Projecting the Incidence of Type 2 Diabetes-Related End-Stage Kidney Disease until 2040: A Comparison between the Effects of Diabetes Prevention and Treatment

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Supplementary Text 1 – Description of data sources for model inputs and uncertainty in model parameters.

To estimate the ESKD incidence and all-cause mortality rates used for estimation of the lifetime risk of ESKD and projections of the incidence of ESKD-D, we used data derived from linkage of the National Diabetes Services Scheme (NDSS) to the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) and the Australian National Death Index (NDI) for 2002-2013, as previously described (1). Briefly, the NDSS was established by the Australian government in 1987 and includes 80-90% of people with diagnosed diabetes in Australia. For model data inputs, we used data from members with type 2 diabetes registered on the NDSS as of 1 January 2002 and all new registrants from this date until 31 December 2013. ANZDATA is a registry that collects data on all people who undergo kidney transplantation and/or dialysis, with complete coverage of all RRT units in Australia. ESKD was defined from ANZDATA as initiation of RRT. The NDI contains records of all registered deaths in Australia.

In the table below the values and sources of all model inputs are outlined, as well as assumed uncertainty distributions used in Monte Carlo simulations.

Table – Source of model inputs and uncertainty. Error distributions were assumed to be normal unless otherwise stated.

Input	Estimated value and standard error	Source
ESKD incidence rate in type 2 diabetes	Sex, age, and duration of diabetes-specific transition probability and standard error. Estimated via Poisson regression (Supplementary Text 2).	National Diabetes Services Scheme linked to the Australia and New Zealand Dialysis and Transplant Registry containing data from 2002-2013.
Mortality rate in type 2 diabetes	Sex, age, and duration of diabetes-specific transition probability and standard error. Estimated via Poisson regression (Supplementary Text 2).	National Diabetes Services Scheme linked to the Australian National Death Index containing data from 2002-2013.
Incidence of type 2 diabetes in the Australian population	2.5 per 1000 Australian population. The standard deviation was assumed to be 10% of the point estimate (±0.25 per 1000).	2.5 per 1000 population was the average incidence of type 2 diabetes from 2015-2019 in Australia. For this calculation the numerator was taken from the National Diabetes Services Scheme data

		snapshots (2), the denominator was taken from the ABS population estimates (3).
Future Australian population size	Actual population estimates were used for 2014-2019. Yearly population projections were used for 2020-2040. The standard error was assumed to be 5% of the point estimate for 2014-2029, and 10% for 2030-2040.	Actual population estimates came from the Australian Bureau of Statistics population estimates (3). Projected population estimates came from the Australian Bureau of Statistics population projections, series B (4).
Diabetes incidence reduction with a sugar sweetened beverage tax	Per cent reduction in diabetes incidence (95% CI) among the Australian population: 	Age	Males	Females
Likely scenario		
<18	7.9% (2.8-13.8)	5.4% (1.9-9.4)
19-64	6.8% (2.4-11.8)	4.7% (1.7-8.2)
≥65	2.7% (1.0-4.8)	2.5% (0.9-4.4)
Best-case scenario		
<18	16.8% (6.2-29.1)	11.5% (4.2-19.9)
19-64	14.4% (5.2-24.9)	10.0% (3.6-17.3)
≥65	5.8% (2.1-10.0)	5.4% (2.0-9.3)		To estimate the proportional reduction in diabetes incidence for each age group, we compared the number of diabetes cases prevented in a modelling study by Briggs et al. (5) to the actual incidence of diabetes in the UK used in that study (6). For the best-case scenario, age-specific estimates for diabetes prevention were not publicly available, so we assumed that the age and sex-distribution of the effect was maintained proportionally to the likely scenario, which was true for all other interventions modelled in that study. Similarly, the published uncertainty intervals by age were not publicly available, and so were assumed to be distributed proportionally among age groups.
Diabetes incidence reduction with a lifestyle modification program	Relative risk of developing type 2 diabetes: 0.71 (95% CI: 0.58-0.88). Applied to 35% of adults with prediabetes under the likely scenario, and 50% of adults under the best-case scenario.	A meta-analysis of real-world diabetes prevention trials (7).

ESKD incidence reduction with wide-spread SGLT2i use	Relative risk of developing ESKD: 0.65 (95% CI: 0.53-0.81). Applied to 50% of people with an eGFR >45 ml/min/1.73m^2 by 2023 under the likely scenario, and 70% of people with an eGFR >30 ml/min/1.73m^2 by 2024 under the best-case scenario.	A meta-analysis of phase III clinical trials (8).

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Supplementary Text 2 – Estimation of sex, age and duration-specific ESKD incidence and all-cause mortality rates

Incidence of ESKD and mortality rates among people without ESKD as a function of sex, age and duration of diabetes were predicted in order to estimate the lifetime risk of ESKD, as well as project the incidence of ESKD, using a framework previously described (1). Briefly, National Diabetes Services Scheme registrants were followed from 1 January 2002 or date of registration, if later, until onset of ESKD, death, or end of follow-up on 31 December 2013. Registrants' follow-up (risk time and ESKD or deaths) was split into intervals of 6 months by current age (0–100 years), calendar time (2002–2013) and diabetes duration (0–40 years). Risk time and ESKD or deaths were then tabulated by current age, date of follow-up, and duration of diabetes, and each cell of the table was assigned age, date, and diabetes duration as continuous variables as the midpoint of the 6 month group. When date of diagnosis was not available for a participant, date of registration was used as a proxy. Data were analysed using a Poisson model, using spline effects of current age, diabetes duration and age at diagnosis, with a linear effect of calendar time. Separate models were fitted for the incidence of ESKD and all-cause mortality among those without ESKD. These models were fitted for males and females separately. Rates are then predicted for each attained age and duration of diabetes, by sex.

Reference

1.   Huo L, Magliano DJ, Rancière F, Harding JL, Nanayakkara N, Shaw JE, et al. Impact of age at diagnosis and duration of type 2 diabetes on mortality in Australia 1997–2011. Diabetologia. 2018;61(5):1055-63.

Supplementary Text 3 – Detailed description of the model used to predict the lifetime risk of ESKD among adults with type 2 diabetes

Step 1: The model begins with a cohort at diagnosis of type 2 diabetes. For this example males diagnosed with type 2 diabetes at age 20 are used, but the methods are the same for any cohort followed from diagnosis of type 2 diabetes.
At this stage the dataset looks as follows:

```
Sex   Age   N
Male  20    100
```

Step 2: transition rates for ESKD are applied, based on the age, age at diagnosis of diabetes, and sex (Supplementary Text 2). Let these rates be denoted by TE, and the number developing ESKD at a given age be denoted N_ESKD (=N*TE). Let the total number who have developed ESKD since diagnosis of type 2 diabetes be denoted C_I (for cumulative incidence).

```
Sex   Age   N     TE        N_ESKD    C_I
Male  20    100   0.0001    0.01      0.01
```

To move forward, N_ESKD is subtracted from N, to track those who remain without ESKD, which is denoted N_EF (Number ESKD-free).

```
Sex   Age   N     TE        N_ESKD    C_I       N_EF
Male  20    100   0.0001    0.01      0.01      99.99
```

Step 3: transition rates for mortality are applied to people without ESKD. Let these rates be denoted by TM, and the number dying be denoted N_Death (=N_EF*TM).

```
Sex   Age   N     TE        N_ESKD    C_I       N_EF      TM        N_Death
Male  20    100   0.0001    0.01      0.01      99.99     0.002     0.2
```

The number of people who remain alive without ESKD at the end of the year is thus N_EF - N_Death = N_Alive.

Sex	Age	N	TE	N_ESKD	C_I	N_EF	TM	N_Death	N_Alive
Male	20	100	0.0001	0.01	0.01	99.99	0.002	0.2	99.79

Step 4: The cohort is followed to age 85 years, repeating the process each year. The number entering the next year is the number who were alive without ESKD at the end of the previous year.

Sex	Age	N	TE	N_ESKD	C_I	N_EF	TM	N_Death	N_Alive
Male	20	100	0.0001	0.01	0.01	99.99	0.002	0.2	99.79
Male	21	99.79	0.0002	0.02	0.03	99.77	0.004	0.4	99.37
Male	23	99.37	0.0003	0.03	0.06	99.34	0.005	0.5	98.84
...									
Male	83	11.19	0.0055	0.06	29.4	11.13	0.161	1.8	9.33
Male	84	9.33	0.0046	0.04	29.5				

Thus, the lifetime risk of ESKD for males aged 20 at diagnosis of type 2 diabetes is 29.5%.

There is a specific and separate ESKD and mortality transition rate for each age, sex, and age at diagnosis combination, resulting from Poisson regression as outlined in Supplementary Text 2.

In the Monte Carlo simulations, transition probabilities were simulated before being applied.

The model is detailed schematically in the following figure:

Step 1: The model begins with a cohort at diagnosis of type 2 diabetes.

Type 2 diabetes

Step 2: Using age, sex, and duration of diabetes-specific ESKD incidence rates, people are transitioned to ESKD.
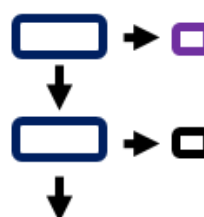
Type 2 diabetes
DKD → ESKD

Step 3: Age, sex, and duration of diabetes-specific mortality rates are applied.

Type 2 diabetes → Death

Step 4: Repeat steps 2 and 3 each year of age until age 85 years.

Supplementary Text 4 – Detailed description of the model used to project the incidence of ESKD-D

The model begins with the NDSS population as at 1 January 2014, in terms of age, sex, and age at diagnosis of diabetes. At this stage the dataset looks as follows:

```
Sex         Age   Age_at_dx N
Male        10    10        1
Male        11    10        3
Male        12    10        2
…
Male        37    29        45
Male        38    29        32
…
Female      10    10        2
…
Female      103   100       1
```

Where dx is short for diagnosis. In this dataset, N represents the number of individuals who fit each age/age at diagnosis category. For example, as at 1 January 2014, there were n=45 males aged 37 years who were diagnosed with type 2 diabetes at age 29 years registered on the NDSS. There is an age, sex, and age at diagnosis category for all NDSS registrants alive at 1 January 2014.

Step 1: transition rates for ESKD are applied, based on the age, age at diagnosis of diabetes, and sex (Supplementary Text 2). Let these rates be denoted by TE, and the number developing ESKD be denoted N_ESKD (=N*TE).

```
Sex         Age   Age_at_dx N     TE        N_ESKD
Male        10    10        1     0.00007   0.00007
Male        11    10        3     0.00008   0.00024
Male        12    10        2     0.00009   0.00018
…
Male        37    29        45    0.00062   0.02790
Male        38    29        32    0.00076   0.02432
…
Female      10    10        2     0.00006   0.00012
…
Female      103   100       1     0.00000   0.00000
```

The total number developing ESKD this year is thus the sum of the variable N_ESKD over the entire dataset. To move forward, N_ESKD is subtracted from N, to track those without ESKD only.

```
Sex        Age   Age_at_dx  N
Male       10    10          0.99993
Male       11    10          2.99976
Male       12    10          1.99982
...
Male       37    29         44.9721
Male       38    29         31.9757
...
Female     10    10          1.99988
...
Female     103   100         1.00000
```

Step 2: transition rates for mortality are applied. Let these rates be denoted by TM, and the number dying be denoted N_Death (=N*TM).

```
Sex        Age   Age_at_dx  N          TM         N_Death
Male       10    10          0.99993    0.00124    0.00124
Male       11    10          2.99976    0.00117    0.00351
Male       12    10          1.99982    0.00114    0.00228
...
Male       37    29         44.9721     0.00294    0.13222
Male       38    29         31.9757     0.00314    0.10040
...
Female     10    10          1.99988    0.00021    0.00042
...
Female     103   100         1.00000    0.64005    0.64005
```

These people are removed from the model by subtracting N_Death from N.

```
Sex        Age   Age_at_dx  N
Male       10    10          0.99869
Male       11    10          2.99625
Male       12    10          1.99754
...
Male       37    29         44.8399
Male       38    29         31.8753
...
Female     10    10          1.99946
...
Female     103   100         0.35995
```

Step 3: The population with type 2 diabetes is aged one year.

```
Sex         Age   Age_at_dx N
Male        11    10          0.99869
Male        12    10          2.99625
Male        13    10          1.99754
…
Male        38    29          44.8399
Male        39    29          31.8753
…
Female      11    10          1.99946
…
Female      104   100         0.35995
```

A population with incident type 2 diabetes is added.

```
Sex         Age   Age_at_dx N
Male        10    10          1
Male        11    10          0.99869
Male        12    10          2.99625
Male        13    10          1.99754
…
Male        29    29          15
…
Male        38    29          44.8399
Male        39    29          31.8753
…
Female      10    10          1
Female      11    10          1.99946
…
Female      104   100         0.35995
```

This process is now repeated for 2015-2040 to obtain estimates for the current trajectory.

There is a specific and separate ESKD and mortality transition rate for each age, sex, and age at diagnosis combination, resulting from Poisson regression as outlined in Supplementary Text 2.

The size of the incident population is given by the product of the ABS population projection estimate for the year in question and 0.0025 (incidence of type 2 diabetes of 2.5 per 1000 Australian population; Supplementary Text 1). For example, in 2022, the size of the Australian population is projected to be 26,727,075, thus the incident population size with type 2 diabetes is 0.0025*26727075 = 66,817.69. The age and sex distribution of the incident population is assumed to remain constant from 2014-2040.

When applying diabetes incidence reductions, the size of the incident population is reduced proportionally to the size of the diabetes incidence reduction specified in Supplementary Text 1. For example, a 29% incidence reduction applied to 35% of the
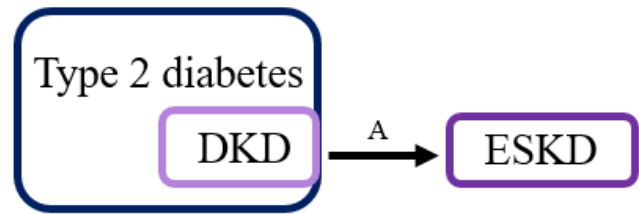
whole population with incident type 2 diabetes in 2022 reduces the number of incident cases from 66,817.69 to 60,035.69 (=66,817.69*(1-0.35*0.29))). (This example is presented for simplicity, in the actual model the incidence reduction applies only to those older than 18 years of age).

When applying ESKD incidence reductions, the ESKD incidence rate is reduced by the amount detailed in Supplementary Text 5. For example, under the best-case scenario in 2030, the incidence of ESKD is reduced by 24.5% (=35%*70%). Thus, if the probability of transition to ESKD for those aged 10 years diagnosed with diabetes at age 10 years was 0.00007 in the current trajectory, it is reduced to 0.00005285 (=0.00007*(1-(0.35*0.7))).

In the Monte Carlo simulations, transition probabilities were simulated before being applied. Simulated parameters from the baseline scenario were held constant for each simulation of an intervention, i.e. each simulation compared the intervention with a paired baseline scenario in which the baseline parameters (incident diabetes rate, ESKD incidence rate, mortality rates in people without ESKD, and future population size) were the same for the baseline and intervention simulation.

The model is detailed schematically in the following figure:

Step 1: The model at this point contains everyone with type 2 diabetes on the NDSS in 2014. Using age, sex, and duration of diabetes-specific ESKD incidence rates, people are transitioned to ESKD. Once ESKD has developed, these people are no longer tracked.
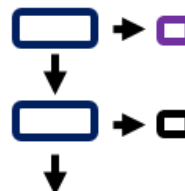
Type 2 diabetes

DKD

A

ESKD

Step 2: Age, sex, and duration of diabetes-specific mortality rates are applied.

Type 2 diabetes

Death

Australian population

Prediabetes

B
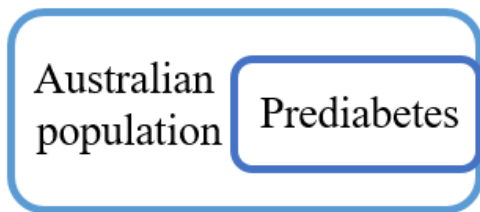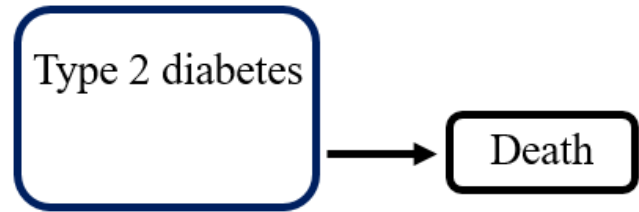
Type 2 diabetes

Step 3: A population with incident type 2 diabetes from the Australian population is added to the model. At the same time, The population with type 2 diabetes is aged one year.
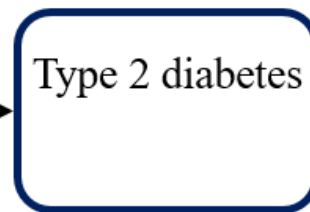
Step 4: Repeat steps 1-3 for 2015-2040.

A: In scenarios involving SGLT2i use, SGLT2is act to decrease the rate of transition from type 2 diabetes to ESKD.

B: In scenarios involving diabetes prevention, diabetes prevention acts to decrease the rate of transition from prediabetes to type 2 diabetes.

DKD: Diabetic kidney disease; ESKD – End-stage kidney disease.

Supplementary Text 5 – Assumptions for modelling ESKD incidence reductions with SGLT2i use

The effect of SGLT2is on the incidence of ESKD was estimated from a meta-analysis of phase III clinical trials (1); SGLT2is were found to reduce ESKD by 35% (RR: 0.65; 95% CI: 0.53-0.81). In Australia, SGLT2is are currently not recommended for individuals with an eGFR of <45 ml/min/1.73m^2, and because there's usually a delay of many years between reaching an eGFR of 45ml/min/1.73m^2 and progression to ESKD, the impact of SGLT2i use on ESKD incidence will not be immediate. Therefore, several assumptions about eGFR trajectories prior to initiation of renal replacement therapy (RRT) were made. Similarly, assumptions about how SGLT2i use will increase over time in the population with type 2 diabetes and DKD were made.

The best available evidence for estimation of eGFR trajectory prior to RRT was considered to be O'Hare et al (2). Among those with diabetes, ~90% had a steady progression to RRT from an eGFR of <60ml/min/1.73m^2 two years prior to RRT, and ~10% had a sudden progression from an eGFR of >60ml/min/1.73m^2. Of this ~90% with steady decline in renal function prior to RRT, we assumed ~80% will take ~6 years from reaching an eGFR of 45ml/min/1.73m^2 to reach an eGFR <30ml/min/1.73m^2 (estimated from (3)), and thus take approximately ~8 years from reaching an eGFR of 45ml/min/1.73m^2 until commencing RRT. The remaining ~20% will progress much faster, and will take ~4 years to reach RRT from reaching an eGFR of 45ml/min/1.73m^2. It is worth noting that these estimates assume linearity in eGFR decline, and while the majority of eGFR decline is linear, a nontrivial proportion is nonlinear (4).

Therefore, we assumed that 10% of individuals will decline from an eGFR of >60ml/min/1.73m^2 to RRT within 2 years, 72% will take 8 years from reaching an eGFR of 45ml/min/1.73m^2 to RRT, and 18% of individuals will take ~4 years from reaching an eGFR of 45ml/min/1.73m^2 to RRT. These times are used to calculate the delay between SGLT2i use and the impact of SGLT2is on the incidence of ESKD. For example, if SGLT2is were used in 20% of the population in 2020, we apply a reduction of 13% (20% of the incidence rate reduction of 0.65) to the incidence of ESKD: 10% of this effect will manifest in 2022, 72% in 2028, and 18% in 2024.

We based the likely SGLT2i use in people with type 2 diabetes and CKD on studies of the prevalence of Renin-Angiotensin-Aldosterone System inhibitor (RAASi) use. These studies show that the prevalence of RAASi use in this population varies with study design from ~20-60% (5,6). We assumed that following publication of the Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy (CREDENCE) trial, which showed clear benefit of these agents for progression of CKD among people with type 2 diabetes and macroalbuminuria (7), use of SGLT2is would reach 50% in this population. Furthermore, use of SGLT2is prior to 2020 in this population would not have been negligible, especially following the publication of several large trials showing benefits of SGLT2is on cardiovascular disease, the first of which was published in 2015 (8).

Therefore, in the likely scenario, we assumed the use of SGLT2is increased to 20% by 2020, and then increased to 50% by 2023, but remained contraindicated for individuals with an eGFR > 45ml/min/1.73m^2.

Because the CREDENCE trial showed evidence of benefit progression to ESKD in individuals with an eGFR as low as 30ml/min/1.73m^2, it is reasonable to expect guidelines might change to expand use of SGLT2is to individuals with an eGFR as low as 30ml/min/1.73m^2. Therefore, in the best-case scenario, we assumed use of SGLT2is increased to 28% in those with an eGFR >45ml/min/1.73m^2 by 2020, increasing to 70% by 2023. Use increased from 0% in 2019 to 70% by 2024 for those with an eGFR 30-45ml/min/1.73m^2.

Ultimately, when these assumptions are applied, the per cent reduction in incidence of ESKD each year applied is as follows:

Year	Likely (%)	Best-case (%)
2018	0.00	0.00
2019	0.07	0.27
2020	0.34	0.58
2021	0.83	0.89
2022	1.52	5.58
2023	2.43	10.40
2024	3.54	15.23
2025	4.87	20.05
2026	6.41	24.50
2027	8.16	24.50
2028	10.11	24.50
2029	12.28	24.50
2030	14.66	24.50
2031-2040	17.50	24.50

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Supplementary Table 1 – Population Characteristics.
Characteristics of the population used for derivation of model data. The model used data derived from the National Diabetes Services Scheme linked to the Australia and New Zealand Dialysis and Transplant Registry and the Australian National Death Index. We included members with type 2 diabetes registered on the NDSS as of 1 January 2002 and all new registrants from this date until 31 December 2013.

		Males	Females	Overall
Total N (%)		636922 (54.2%)	537641 (45.8%)	1174563 (100.0%)
Incident ESKD (N)		4902	2773	7675
Deaths without ESKD (N)		127614	98321	225935
Person-years of follow-up		4233208	3838415	8071623
Age of onset of diabetes – N (%)	10-39	47583 (7.5%)	66327 (12.3%)	113910 (9.7%)
	40-54	200249 (31.4%)	140146 (26.1%)	340395 (29.0%)
	55-69	268745 (42.2%)	207370 (38.6%)	476115 (40.5%)
	≥70	120345 (18.9%)	123798 (23.0%)	244143 (20.8%)
Duration of diabetes at end of follow-up – median (IQR)		7.9 (3.7-13.7)	8.9 (4.2-14.8)	8.3 (3.9-14.2)

Supplementary Table 2 – Remaining lifetime risk of ESKD, to age 85 years, by age of onset of diabetes and sex.
Estimated using multistate life table modelling.
Data are presented as median (95% uncertainty interval).

Age of onset of diabetes	Males	Females
20	29.5% (23.1-37.9)	17.7% (11.6-25.3)
30	17.7% (14.9-21.4)	12.5% (9.5-16.1)
40	9.0% (8.0-10.2)	8.4% (7.1-10.0)
50	4.7% (4.2-5.2)	4.4% (3.9-5.2)
60	2.5% (2.3-2.8)	1.8% (1.6-2.1)
70	1.2% (1.1-1.4)	0.7% (0.6-0.8)
80	0.3% (0.3-0.4)	0.1% (0.1-0.2)

Supplementary Table 3 – Number of incident diabetes cases expected and reduced by interventions between 2020 and 2040 under various modelled scenarios.
Data are presented as number of expected cases for current trajectory, and number of cases reduced (%) for each scenario.

Age	Number of cases expected	Number of cases reduced (%)					
	Current Trajectory	Lifestyle modification program		Sugar sweetened beverage tax		Combination of all interventions	
		Likely	Best-case	Likely	Best-case	Likely	Best-case
Males		Males					
10-39	61000	5883 (9.6%)	8412 (13.8%)	4106 (6.7%)	8736 (14.3%)	9516 (15.6%)	15840 (26.0%)
40-54	248230	24565 (9.9%)	35127 (14.2%)	16635 (6.7%)	35399 (14.3%)	39257 (15.8%)	65097 (26.2%)
55-69	352664	34900 (9.9%)	49905 (14.2%)	19415 (5.5%)	41320 (11.7%)	52001 (14.7%)	84643 (24.0%)
70-84	160607	15894 (9.9%)	22727 (14.2%)	4212 (2.6%)	8992 (5.6%)	19727 (12.3%)	30438 (19.0%)
Total; 95% uncertainty interval	822501; 641981 to 1035481	81241 (9.9%); 31270 to 131046	116171 (14.1%); 44687 to 187478	44376 (5.4%); 10514 to 76630	94441 (11.5%); 20760 to 162054	120373 (14.6%); 63421 to 183419	195473 (23.8%); 103337 to 298096
Females		Females					
10-39	60009	5759 (9.6%)	8234 (13.7%)	2808 (4.7%)	5975 (10.0%)	8241 (13.7%)	13297 (22.2%)
40-54	167909	16640 (9.9%)	23793 (14.2%)	7821 (4.7%)	16639 (9.9%)	23552 (14.0%)	37753 (22.5%)
55-69	257425	25511 (9.9%)	36478 (14.2%)	10230 (4.0%)	21819 (8.5%)	34691 (13.5%)	54815 (21.3%)
70-84	149015	14767 (9.9%)	21116 (14.2%)	3638 (2.4%)	7862 (5.3%)	18115 (12.2%)	27843 (18.7%)
Total; 95% uncertainty interval	634358; 494942 to 798935	62676 (9.9%); 24125 to 101188	89621 (14.1%); 34475 to 144747	24506 (3.9%); 5916 to 42413	52293 (8.2%); 12503 to 89897	84701 (13.4%); 42760 to 128962	133637 (21.1%); 71372 to 201863
Overall		Overall					
Total; 95% uncertainty interval	1456859; 1136923 to 1834415	143927 (9.9%); 55395 to 232234	205803 (14.1%); 79161 to 332225	68882 (4.7%); 16430 to 119043	146686 (10.1%); 33393 to 251947	204824 (14.1%); 106004 to 312035	328911 (22.6%); 175026 to 498479

Supplementary Figure 1 – Number of annual incident diabetes-related end-stage kidney disease (ESKD-D) cases among people with type 2 diabetes in Australia, by current trajectory and different interventions.
A – Likely scenarios. **B –** Best-case scenarios.
Abbreviations: LSM – Lifestyle modification; SSB – Sugar Sweetened Beverage; SGLT2i – Sodium-glucose co-transporter 2 inhibitor.