly caused by differences in diabetes and CKD prevalence, and in the burden of linked diseases. However, other factors may also play a role, such as potential genetic predisposition—for example, smaller coronary arteries in women, which could lead to greater cardiovascular disease complications (Hiteshi et al. 2014)—and environmental factors. An analysis of the indirect diabetes and CKD burden in the Indigenous population would be an important area of work to progress in future burden of disease studies.

As part of the ABDS 2011, the AIHW has developed a system that will allow estimates of burden of disease in Australia to be updated and kept current with emerging information. This offers potential to monitor and update the estimates included in this study as new evidence emerges about the association between diseases-as-risks and linked diseases, and as exposure to risk factors in the population changes over time.

5.6 Conclusion

The impact of diabetes and CKD on population health is emphasised by their respective collective burden. When the indirect burden of diabetes and CKD was added to their direct burden, the collective burden was 1.9 and 2.1 times, respectively, higher than their direct burden. This highlights the contribution of diabetes and CKD to disease burden, both in their own right and as risk factors for other diseases, such as cardiovascular diseases.

Results from this study provide information about the association between diabetes and CKD and their linked diseases. The collective burden of diabetes and CKD gives a more comprehensive picture on the health loss attributable to these conditions. The results in this study could be used to inform population health monitoring and may assist in the development of chronic disease policy for prevention initiatives.

Appendix A: Selection of effect sizes for diabetes

In this report, diabetes includes type 1 and type 2, but not gestational, diabetes. This is consistent with the ABDS 2011. Selected literature on diabetes described in this appendix mainly refers to type 2 diabetes unless otherwise stated.

Burden of disease studies use effect sizes to measure the strength of association between a risk factor (disease-as-risks in this study) and a linked disease. In this appendix, effect size measures the risk of developing the specific linked disease among those with and without diabetes. Effect sizes used in this study were identified following review of relevant literature and were restricted to studies with a prospective longitudinal design where the outcome was a clinically diagnosed linked disease. Sex-specific effect sizes were applied where possible.

Selected studies showed that, if an individual has diabetes, there is an increased risk of developing a number of diseases: these are identified in Table A1. Appendix Table A1 also lists the effect sizes used in this study to estimate the indirect burden of diabetes and their sources. For further information on the selection of linked diseases and effect sizes see Chapter 2. A summary of selected studies is presented in Table A2.

Table A1: Effect size and sources for diabetes and linked disease pair analysis.

Linked disease	Level of evidence	Effect size (95% CI)	Source of effect size
Coronary heart disease	Convincing	Males: HR 1.89 (1.73–2.06) Females: HR 2.59 (2.29–2.93)	Emerging Risk Factor Collaboration 2010
Stroke (all types)	Convincing	Males: HR 2.16 (1.84–2.52) Females: HR 2.83 (2.35–3.40)	Emerging Risk Factor Collaboration 2010
Peripheral vascular disease	Convincing	OR 1.88 (1.66–2.14)	Fowkes et al. 2013
Dementia (all types; age 65+)	Convincing	RR 1.50 (1.33–1.70)	Prince et al. 2014
Chronic kidney disease[(a)]	—	—	ANZDATA 2011
Liver cancer	Convincing	RR 2.31 (1.87–2.84)	Wang et al. 2012
Pancreatic cancer	Probable	OR 1.82 (1.66–1.89)	Huxley et al. 2005
Bowel cancer	Probable	RR 1.30 (1.20–1.40)	Larsson et al. 2005
Uterine cancer	Probable	RR 2.10 (1.75–2.53)	Friberg et al. 2007
Breast cancer (age 45+)	Convincing	RR 1.20 (1.12–1.28)	Larsson et al. 2007
Kidney cancer	Convincing	RR 1.40 (1.16–1.69)	Bao et al. 2013
Bladder cancer	Convincing	RR 1.24 (1.08–1.42)	Larsson et al. 2006

(a) Population attributable fraction for CKD was derived directly from the ANZDATA, 2011.

Diabetes and cardiovascular disease

Diabetes is an established risk factor for coronary heart disease and stroke (AIHW 2014). Studies have shown that patients with diabetes have increased risk of stroke. For example, Liao et al. (2015) found the incidents of stroke in cohorts with and without diabetes were 10.1 and 4.5 per 1,000 persons-years, respectively. The increased risk of ischaemic stroke has been

linked to pathophysiological changes seen in cerebral vessels of individuals with diabetes (Tuttolomondo et al. 2015).

People with diabetes are at higher risk of developing atherosclerosis: the most common cause of peripheral vascular disease. Individuals with peripheral vascular disease have a much higher risk of heart attack or stroke. The pathophysiology of vascular disease in diabetes involves abnormalities in endothelial, vascular smooth muscle cells and platelet functions. In people with diabetes, the risk of peripheral vascular disease is increased by age, duration of diabetes and presence of peripheral neuropathy (Fowkes et al. 2013), as well as other risk factors such as smoking, hypertension and high cholesterol.

Diabetes and coronary heart disease

There have been several cohort studies conducted supporting diabetes as an independent risk factor for coronary heart disease in people with diabetes (Selvin et al. 2005; Soedamah-Muthu et al. 2006; Tonelli et al. 2012).

The effect size used in this study was drawn from a meta-analysis by the Emerging Risk Factors Collaboration (2010) where diabetes and the risk of vascular disease was assessed. It was a collaborative meta-analysis of 102 prospective studies, involving 1.27 million people. This was considered the most comprehensive meta-analysis, including the largest number of studies with an outcome of coronary heart disease and stroke by age and sex.

The adjusted hazard ratio for the association between diabetes and coronary heart disease was 1.89 (95% CI 1.73–2.06) for males and 2.59 (95% CI 2.29–2.93) for females (Emerging Risk Factors Collaboration 2010). This was comparable to the relative risks reported in a meta-analysis by Peters et al. (2014a) of 2.16 for males and 2.82 for females. Both meta-analyses suggest that the effect of diabetes on the relative risk of coronary heart disease is greater in females than males.

Diabetes and stroke

In this study, stroke as a linked disease referred to all types of stroke, not specific subtypes of stroke (that is, ischaemic and haemorrhagic stroke). Several cohort studies found diabetes is associated with increased risk of total and subtypes of stroke (Janghorbani et al. 2007; Liao et al. 2015; Najarian et al. 2006). A meta-analysis by Shou et al. (2015) further showed that stroke patients with diabetes had significantly higher stroke recurrence risks than those without diabetes.

The effect size used in this study was also drawn from the Emerging Risk Factors Collaboration (2010). The adjusted hazard ratio for the association between diabetes and ischaemic stroke was 2.16 (95% CI 1.84–2.52) for males and 2.83 (95% CI 2.35–3.40) for females. This meta-analysis was selected as it included the largest number of studies with an outcome of stroke subtypes. The effect size was comparable to a meta-analysis by Peters et al. (2014b), where the relative risk of stroke associated with diabetes was 1.83 for males and 2.28 for females. The sex difference was consistent across total and subtypes of stroke.

Diabetes and peripheral vascular disease

There is convincing evidence on diabetes as a risk factor for peripheral vascular disease. A meta-analysis by Fowkes et al. (2013) assessed the odds ratios for 15 risk factors for peripheral vascular disease for high-income and low-income countries, and included diabetes as a risk factor. The odds ratio (1.88, 95% CI 1.66–2.14) used for the association

between diabetes and peripheral vascular disease was drawn from this meta-analysis, using the effect size found for diabetes for high-income countries.

Diabetes and dementia

There is strong and consistent evidence of a causal association between diabetes and dementia (Prince et al. 2014). Numerous prospective studies have demonstrated this as summarised in several systematic reviews (Biessels et al. 2006; Cukierman et al. 2005; Lu et al. 2009; Luchsinger 2010; Profenno et al. 2010). The association is also supported by recent meta-analyses (Cheng et al. 2012; Gudala et al. 2013; Lu et al. 2009; Ninomiya 2014; Prince et al. 2014).

The relative risk used in this study is from Prince et al. (2014) because this was assessed to be the most up-to-date meta-analysis, and included the largest number of studies with an outcome of any dementia.

In total, 11 studies were included in Prince et al. (2014) with a pooled relative risk of 1.50 for the association between any dementia and diabetes in late life (aged 65 and over). This relative risk was consistent when analysis was restricted to 7 studies that included both diagnosed and undiagnosed diabetes.

The results from Prince et al. (2014) are in accordance with previous reviews and are comparable to other recent meta-analyses (Barnes & Yaffe 2011; Lu et al. 2009; Ninomiya 2014; Rönnemaa et al. 2011).

There are several biologically plausible mechanisms through which diabetes could increase dementia risk. However, there is currently no clear consensus on the direct causal relationship (Ninomiya 2014; Prince et al. 2014). Diabetes is associated with atherosclerosis and stroke (Mankovsky & Ziegler 2004) which, in turn, increase the risk of dementia (Savva & Stephan 2010). In addition, defective binding of insulin to receptors in the brain may contribute to accumulation of amyloid, which is toxic to brain cells (Bedse et al. 2015). Brain imaging studies demonstrate an association between brain metabolism, consistent with Alzheimer's disease and insulin resistance (Baker et al. 2011) and diabetes (Roberts et al. 2014). Finally, common genetic pathways may underlie the development of both diabetes and dementia (Akomolafe et al. 2006).

Diabetes and chronic kidney disease

Direct evidence from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) was used to ascertain a proportion of people in the database who have CKD due to diabetes (the population attributable fraction). The registry captures data for most cases of treated ESKD in Australia and provides evidence to attribute CKD to diabetes. The proportions were modelled for people aged 75 and over due to limited data on the registry for these ages.

It is understood that people aged 85 and over are less likely to undergo renal replacement therapy, so the proportion due to diabetes for ESKD may be underestimated. Other issues and limitation of ANZDATA are considered in Chapter 5. Nevertheless, ANZDATA is considered to be of high quality and is a register of all people in Australia receiving dialysis or kidney transplant, where the intention to treat is long-term survival (AIHW 2012a).

Diabetes and cancer

The literature indicates there is a strong association between diabetes (mainly Type 2) and certain types of cancer. Results of several studies have been combined for meta-analysis and have shown that some cancers develop more commonly in people with Type 2 diabetes, including cancer of the liver (Wang et al. 2012), pancreas (Huxley et al. 2005), kidney (Larsson and Wolk 2011), endometrium (Friberg et al. 2007), colon and rectum (Guraya 2015), bladder (Xu et al. 2013) and breast (Boyle et al. 2012). Diabetes has been associated with a decreased risk of prostate cancer (Suh and Kim 2011). This possible protective effect was not included in our study because only linked diseases with increased risk were considered. There have been limited studies on the risk of cancer among people with type 1 diabetes.

The exact mechanism of this increased risk of cancer among people with diabetes is unclear, but it is thought that hyperglycaemia and the hyperinsulinemia characteristic of diabetes promotes the growth of cancerous cells, as well as inhibiting the death of these cells (Suh and Kim 2011). Other possible mechanisms include diabetes as a marker of underlying biological factors that alter cancer risk (for example, insulin resistance and hyperinsulinemia). It is also possible, for type 2 diabetes, that the cancer–diabetes association is indirect and due to common risk factors such as obesity and physical inactivity. However, in the selected meta-analyses, these confounders were adjusted in their pooled analysis of effect sizes.

Several meta-analyses indicate that the strongest association between type 2 diabetes and cancer risk is with pancreatic and liver cancer (Vigneri et al. 2009); that is, the 2 organs involved in the metabolic problems typical of diabetes.

Diabetes and liver cancer

Meta-analyses showed consistent evidence that diabetes is associated with increased risk of liver cancer incidence (El-Serag et al. 2006; Wang et al. 2012, 2014; Yang et al. 2011). Covariates were adjusted; that is, the association found was independent of alcohol use, smoking, hepatitis, liver cirrhosis and high body mass (El-Serag et al. 2006; Wang et al. 2012). It is noted that more than 80% of liver cancer incidence develop in Asian and African countries, and the incidence is relatively low in Australia, USA and Europe (Yang et al. 2011). This is in part explained by the geographical variations in the prevalence of chronic infection with the hepatitis B or hepatitis C viruses: the incidence rate is higher in Eastern Asia and sub-Saharan Africa (Yang et al. 2011).

The relative risk used was drawn from Wang et al. (2012), which was assessed as the most up-to-date meta-analysis, including the largest number of studies with an outcome of liver cancer. A total of 17 case-control studies and 32 cohort studies were included in the meta-analysis. The pooled relative risk was 2.31 (95% CI 1.87–2.84) for the association between diabetes and liver cancer with adjusted covariates as described. This was compared with the effect size of 2.50 reported in an earlier meta-analysis by El-Serag et al. (2006) and relative risk of 1.87 reported by Yang et al. (2011).

Diabetes and pancreatic cancer

Findings in meta-analyses show increased relative risks of pancreatic cancer in individuals with chronic diabetes and support a modest causal relationship between diabetes and pancreatic cancer (Huxley et al. 2005; Song et al. 2015). One study found that individuals with recently diagnosed diabetes (<4 years) had a 50% greater risk of pancreatic cancer

compared with those who had chronic diabetes (≥5 years) (Huxley et al. 2005). This was consistent with the finding in Song et al. (2015) suggesting diabetes may be an early indicator of pancreatic cancer.

There is a study by Wang et al. (2003), however, which suggests that pancreatic cancer can induce diabetes. Patients with pancreatic cancer may have peptides (molecules) that are suggested to have the potential to cause diabetes (Wang et al. 2003). From this inconsistent finding, this study suggests a probable level of evidence of a causal association between diabetes and pancreatic cancer.

The odds ratio (1.82; 95% CI 1.66–1.89) for the association between diabetes and pancreatic cancer was drawn from Huxley et al. (2005). This is similar to the relative risk of 1.64 reported by Song et al. (2015) for individuals with duration of diabetes ≥2 years. Song et al. (2015) did not provide an overall relative risk independent of the duration of diabetes. Other meta-analyses found that diabetes was associated with higher mortality in patients with pancreatic cancer (Mao et al. 2015).

Diabetes and bowel cancer

There is probable evidence of a causal association between diabetes and bowel cancer as there are some inconsistent findings. Three meta-analyses support a relationship between diabetes and increased risk of bowel cancer (Deng et al. 2012; Guraya 2015; Larsson et al. 2005). Further, a retrospective cohort study by Yang et al. (2004) showed long-term insulin therapy is associated with an increased risk of bowel cancer among patients with type 2 diabetes. This was also supported by Deng et al. (2012). Because it was inferred that insulin use is linked to severity of type 2 diabetes, it is possible that the observed association was due to the severity of diabetes rather than a true effect of exogenous insulin; whether insulin therapy increases bowel cancer risk needs further investigation. Despite this, given the number of meta-analyses available, it was deemed sufficient to include bowel cancer as a linked disease to diabetes for this analysis.

The relative risk used was drawn from a meta-analysis by Larsson et al. (2005). This study is older than other meta-analysis available, but it provided details of the studies chosen and the studies were mostly from the USA, Europe and Australia. It included 6 case-control and 9 cohort studies. The pooled relative risk from Larsson et al. (2005) for the association between diabetes and bowel cancer was 1.30 (95% CI 1.20–1.40). It was comparable to other meta-analyses: Deng et al. (2012) reported a relative risk of 1.26 and Guraya (2015) found a relative risk of 1.21, for the association of diabetes and bowel cancer incidence.

Diabetes and uterine and breast cancer

Both uterine and breast cancer risks are increased in women with diabetes, and this risk is independent from obesity. Several biological mechanisms have been proposed, most regarding sex hormone abnormalities (Vigneri et al. 2009). High levels of insulin and oestrogens have been suggested to increase endometrial cancer risk by stimulating proliferation of endometrial cells (Friberg et al. 2007).

Diabetes and uterine cancer

A meta-analysis by Friberg et al. (2007) found consistent evidence in both case-control and cohort studies on the increased risk of uterine cancer in women with diabetes (largely Type 2) compared with those without diabetes. Studies were conducted in the USA (8), Europe (6), South America (1) and Asia (1). Their pooled relative risk was 2.10 (95% CI 1.75–2.53) for the

association between diabetes and uterine cancer used in this study. There was no other meta-analysis found in the literature.

Diabetes and breast cancer

There is convincing evidence that diabetes is associated with an increased risk of breast cancer. However, studies found this risk in post-menopausal women and not in pre-menopausal women (Boyle et al. 2012; Larsson et al. 2007). To account for this, the analysis used exposure data for women aged over 45.

The relative risk used was drawn from Larsson et al. (2007). It included 5 case-control and 15 cohort studies conducted mostly in North America and Europe. The association between diabetes and breast cancer was consistent for these selected studies. It supports a positive association between diabetes and breast cancer risk. The pooled relative risk was 1.20 (95% CI 1.12–1.28), for the association between diabetes and breast cancer in women. This is consistent with a relative risk of 1.27 reported by Boyle et al. (2012). The relative risk from Larsson et al. (2007) was selected as their meta-analysis consisted of a greater proportion of cohort studies (rather than case-control studies) than Boyle et al. (2012).

Diabetes and kidney cancer

There is convincing evidence of an association between diabetes and risk of kidney cancer. Meta-analyses found consistent positive association between these conditions (Bao et al. 2013; Larsson & Wolk 2011). Diabetes may affect the risk of kidney cancer by increasing insulin resistance and levels of insulin in the blood that could affect tumour growth (Larsson & Wolk 2011).

The relative risk used for this report was from Bao et al. (2013). This large meta-analysis provided details of 18 studies conducted in North America (8), Europe (6) and Asia (4), compared with a higher proportion of studies conducted in Asia used in the meta-analysis by Larsson & Wolk (2011).

The pooled relative risk used in this study was 1.40 (95% CI 1.16–1.69) for the association between diabetes and kidney cancer (Bao et al. 2013). This was compared to the relative risk of 1.42 reported by Larsson & Wolk (2011).

Diabetes and bladder cancer

There is a strong causal association between diabetes and bladder cancer. This is supported by meta-analyses (Larsson et al. 2006; Xu et al. 2013; Zhu et al. 2013), cohort and case-control studies (Attner et al. 2012; Lo et al. 2013; MacKenzie et al. 2011).

The relative risk selected is from a meta-analysis by Larsson et al. (2006); this was assessed to be most applicable for Australian prevalence estimates. The selected studies in this meta-analysis were conducted mostly in North America and Europe, where other meta-analyses included more studies from Asia (Xu et al. 2013; Zhu et al. 2013). It is thought that dietary intake may influence the onset of diabetes, therefore relative risks from countries with a predominantly western diet were selected as being comparable to Australia.

Larsson et al. (2006) included 16 studies with a pooled relative risk of 1.24 (95% CI 1.08–1.42), for the association between diabetes and bladder cancer. These results were also similar to other meta-analyses: Xu et al. (2013) reported relative risk of 1.11 and Zhu et al. (2013) found relative risk of 1.35, on the association of diabetes and bladder cancer incidence.

Table A2: Source of effect size used in calculation of attributable burden for diabetes

Linked disease	Reference	Study type	Number of studies	Study date	Sample size	Age at exposure	Length of follow-up	Diabetes definition	Outcome definition	Effect size (95% CI)	Notes
Coronary heart disease	Emerging Risk Factor Collaboration 2010	Meta-analysis	102 studies	Up to May 2010	698,782	Mean = 52 years	More than 1 year	Self-report, medication usage and/or baseline fasting glucose concentration ≥7 mmol/L	First ever myocardial infarction or fatal coronary heart disease	Male HR 1.89 (1.73–2.06) Females HR 2.59 (2.29–2.93)	Adjusted for age, smoking status, body mass index and systolic blood pressure and, where appropriate, stratified by sex and trial arm. Includes both fatal and non-fatal events.
Stroke	Emerging Risk Factor Collaboration 2010	Meta-analysis	102 studies	Up to May 2010	698,782	Mean = 52 years	More than 1 year	Self-report, medication usage and/or baseline fasting glucose concentration ≥7 mmol/L	Incident ischaemic stroke	Males HR 2.16 (1.84–2.52) Females HR 2.83 (2.35–3.40)	Adjusted for age, smoking status, body mass index and systolic blood pressure and, where appropriate, stratified by sex and trial arm. Includes both fatal and non-fatal events.
Peripheral vascular disease	Fowkes et al. 2013	Meta-analysis	34 studies	1997–2011	112,027	Range = 25–104 years	Not noted	Fasting glucose level >7 mmol/L, diabetes medication or doctor's diagnosis	Ankle brachial index ≤0.90	OR 1.88 (1.66–2.14)	Odd ratios were based on multivariate study design in which similar definitions of risk factors (e.g. body mass index, hypertension, smoking and high cholesterol) were used.
Dementia	Prince et al. 2014	Meta-analysis	11 studies	Up to January 2012	35,342	Range = 60–88 years	2–13 years	Diagnosed and undiagnosed diabetes	All-cause dementia (clinically diagnosed)	RR 1.50 (1.33–1.70)	Adjusted for age, sex, education and other potential risk factors.

(Continued)

Table A2 (continued): Source of effect size used in calculation of attributable burden for diabetes

Linked disease	Reference	Study type	Number of studies	Study date	Sample size	Age at exposure	Length of follow-up	Diabetes definition	Outcome definition	Effect size (95% CI)	Notes
Liver cancer	Wang et al. 2012	Meta-analysis	49 studies	Up to February 2011	Not reported	Range = 17–80 years	3–15 years	Self-report, medical records or database review, blood glucose level or medications	Liver cancer confirmed by histological and cytological examinations, laboratory tests or imaging findings	RR 2.31 (1.87–2.84)	Adjusted risk estimates were used. Studies adjusted for age, sex, hepatitis, alcohol, smoking, body mass index and liver cirrhosis.
Pancreatic cancer	Huxley et al. 2005	Meta-analysis	36 studies	Up to January 2005	9,220	Not reported	Not reported	Self-report, medical records or blood glucose level	Pancreatic cancer confirmed by laboratory tests, imaging findings, cancer registry	OR 1.82 (1.66–1.89)	Adjusted for sex, age, smoking, social class and dietary risk factors.
Bowel cancer	Larsson et al. 2005	Meta-analysis	15 studies	Up to July 2005	2,593,935	Not reported	Not reported	Self-report, medical records or fasting glucose level ≥7 mmol/L	Incident bowel cancer diagnosis	RR 1.30 (1.20–1.40)	Adjusted for age, sex, body mass index, smoking, alcohol, hormone replacement therapy use and dietary risk factors.
Breast cancer	Larsson et al. 2007	Meta-analysis	20 studies	Up to February 2007	1,400,000	Range = 20–95 years	Not reported	Self-report, medical records or blood glucose level	Incident breast cancer diagnosis	RR 1.20 (1.12–1.28)	Adjusted for age, body mass index, smoking, alcohol, social class and dietary risk factors.
Uterine cancer	Friberg et al. 2007	Meta-analysis	16 studies	Up to January 2007	96,003	≥20 years	Not reported	Self-report, medical records or medical registers	Incident uterine cancer diagnosis	RR 2.10 (1.75–2.53)	Adjusted for age, body mass index, smoking, alcohol, hypertension, education, physical activity, parity and dietary risk factors.

(Continued)

Table A2 (continued): Source of effect size used in calculation of attributable burden for diabetes

Linked disease	Reference	Study type	Number of studies	Study date	Sample size	Age at exposure	Length of follow-up	Diabetes definition	Outcome definition	Effect size (95% CI)	Notes
Kidney cancer	Bao et al. 2013	Meta-analysis	24 studies	Up to February 2012	6,025,827	Not reported	6–40 years	Self-report or medical records	Incident kidney cancer diagnosis	RR 1.40 (1.16–1.69)	Adjusted for age, sex, ethnicity, body mass index, smoking, alcohol, physical activity and dietary risk factors.
Bladder cancer	Larsson et al. 2006	Meta-analysis	16 studies	Up to July 2006	Not reported	Not reported	Not reported	Self-report, medical records or fasting glucose level	Incident bladder cancer diagnosis	RR 1.24 (1.08–1.42)	Adjusted for age, sex, smoking, body mass index and dietary risk factors.

Appendix B: Selection of effect sizes for chronic kidney disease

A review of the relevant literature identified that if an individual has CKD, there is an increased risk of developing a number of diseases: 4 diseases were identified for this study. In this appendix, effect size measures the risk of developing the specific linked disease among those with and without CKD. The effect sizes used in this study to estimate the indirect burden of CKD and their sources are listed in Table B1. For further information on the selection of linked diseases and effect sizes see Chapter 2. A summary of selected studies is presented in Table B2.

CKD in this appendix mainly refers to stages 3 to 5, defined in the literature by eGFR of less than 60 mL/min/1.73 m^2 or the levels of urinary protein or albumin. The definition of eGFR is consistent with stage 3 to 5 of CKD used in the ABDS 2011.

Table B1: Effect size and sources for chronic kidney disease and linked disease pair analysis

Linked disease	Level of evidence	Effect size (95% CI)	Source of effect size
Coronary heart disease	Convincing	RR 1.47 (1.23–1.74)	Perkovic et al. 2008
Stroke (all types)	Convincing	RR 1.43 (1.31–1.57)	Lee et al. 2010a
Peripheral vascular disease	Probable	OR 2.5 (1.2–5.1)	O'Hare et al. 2003
Dementia (all types; age 65+)	Possible/probable	RR 1.37 (1.06–1.78)	Seliger et al. 2004

CKD and cardiovascular disease

There is strong evidence to suggest that CKD is an independent risk factor for cardiovascular disease (Herzog et al. 2011; Sarnack et al. 2003). Many studies have shown markers of kidney dysfunction such as raised proteinuria (urinary protein excretion) or albuminuria (urinary albumin excretion), and low estimated glomerular filtration rate (eGFR) are associated with cardiovascular disease (Perkovic et al. 2008). Morbidity and mortality from cardiovascular disease are inversely and independently associated with kidney function; the incidence and severity of cardiovascular disease increases as eGFR declines (Gansevoort et al. 2013). Meta-analyses also show the risk of cardiovascular mortality increases linearly with decreasing eGFR, after adjustment of cardiovascular risk factors (Matsushita et al. 2010; Van der Velde et al. 2011).

Mechanisms specific to CKD promote vascular disease. Patients with CKD have higher risk of multi-vessel coronary calcification (Herzog et al. 2011) and in patients with advancing CKD, the prevalence of left-ventricular hypertrophy is increased, which leads to reduced coronary reserve (Gansevoort et al. 2013). Other studies have shown that CKD promotes hypertension and dyslipidaemia (Kokubo et al. 2009; Schiffrin et al. 2007), which could accelerate atherosclerosis and lead to increased prevalence of coronary artery disease, heart failure, stroke and peripheral vascular disease.

CKD and coronary heart disease

There is strong and consistent evidence for an association between proteinuria and albuminuria with subsequent risk of coronary heart disease. Cohort studies have shown that microalbuminuria is a strong and independent determinant of coronary heart disease and

death (Klausen et al. 2004; Ryoo et al. 2011). Further, CKD is associated with risk for recurrent coronary heart disease that is similar to other high-risk conditions, such as diabetes, metabolic syndrome or cigarette smoking (Baber et al. 2013).

The pooled relative risk used (1.47, 95% CI 1.23–1.74) for the association between CKD and coronary heart disease was sourced from a meta-analysis by Perkovic et al. (2008). The results from this meta-analysis of 26 cohort studies, including information on over 7,000 coronary heart disease events among almost 170,000 individuals, suggested that people with proteinuria have a risk of coronary heart disease that is 50% greater than those without. Furthermore, there was evidence to indicate a dose–response relationship where the strength of the association was higher among individuals with macroalbuminuria compared with those with microalbuminuria. The relationship was consistent across predefined population subgroups, including sex, ethnicity and individuals with and without diabetes. This meta-analysis confirmed a strong and independent association between chronic kidney dysfunction and risk of coronary heart disease.

CKD and stroke

There is strong and consistent evidence for an association between CKD and stroke. Several meta-analyses found the risk of stroke increases linearly with decreasing eGFR or increasing albuminuria (Lee et al. 2010a, 2010b ; Masson et al. 2015). People with a low eGFR (<60 mL/min/1.73 m^2) had an independent risk of stroke greater than those with a normal baseline eGFR (Lee et al. 2010a; Weiner et al. 2004).

The pooled relative risk used (1.43, 95% CI 1.31–1.57) for the association between CKD and stroke was sourced from a meta-analysis by Lee et al. (2010a). This meta-analysis was assessed to be the most up to date, including the largest number of studies with an outcome of any stroke. It included 21 articles derived from 33 prospective studies and over 280,000 persons experiencing almost 8,000 stroke events. The results found a link between low eGFR and risk of future stroke. This relationship was consistent across diverse population subgroups—that is, those with or without cardiovascular risk factors.

The pooled relative risk of 1.43 for the risk of stroke was similar to the hazard ratio of 1.17 reported by Weiner et al. (2004), where CKD was also defined by low eGFR. In contrast, the relative risk reported by Lee et al. (2010b) for macroalbuminuria was 2.65 and for microalbuminuria was 1.58, while the relative risk for proteinuria was 1.71 reported in a meta-analysis by Ninomiya et al. (2009).

CKD and peripheral vascular disease

There are few high-quality observational studies on CKD and the risk of peripheral vascular disease. The cohort study by O'Hare et al. (2004) found a strong association between renal insufficiency and lower-extremity peripheral vascular disease, independent of potential confounders such as age, diabetes, hypertension, coronary heart disease, stroke history and high cholesterol. The odds ratio was 2.5 (95% CI 1.2–5.1). This study was selected because it had a large sample size of 2,229 persons and clearly defined methodology.

The level of evidence for CKD was assessed to be probable in this report, because evidence was obtained from observational studies.

CKD and dementia

The level of evidence for CKD was assessed to be possible/probable in this report. This is because there are limited studies demonstrating a causal association between CKD and clinically defined dementia (Helmer et al. 2011; Miwa et al. 2014; Sasaki et al. 2011; Seliger et al. 2004).

A systematic review of the evidence found the association to be consistent between studies for CKD as a risk factor for cognitive decline, but no meta-analyses have been conducted (Deckers et al. 2015). Cognitive decline is less severe than dementia and not all persons with cognitive decline go on to have dementia, with a dementia diagnosis requiring severe cognitive decline and meeting diagnostic criteria.

Three studies have reported that impaired kidney function is associated with higher risk of dementia after adjusting for confounding factors: brain atrophy and small blood vessel disease (Miwa et al. 2014; Sasaki et al. 2011; Seliger et al. 2004). Another study showed no association between low kidney function at baseline and dementia, but found that a fast decline in kidney function—probably reflecting more severe kidney damage or impairment—was associated with an increased risk of dementia (Helmer et al. 2011).

The relative risk of 1.37 used in this project is taken from a 2004 study of 3,349 persons aged over 65 undertaken in the USA (Seliger et al. 2004). Moderate renal impairment was defined as elevated serum creatinine levels according to gender specific cut-offs (≥1.3 mg/dL for women and ≥1.5 mg/dL for men) (Seliger et al. 2004). Based on available evidence, this was the most applicable measure of CKD for Australian prevalence estimates. It was also the most comparable study for an Australian context, with other prospective longitudinal studies undertaken in Japanese and South-East Asian populations (Miwa et al. 2014; Sasaki et al. 2011).

Several biologically plausible mechanisms may explain how impaired kidney function leads to increased risk of dementia (Bugnicourt et al. 2013). Among these are anaemia, atherosclerosis and increased risk of stroke and micro infarcts, as well as elevated homocysteine—all more common in people with CKD and associated with increased dementia risk (Bugnicourt et al. 2013; Etgen 2015).

Table B2: Source of effect size used in calculation of attributable burden for chronic kidney disease

Linked disease	Reference	Study type	Number of studies	Study date	Sample size	Age at exposure	Length of follow-up	CKD definition	Outcome definition	Effect size (95%CI)	Notes
Coronary heart disease	Perkovic et al. 2008	Meta-analysis	26 cohort studies	Up to November 2006	169,949	>20 years	4–27 years	Proteinuria or albuminuria	Fatal or non-fatal coronary heart disease	RR 1.47 (1.23–1.74)	Adjusted for age, sex, body mass index, smoking, alcohol, hypertension, diabetes, education, total cholesterol and physical activity.
Stroke	Lee et al. 2010a	Meta-analysis	21 studies	Up to October 2009	284,672	Range = 53–78 years	3–15 years	eGFR <60 mL/min/1.73 m^2	All fatal and non-fatal stroke (ischaemic and haemorrhagic)	RR 1.43 (1.31–1.57)	Adjusted for age, sex, body mass index, smoking, alcohol, hypertension, diabetes, education, coronary heart disease, diabetes, cholesterol and selected medications.
Peripheral vascular disease	O'Hare et al. 2003	Prospective population study	1 study	1999–2000	2,229	≥40 years	Not reported	eGFR <60 mL/min/1.73 m^2	Ankle brachial index <0.90	OR 2.5 (1.2–5.1)	Adjusted for age, sex, body mass index, ethnicity, diabetes, hypertension, coronary artery disease, stroke history.
Dementia	Seliger et al. 2004	Prospective longitudinal population study	1 study	1989–1990 and 1992–1999	3,349	Mean = 76 ± 4.9 years	Median 6 years	Elevated serum creatinine Males ≥1.5 mg/dL Females ≥1.3 mg/dL	All-cause dementia (clinically diagnosed DSM-IV[(a)])	RR 1.37 (1.06–1.78)	Adjusted for age, sex, education, ethnicity, body mass index, coronary heart disease, hypertension, diabetes, smoking, apolipoprotein (apoE) genotype.

Appendix C: Methods for scenario modelling

In this report, the collective burden due to diabetes and CKD was extrapolated to 2020 using 2 scenarios. The difference between these scenarios provide an indication of the amount of burden that may be avoided if the rise of diabetes or CKD is halted, compared with the amount of burden if the current trends continue. Results from both methods were compared with the 2011 burden to estimate the extent of impact between the 2 scenarios (chapters 3 and 4).

The year 2020 was chosen because it aligns with the National Strategic Framework for Chronic Conditions and the World Health Organization's Global Action Plan for the Prevention and Control of Non-communicable Diseases 2013–2020 (WHO 2013).

Indirect burden

Projected indirect burden is dependent on both the future exposure of the risk factor (in this case exposure to diabetes and CKD) and the future *burden* of the linked diseases, which may be influenced by many factors such as diagnosis and treatment, as well as exposure to other risk factors.

Diabetes and CKD exposure

To estimate the indirect burden of diabetes and CKD in 2020, diabetes and CKD exposure (in this case, disease prevalence) were extrapolated using 2 scenarios. Scenario A assumes the past trend of prevalence rate (between 2003 and 2011) continues to 2020, while scenario B assumes that the 2011 prevalence rate will remain the same to 2020. Both scenarios account for expected changes in the population structure.

The 2 scenarios used to extrapolate diabetes and CKD prevalence in 2020 used the following methods:

- **Scenario A**

  The annual rate of change between the prevalence rate in 2003 and 2011 from the ABDS 2011 and extrapolated to 2020, was applied to projected 2020 populations. Other information about past trends in these conditions was used to determine if the rate of change is likely to continue.

  Assumption: the annual prevalence rate of change between 2003 and 2011 will continue to 2020.

- **Scenario B**

  Applying the prevalence rate in 2011 to projected 2020 populations; obtained from the Australian Bureau of Statistics population projections series B (ABS 2013).

  Assumption: the prevalence rate in 2011 is the same in 2020. The only change in burden is due to population growth and ageing.

The results show the differences in attributable burden that could be expected if these scenarios were to reflect the population exposure.

The data sources and methods used to derive prevalence for diabetes and CKD in 2011 and 2003 are described in Appendix D.

The annual rate of change in prevalence and fatal burden between 2003 and 2011 was derived for each sex and age group (see tables C1–C4). The annual rate of change in non-fatal burden between 2003 and 2011 were calculated at the sequela level for each sex and age group. Sequelae are consequences associated with the disease (see Appendix D) and extrapolation of trends at the sequelae level provides more accurate estimates of non-fatal burden.

Linked diseases

For both scenarios, it was assumed the 2011 burden rates of the linked diseases will remain the same to 2020, adjusted for expected changes in the population structure. Due to the complexity of possible associations between diseases, expected future changes in linked disease burden will require more consideration. This assumption was made for simplicity in our analysis.

The indirect diabetes and CKD burden estimated in 2020 under different prevalence scenarios for each linked disease are summarised in tables C5 and C6.

Direct burden

The direct burden for diabetes and CKD was also extrapolated to 2020 using similar scenarios. Scenario A assumes that the past trend of fatal and non-fatal burden rate (between 2003 and 2011) continues to 2020, while scenario B assumes the 2011 fatal and non-fatal burden rate will remain the same in 2020, where the only change in burden is due to population growth and ageing. Both scenarios account for expected changes in the population structure.

Collective burden

For each scenario A and B, the sum of indirect and direct burden provides estimates of the collective burden in 2020.

Assumptions and limitations

In our scenario analysis, we extrapolated diabetes and CKD exposure to 2020 and examined their impact on linked diseases. These extrapolations are, by nature, estimates about what might reasonably be expected in the future. Estimates based on historical trends and other available information can generate the best estimates. However, there is no guarantee of their realisation in the future. Scenario A and B generated different estimates of attributable burden in 2020. A major limitation for scenario A is that the assumption on the rate of change was based on 2 time points (2003 and 2011). Updated burden of disease estimates may provide opportunity for future extrapolations based on more than 2 time points, leading to increased mathematical accuracy.

A limitation is that, when using scenarios to estimate the impact of reduced exposure to diabetes or CKD on linked disease burden, it is not possible to quantify the flow-on effects to other possible diseases in the causal pathway that may occur in reality. For example, estimating the impact of reducing exposure to diabetes on coronary heart disease burden is

independent of measuring the impact of any potential reduction in CKD that might arise from reducing exposure to diabetes.

In this study, the impact of diabetes and CKD on linked diseases was assessed independently. Similarly, due to the complexity of possible associations between diseases, expected future changes in linked disease burden will require more consideration. It was assumed the 2011 burden rates of the linked diseases will remain constant to 2020. This assumption was made for simplicity in our analysis.

Table C1: Estimated diabetes prevalence rates (number per 1,000) for 2003 and 2011 used in scenario modelling

Age group (years)	2003		2011		Annual rate difference		Rate change between 2003 and 2011		Rate change between 2011 and 2020	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1–4	0.5	0.4	0.4	0.3	0.0	0.0	–0.1	0.0	–0.1	0.0
5–9	1.6	1.6	1.3	1.4	0.0	0.0	–0.3	–0.3	–0.4	–0.3
10–14	3.7	3.6	2.9	2.9	–0.1	–0.1	–0.8	–0.7	–0.9	–0.7
15–19	3.0	3.0	2.5	2.5	–0.1	–0.1	–0.5	–0.4	–0.6	–0.5
20–24	2.8	1.3	2.6	1.3	0.0	0.0	–0.1	0.0	–0.2	0.0
25–29	9.9	3.9	9.7	3.9	0.0	0.0	–0.2	0.0	–0.2	0.0
30–34	19.5	8.9	15.8	7.4	–0.5	–0.2	–3.7	–1.5	–4.1	–1.7
35–39	22.5	13.7	23.1	23.9	0.1	1.3	0.6	10.3	0.7	11.5
40–44	30.1	19.6	42.0	31.2	1.5	1.4	12.0	11.6	13.4	13.0
45–49	40.4	25.1	63.7	36.6	2.9	1.4	23.3	11.5	26.2	12.9
50–54	54.2	31.2	90.0	37.0	4.5	0.7	35.8	5.9	40.3	6.6
55–59	100.7	53.4	107.9	85.8	0.9	4.1	7.2	32.4	8.1	36.5
60–64	125.1	67.6	177.2	93.5	6.5	3.2	52.1	25.8	58.6	29.1
65–69	125.5	72.6	245.3	127.2	15.0	6.8	119.8	54.6	134.8	61.4
70–74	148.0	90.0	225.5	113.5	9.7	2.9	77.5	23.4	87.2	26.4
75–79	158.4	99.5	190.2	134.0	4.0	4.3	31.8	34.5	35.7	38.8
80–84	126.9	85.7	211.4	104.0	10.6	2.3	84.5	18.3	95.0	20.6
85–89	119.3	85.3	184.0	117.4	8.1	4.0	64.7	32.2	72.8	36.2
90–94	141.7	108.8	215.9	148.0	9.3	4.9	74.1	39.2	83.4	44.1
95–99	122.7	160.6	183.0	235.7	7.5	9.4	60.3	75.1	67.8	84.5
100+	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Source: AIHW burden of disease database, 2011.

Table C2: Diabetes YLL rates (number per 1,000) for 2003 and 2011 used in scenario modelling

Age group (years)	2003		2011		Annual rate change		Rate change between 2003 and 2011		Rate change between 2011 and 2020	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1–4	0.0	0.2	0.0	0.0	0.0	0.0	0.0	–0.2	0.0	–0.2
5–9	0.0	0.0	0.2	0.0	0.0	0.0	0.2	0.0	0.2	0.0
10–14	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.1
15–19	0.2	0.2	0.1	0.2	0.0	0.0	–0.1	0.0	–0.1	0.0
20–24	0.1	0.1	0.2	0.2	0.0	0.0	0.1	0.1	0.1	0.1
25–29	0.3	0.2	0.2	0.1	0.0	0.0	–0.1	0.0	–0.2	0.0
30–34	0.8	0.4	0.2	0.4	–0.1	0.0	–0.6	0.0	–0.7	0.0
35–39	0.8	0.2	0.6	0.1	0.0	0.0	–0.2	–0.1	–0.2	–0.1
40–44	1.3	0.6	1.0	0.6	0.0	0.0	–0.3	0.0	–0.3	0.0
45–49	1.1	1.2	1.4	1.1	0.0	0.0	0.3	–0.1	0.4	–0.2
50–54	3.1	1.1	2.7	1.6	–0.1	0.1	–0.4	0.5	–0.5	0.5
55–59	4.6	1.5	3.0	1.7	–0.2	0.0	–1.6	0.1	–1.8	0.2
60–64	7.6	3.6	5.3	2.8	–0.3	–0.1	–2.3	–0.8	–2.6	–0.9
65–69	11.8	6.1	9.6	4.7	–0.3	–0.2	–2.2	–1.4	–2.5	–1.6
70–74	17.5	8.4	11.7	7.2	–0.7	–0.1	–5.8	–1.2	–6.5	–1.3
75–79	17.3	12.8	17.4	10.1	0.0	–0.3	0.0	–2.7	0.0	–3.1
80–84	21.1	13.9	22.3	14.1	0.2	0.0	1.2	0.2	1.4	0.2
85–89	27.0	18.5	24.0	19.9	–0.4	0.2	–3.0	1.4	–3.4	1.5
90–94	26.6	17.9	27.0	20.0	0.1	0.3	0.4	2.0	0.5	2.3
95–99	16.3	18.0	24.7	20.7	1.1	0.3	8.4	2.7	9.5	3.1
100+	11.3	11.8	25.1	21.6	1.7	1.2	13.9	9.8	15.6	11.0

Source: AIHW burden of disease database, 2011.

Table C3: Estimated chronic kidney disease prevalence rates (number per 1,000) for 2003 and 2011 used in scenario modelling

Age group (years)	2003		2011		Annual rate difference		Rate change between 2003 and 2011		Rate change between 2011 and 2020	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1–4	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5–9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
10–14	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
15–19	0.3	0.3	0.3	0.4	0.0	0.0	0.1	0.1	0.1	0.1
20–24	0.9	0.8	1.0	0.9	0.0	0.0	0.1	0.1	0.1	0.1
25–29	1.5	1.6	1.6	1.8	0.0	0.0	0.1	0.1	0.2	0.1
30–34	1.6	1.9	2.0	2.4	0.0	0.1	0.4	0.5	0.4	0.6
35–39	2.7	3.0	3.4	3.7	0.1	0.1	0.7	0.7	0.8	0.8
40–44	3.3	3.6	4.5	4.6	0.1	0.1	1.2	1.1	1.3	1.2
45–49	5.0	5.0	6.5	6.1	0.2	0.1	1.5	1.2	1.7	1.3
50–54	6.7	6.4	8.5	7.6	0.2	0.2	1.8	1.3	2.0	1.4
55–59	10.1	9.0	13.0	10.6	0.4	0.2	3.0	1.6	3.3	1.8
60–64	19.1	15.8	20.4	15.3	0.2	–0.1	1.3	–0.5	1.5	–0.6
65–69	83.3	61.9	91.5	64.2	1.0	0.3	8.2	2.3	9.2	2.6
70–74	133.4	92.1	165.1	111.5	4.0	2.4	31.7	19.3	35.7	21.8
75–79	129.8	145.7	176.3	197.7	5.8	6.5	46.5	52.0	52.3	58.5
80–84	255.8	276.2	286.1	329.5	3.8	6.7	30.3	53.4	34.1	60.0
85–89	285.8	302.7	264.4	305.2	–2.7	0.3	–21.4	2.4	–24.1	2.7
90–94	333.6	337.7	312.7	344.5	–2.6	0.8	–20.9	6.8	–23.6	7.6
95–99	320.4	376.9	308.0	357.7	–1.5	–2.4	–12.4	–19.2	–13.9	–21.6
100+	167.0	262.2	244.2	255.5	9.7	–0.8	77.2	–6.6	86.9	–7.5

Source: AIHW burden of disease database, 2011.

Table C4: Chronic kidney disease YLL rates (number per 1,000) for 2003 and 2011 used in scenario modelling

Age group (years)	2003		2011		Annual rate change		Rate change between 2003 and 2011		Rate change between 2011 and 2020	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1–4	0.0	0.2	0.0	0.0	0.0	0.0	0.0	–0.2	0.0	–0.2
5–9	0.0	0.0	0.2	0.0	0.0	0.0	0.2	0.0	0.2	0.0
10–14	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.1
15–19	0.2	0.2	0.1	0.2	0.0	0.0	–0.1	0.0	–0.1	0.0
20–24	0.1	0.1	0.2	0.2	0.0	0.0	0.1	0.1	0.1	0.1
25–29	0.3	0.2	0.2	0.1	0.0	0.0	–0.1	0.0	–0.2	0.0
30–34	0.8	0.4	0.2	0.4	–0.1	0.0	–0.6	0.0	–0.7	0.0
35–39	0.8	0.2	0.6	0.1	0.0	0.0	–0.2	–0.1	–0.2	–0.1
40–44	1.3	0.6	1.0	0.6	0.0	0.0	–0.3	0.0	–0.3	0.0
45–49	1.1	1.2	1.4	1.1	0.0	0.0	0.3	–0.1	0.4	–0.2
50–54	3.1	1.1	2.7	1.6	–0.1	0.1	–0.4	0.5	–0.5	0.5
55–59	4.6	1.5	3.0	1.7	–0.2	0.0	–1.6	0.1	–1.8	0.2
60–64	7.6	3.6	5.3	2.8	–0.3	–0.1	–2.3	–0.8	–2.6	–0.9
65–69	11.8	6.1	9.6	4.7	–0.3	–0.2	–2.2	–1.4	–2.5	–1.6
70–74	17.5	8.4	11.7	7.2	–0.7	–0.1	–5.8	–1.2	–6.5	–1.3
75–79	17.3	12.8	17.4	10.1	0.0	–0.3	0.0	–2.7	0.0	–3.1
80–84	21.1	13.9	22.3	14.1	0.2	0.0	1.2	0.2	1.4	0.2
85–89	27.0	18.5	24.0	19.9	–0.4	0.2	–3.0	1.4	–3.4	1.5
90–94	26.6	17.9	27.0	20.0	0.1	0.3	0.4	2.0	0.5	2.3
95–99	16.3	18.0	24.7	20.7	1.1	0.3	8.4	2.7	9.5	3.1
100+	11.3	11.8	25.1	21.6	1.7	1.2	13.9	9.8	15.6	11.0

Source: AIHW burden of disease database, 2011.

Table C5: Indirect diabetes burden estimated in 2020 under different prevalence scenarios, by linked disease

		Scenario A		Scenario B		Scenario B compared with Scenario A	
		Continued trend in diabetes prevalence rate to 2020		Stable diabetes prevalence rate to 2020		DALY that would be avoided in 2020	
Linked disease	**Attributable DALY in 2011**	**Attributable DALY in 2020**	**Percentage change from 2011 attributable DALY[(a)]**	**Attributable DALY in 2020**	**Percentage change from 2011 attributable DALY[(a)]**	**DALY number**	**DALY (%)[(b)]**
Coronary heart disease	38,852	79,588	104.8	50,964	31.2	28,624	36.0
Stroke	18,730	37,420	99.8	24,611	31.4	12,808	34.2
Chronic kidney disease	8,945	16,950	89.5	11,547	29.1	5,403	31.9
Dementia	8,018	18,033	124.9	10,849	35.3	7,184	39.8
Liver cancer	3,655	7,395	102.3	4,728	29.4	2,667	36.1
Pancreatic cancer	3,655	7,002	91.6	4,660	27.5	2,342	33.4
Bowel cancer	2,993	6,420	114.5	3,910	30.6	2,510	39.1
Breast cancer	875	1,783	103.8	1,106	26.4	677	38.0
Peripheral vascular disease	771	1,651	114.1	1,025	33.0	626	37.9
Kidney cancer	739	1,553	110.1	949	28.5	603	38.8
Uterine cancer	610	1,192	95.3	783	28.3	409	34.3
Bladder cancer	489	1,097	124.3	655	33.9	442	40.3
Indirect burden total	**88,332**	**180,084**	**103.9**	**115,788**	**31.1**	**64,297**	**35.7**

(a) Percentage change is the change in attributable DALY between 2020 and 2011 divided by the attributable DALY in 2011 for each scenario.

(b) Percentage difference is the difference in attributable DALY in 2020 between Scenario A and B divided by the attributable DALY in 2020 for Scenario A.

Source: AIHW analysis of burden of disease database, 2011.

Table C6: Indirect chronic kidney disease burden under different exposure scenarios, by linked disease

		Scenario A		Scenario B		Scenario B compared with Scenario A	
		Continued trend in CKD prevalence rate to 2020		Stable CKD prevalence rate to 2020		DALY that would be avoided in 2020	
Linked disease	**Attributable DALY in 2011**	**Attributable DALY in 2020**	**Percentage change from 2011 attributable DALY[(a)]**	**Attributable DALY in 2020**	**Percentage change from 2011 attributable DALY[(a)]**	**DALY number**	**DALY (%)[(b)]**
Coronary heart disease	22,728	33,134	45.8	30,401	33.8	2,733	8.2
Dementia	12,678	17,868	40.9	16,789	32.4	1,079	6.0
Stroke	9,859	14,097	43.0	12,978	31.6	1,119	7.9
Peripheral vascular disease	1,621	2,312	42.6	2,173	34.1	139	6.0
Indirect burden total	**46,886**	**67,410**	**43.8**	**62,342**	**33.0**	**5,068**	**7.5**

(a) Percentage change is the change in attributable DALY between 2020 and 2011 divided by the attributable DALY in 2011 for each scenario.

(b) Percentage difference is the difference in attributable DALY in 2020 between Scenario A and B divided by the attributable DALY in 2020 for Scenario A.

Source: AIHW analysis of burden of disease database, 2011.

Appendix D: Data sources

Prevalence estimates and direct burden estimates for diabetes and CKD were obtained from the ABDS 2011. Detailed methodology on the methods and assumptions used by the ABDS 2011 can be found in *Australian Burden of Disease Study 2011: methods and supplementary material* (AIHW 2016b).

For diabetes and CKD, prevalence estimates were calculated at the sequela level (consequences associated with diabetes); estimates for each sequela were then combined to produce burden estimates for diabetes and CKD, respectively.

Diabetes

Diabetes includes type 1, type 2 and other diabetes types, with the exception of gestational diabetes (included in reproductive and maternal conditions). Two sequelae were included for analysis: undiagnosed and diagnosed diabetes.

Prevalence estimates for undiagnosed and diagnosed diabetes in people aged 18 and over were derived from the biomedical component of the Australian Health Survey (AHS) 2011–12. For those aged under 18, diagnosed diabetes prevalence estimates were obtained from the National Diabetes Registry. It was assumed that there were no people with undiagnosed diabetes aged under 18.

2003 prevalence estimates (used to inform current trends in scenario modelling)

For diagnosed diabetes, because the health surveys before the AHS did not have biomedical components, the 2003 prevalence estimates were modelled using the self-report data from the 2001, 2004–05, 2007–08 National Health Survey and the AHS.

Chronic kidney disease

The primary data source for estimating prevalence of chronic kidney disease (with and without anaemia) was the AHS 2011–12, while the primary data source for estimating prevalence of ESKD was the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) 2011. There were 6 sequelae included for analysis: asymptomatic; anaemia due to stage 3 chronic kidney disease; stage 4 chronic kidney disease; anaemia due to stage 4 chronic kidney disease; ESKD treated with dialysis or transplant; and untreated ESKD.

Asymptomatic

The prevalence of asymptomatic stage 3 CKD was estimated using measured data from the AHS 2011–12. Stages were determined by combining the participants' estimated glomerular filtration rate results with their albumin:creatinine ratio results as described in *Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: prevalence and incidence* (AIHW 2014).

It is important to note that asymptomatic CKD was given an asymptomatic health state, so it did not contribute to the non-fatal burden.

Anaemia due to stage 3 chronic kidney disease

The AHS 2011–12 was used to calculate the proportion of people with stage 3 chronic kidney disease by broad age group and sex. The age and sex distribution was further refined using hospitalisations data from the National Hospital Morbidity Database.

Stage 4 chronic kidney disease and *Anaemia due to stage 4 chronic kidney disease*

The prevalence of stage 4 CKD was also estimated using measured data from the AHS 2011–12, using the estimate of persons with stage 4 and 5 chronic kidney disease minus those with ESKD (stage 5 only) sourced from the ANZDATA.

The age and sex distribution was based on the AHS 2011–12 results but disaggregated further by the age and sex of persons who were hospitalised in 2011.

End stage kidney disease treated with dialysis or transplant

Registry data from the 2011 ANZDATA was used to determine the prevalence of ESKD treated by dialysis or transplant.

Untreated ESKD

Untreated ESKD refers to people were not receiving kidney replacement therapy, although they may be receiving palliative treatments. The prevalence of people with untreated ESKD was estimated from an analysis of the 2010 ANZDATA linked with the AIHW National Mortality Database and National Death Index to identify persons who died from ESKD that were not treated with kidney replacement therapy or were not in the registry (AIHW 2011). The prevalence for 2010 was assumed to be the same as 2011.

2003 prevalence estimates (used to inform current trends in scenario modelling)

The ratio of the prevalence of treated ESKD to the prevalence of stage 3 CKD and stage 4 CKD in 2011 was used to estimate prevalence in 2003, due to lack of biomedical measurement data consistent with the 2011 method. The age and sex distribution from 2011 were then applied to these estimates because the hospital codes used to estimate these were not in use in 2003.

Population attributable fraction for CKD attributable to diabetes

The proportion of CKD that was attributable to diabetes (population attributable fraction) was calculated based on the ANZDATA, because the ANZDATA only includes data on ESKD receiving treatment (stage 5 CKD). In our analysis, the population attributable fraction was assumed to apply to all stages of CKD. The variable used to calculate the proportion of people with CKD due to diabetes in the ANZDATA is the 'primary group'—specifically the proportion of individuals with diabetic nephropathy by age and sex. The registry includes limited information on people aged 90 and over because they are less likely to get renal replacement therapy over time. As such, the PAFs were modelled for age 90 and over.

Linked diseases

The data sources for the DALY estimates of each linked diseases are summarised in Table D1.

Table D1: The Australian Burden of Disease Study 2011 main data sources for YLD estimation

Linked disease	Key national data sources
Cancers	Australian Cancer Database
	National Mortality Database
	National Hospital Morbidity Database
	Epidemiological studies
Cardiovascular diseases (coronary heart disease, stroke, peripheral vascular disease)	National Hospital Morbidity Database
	Western Australian linked data
	New Zealand Burden of Disease Study
Dementia	AIHW dementia analyses
	International epidemiological studies

Glossary

attributable burden: The disease burden attributed with a particular risk factor. It is the reduction in fatal and non-fatal burden that would have occurred if exposure to the risk factor had been avoided (or, more precisely, had been at its theoretical minimum).

chronic: Persistent and long-lasting.

collective burden: The sum of the direct and indirect burden**.**

comorbidity: A situation where a person has 2 or more health problems at the same time.

comparative risk assessment: The process for estimating the burden of disease attributable to selected risk factors. It involves 5 key steps: selection of risk–outcome pairs; estimation of exposure distribution; estimation of effect sizes; choice of theoretical minimum risk exposure level; and finally the calculation of attributable burden.

DALY (disability-adjusted life years): Measure (in years) of healthy life lost, either through premature death defined as dying before the expected life span (YLL) or, equivalently, through living with ill health due to illness or injury (YLD).

direct burden: In burden of disease analysis, it is the burden calculated to capture the main disabling consequences of the disease. For example, the direct diabetes burden includes diabetic nephropathy, neuropathy and retinopathy.

disability: In burden of disease analysis, any departure from an ideal health state.

disease: A broad term that can be applied to any health problem, including symptoms, diseases, injuries and certain risk factors, such as high blood cholesterol and obesity. Often used synonymously with condition, disorder or problem.

diseases-as-risks: Diseases act as risk factors for other diseases. To fully account for the health loss attributable to diseases-as-risks requires that their 'indirect' burdens be calculated and then added to their 'direct' burdens in order to estimate their collective burdens.

effect size: A statistical measure of the strength of the relationship between 2 variables (in this context, between a risk exposure and a disease outcome), expressed, for example, as a relative risk.

fatal burden: The burden from dying 'prematurely' as measured by years of life lost. Often used synonymously with YLL, and also referred to as 'life lost'.

hazard ratio (HR): Hazard ratio has similar interpretation to relative risk. It is the ratio of the probability of an event (e.g. disease outcome) in the exposed group to the probability in the control group. Hazard ratios differ from relative risks in that the latter are cumulative over an entire study, using a defined endpoint, while the former represent instantaneous risk at some particular time period during the study.

indirect burden: In burden of disease analysis, where the disease of interest is considered to be a risk factor (that is, disease-as-risk) for associated or 'linked' diseases, it is the burden from these linked diseases due to the disease-as-risk. For example, diabetes is considered to be a risk factor for coronary heart disease, stroke, dementia and other diseases, so the indirect burden is the burden attributable to diabetes for these linked diseases.

linked disease: Many risk factors are associated with developing certain diseases; for example, diabetes is associated with increased risk of developing coronary heart disease. The disease in association is a linked disease to the risk factor.

meta-analysis: A statistical technique for combining findings from previous independent studies. It provides a quantitative estimate of the overall effect of an intervention or variable on a defined outcome, giving due weight to the size of the different studies included.

morbidity: Ill health in an individual, and levels of ill health in a population or group.

mortality: Death.

non-fatal burden: The burden from living with ill health as measured by years lived with disability. Often used synonymously with YLD, and also referred to as 'health loss' in this report.

odds ratio (OR): Odds ratio is a measure of association which compares the odds of disease in those exposed, to the odds of disease in those unexposed.

population attributable fraction (PAF): The proportion (fraction) of a disease, illness, disability or death in a population that can be attributed to a particular risk factor or combination of risk factors.

prevalence: The number of cases of a disease or injury in a population at a given time.

relative risk (RR): The risk of an event relative to exposure, calculated as the ratio of the probability of the event occurring in the exposed group to the probability of it occurring in the non-exposed group. A relative risk of 1 implies no difference in risk; a RR <1 implies the event is less likely to occur in the exposed group; and a RR >1 implies the event is more likely to occur in the exposed group.

risk factor (for health): Any factor that causes or increases the likelihood of a health disorder or other unwanted condition or event.

risk–outcome pairs: Conditions that are causally linked to a risk factor.

YLD (years lived with disability): A measure of the years of what could have been a healthy life but were instead spent in states of less than full health. YLD represent non-fatal burden.

YLL (years of life lost): Years of life lost due to premature death, defined as dying before the global ideal life span. YLL represent fatal burden.

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Related publications

This report, *Diabetes and chronic kidney disease as risks for other diseases*, and other AIHW publications can be downloaded for free from the AIHW website <http://www.aihw.gov.au>. The website also includes information on ordering printed copies.

The following AIHW publications relating to burden of disease in Australia might also be of interest:

- AIHW 2016a. Australian Burden of Disease Study: impact and causes of illness and death in Australia 2011. Australian Burden of Disease Study series no. 3. Cat. no. BOD 4. Canberra: AIHW.
- AIHW 2016b. Australian Burden of Disease Study 2011: methods and supplementary material. Australian Burden of Disease Study series no. 5. Cat. no. BOD 6. Canberra: AIHW.
- AIHW 2016c. Australian Burden of Disease Study: impact and causes of illness and death in Aboriginal and Torres Strait Islander people 2011. Australian Burden of Disease Study series no. 6. Cat. no. BOD 7. Canberra: AIHW.
- AIHW 2016d. Contribution of vascular diseases and risk factors to the burden of dementia in Australia: Australian Burden of Disease Study 2011. Australian Burden of Disease Study series no. 9. Cat. no. BOD 10. Canberra: AIHW.

This report aims to provide a more comprehensive picture of the full health loss attributable to diabetes and chronic kidney disease (CKD). It quantifies the impact of diabetes and CKD on the burden of other diseases for which there is evidence of a causal association ('linked diseases') to estimate the indirect burden caused by these 2 diseases. It uses disease burden estimates from the Australian Burden of Disease Study 2011 and extends the standard approach for analysis of risk factors to model diabetes and CKD as risk factors. When the indirect burden due to linked diseases was taken into account, the collective burden due to diabetes was 1.9 times as high, and CKD was 2.1 times as high, as their direct burden.