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FULL RESEARCH PAPER
Cardiovascular disease

The reduction of the productivity burden of cardiovascular disease by improving the risk factor control Among Australians with type 2 diabetes: a 10-year dynamic analysis

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Aims To quantify the productivity burden of cardiovascular disease (CVD) in type 2 diabetes and the potential benefits of improved CVD risk factor control.

Methods and results We designed models to quantify the productivity burden (using the productivity-adjusted life-year; PALY) of CVD in Australians with type 2 diabetes aged 40–69 years from 2023–2032. PALYs were ascribed a financial value equivalent to gross domestic product (GDP) per full-time worker (AU$204 167 (€124 542)). The base-case model was designed to quantify the productivity burden of CVD in the target population. Then, other hypothetical scenarios were simulated to estimate the potential productivity gains resulting from improved control of risk factors. These scenarios included reductions in systolic blood pressure (SBP), number of smokers, total cholesterol, and incidence of type 2 diabetes. All future costs and outcomes were discounted at an annual rate of 5%. In the base-case (i.e. current projections), the estimated total PALYs lost due to CVD in type 2 diabetes were 1.21 million [95%CI (1.10–1.29 million)], contributing to an AU$258.93 (€157.94) billion [95%CI (AU$258.73–261.69 (€157.83–159.63) billion)] lost in the country's GDP. If there were reductions in SBP, number of smokers, total cholesterol, and incidence of type 2 diabetes, there would be gains of 7,889, 28,971, 7,117, and 320 124 PALYs, respectively. These improvements would also lead to economic gains of AU$1.72 (€1.05) billion, AU$6.21 (€3.79) billion, AU$1.55 billion (€947.33 million), and AU$68.34 (€41.69) billion, respectively.

Conclusion Targeted 'early lifestyle' strategies that can prevent CVD in Australians with type 2 diabetes are likely to positively impact Australian health and work productivity.

Lay summary This study aimed to assess the productivity burden of cardiovascular disease (CVD) in individuals with type 2 diabetes and the potential benefits of improving the control of CVD risk factors. We developed models to estimate the productivity burden using a measure called productivity-adjusted life-years (PALY). We assigned a financial value to PALYs based on the country's gross domestic product (GDP) per full-time worker.

The base-case model showed that the estimated total PALYs lost due to CVD in type 2 diabetes were 1.21 million (95%CI (1.10–1.29 million), contributing AU$258.93 (€157.94) billion (95%CI (AU$258.73–261.69 (€157.83–159.63) billion) lost in the country's GDP.

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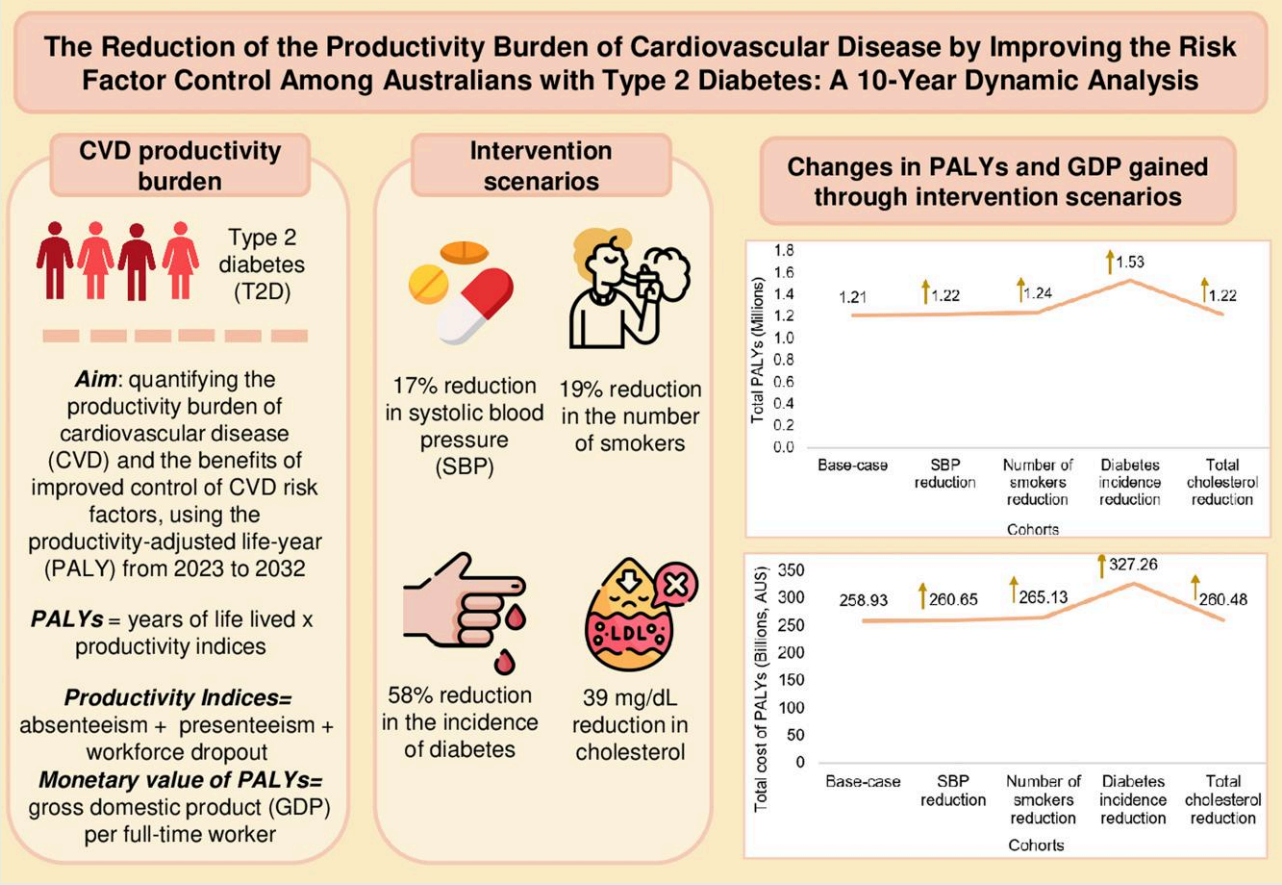
We also simulated hypothetical scenarios to explore the potential gains from reducing risk factors. We found that reductions in systolic blood pressure (SBP), smoking rates, total cholesterol, and the incidence of type 2 diabetes could lead to gains of 7,889, 28,971, 7,117, and 320 124 PALYs, respectively. These improvements would also result in economic gains of AU$1.72 (€1.05) billion, AU$6.21 (€3.79) billion, AU$1.55 billion (€947.33 million), and AU$68.34 (€41.69) billion, respectively.

Targeted strategies focusing on early lifestyle interventions to prevent CVD in individuals with type 2 diabetes can have a positive impact on both health outcomes and work productivity in Australia.

Graphical Abstract



The Reduction of the Productivity Burden of Cardiovascular Disease by Improving the Risk Factor Control Among Australians with Type 2 Diabetes: A 10-Year Dynamic Analysis.

Keywords Cardiovascular disease • Diabetes • Productivity • Economics • Health • Projection

Introduction

Diabetes prevalence is rising among younger adults, driven by increasing obesity rates, where the lifetime burden of diabetes is also greater due to the longer lifespans.[1] Type 2 diabetes (T2D) is an independent risk factor for several forms of cardiovascular disease (CVD), affecting 32.2% of the type 2 diabetic patients.[2,3]

Recently, there has been a growing interest in examining how health conditions affect work productivity at the population level.[4] Our group previously assessed the productivity burden attributable to diabetes, utilizing a novel measure known as the productivity-adjusted life-year (PALY).[4] PALYs have been developed to account for years of life lived adjusted for productivity loss attributed to diseases or complications.

Numerous studies on PALY and diabetes among working-age populations have shown varying results across different countries.[5–10] For instance, in Australia, diabetes is projected to reduce PALYs by 791 428 (11.1%), contributing to an AU$80 billion decline in gross domestic product (GDP).[5] However, data examining the impact of CVD as a complication of diabetes on work productivity are lacking. Moreover, as T2D progresses gradually, the benefits of enhancing risk factor control build up over decades.

In a study utilizing the Swedish National Diabetes Register,[11] authors analyzed data from 29 471 individuals with T2D who did not have CVD, each with at least five measurements of risk factors over three years. The

study assessed the incidence of myocardial infarction (MI), stroke, and all-cause mortality over an average follow-up of 4.8 years, revealing significant associations between the variability of haemoglobin A1C, body weight, systolic blood pressure (SBP), and total cholesterol with cardiovascular outcomes. Notably, individuals with high variability in both body weight and blood pressure exhibited the highest risk (hazard ratio (HR) = 1.81) compared to those with low variability. Similarly, a study conducted in the Netherlands[12] assessed 2011 individuals with CVD from the Utrecht Cardiovascular Cohort, who were re-evaluated after 10 years. Those maintaining a persistently healthy lifestyle had lower risks of cardiovascular mortality (HR = 0.57) and incident T2D (HR = 0.46) compared to those with a persistently unhealthy lifestyle. Also, people who improved their lifestyle also experienced reduced risks for cardiovascular mortality (HR = 0.46) and incident T2D (HR = 0.50).

Implementing strategies to improve risk factor control often requires substantial upfront investments. Therefore, evaluating the long-term value of improved risk factor control is crucial for decision-making, especially when healthcare resources are limited.

In the current study, we adapted a validated model published by our group,[13] designed to estimate the future burden of CVD among Australians with T2D using dynamic population modelling. Using this approach, we quantified the long-term nationwide productivity burden of CVD and the potential benefits of improved control of CVD risk factors in people with T2D. We focused on measuring the impact in terms of PALYs from 2023 to 2032.

Methods

Model structure

We adapted a previously validated model of CVD in T2D[13] to quantify the burden of CVD in terms of years of life lived and PALYs for Australians with T2D. Age- and sex-specific models were developed for Australians aged 40–69 years from 2023 to 2032, applying yearly cycles. The models were dynamic in that they accounted for people entering and leaving the simulation over the ten years (deaths, immigration and emigration, and incident T2D). The assumed retirement age in Australia was 69 years, as per Australian labor statistics.[14] Therefore, individuals enter the models at age 40 and exit at age 70, representing the working-age population. The starting age of 40 was chosen based on our previous model, which focused on capturing the CVD burden in individuals aged 40 to 89 with T2D (19). Additionally, this age range was identified as experiencing the most significant economic impact due to T2D. Data indicate that T2D affects 3.1% to 9.2% of people aged 40–59 years.[15]

As described in our previously published study,[14] we built the current model based on the published model from that work. In the present study, two-stage dynamic multistate Markov models were developed using Microsoft Excel to estimate the burden of CVD among Australians with T2D in terms of PALYs, utilizing yearly cycles. The models tracked individuals for a period of 10 years, following them until their death or until they reached 70 years of age within the simulation. The models accounted for both incident and recurrent non-fatal cardiovascular events (such as MI and stroke), as well as mortality from cardiovascular and non-cardiovascular causes among individuals with T2D, with and without established CVD.

Individuals aged 40–69 years with T2D and no prior CVD were assumed to enter the 'Alive with T2D without established CVD' health state. Within this state, individuals could experience non-fatal or fatal cardiovascular events, leading them to transition to the 'Alive with T2D with established CVD' or 'Dead' health state. The half-cycle corrections were applied in the models between years.

Based on our published model,[13] the base-case analysis was designed to quantify the burden of CVD in T2D in terms of PALYs lost using real-world estimates from the Australian National Health Survey (NHS) (2011/12).[16] A detailed description of the model was provided previously.[13] Briefly, the risk of incident CVD among individuals with T2D was calculated using the 2013 Pooled Cohort Equation-Atherosclerotic Cardiovascular Disease (PCE-ASCVD),[17] which estimates the 10-year absolute rate of incident CVD. The PCE-ASCVD equation incorporates risk factors (sex, age, smoking status, SBP, diabetes status, hypertension treatment status, total cholesterol, and high-density lipoprotein cholesterol levels (HDL)). We parameterized the model using risk estimates from the Australian NHS.[16] The rate of recurrent CVD events in individuals with T2D and established CVD was derived from the Reduction of Atherothrombosis for Continued Health (REACH) registry.[18]

Subsequently, we repeated the simulation under various hypothetical scenarios that reflected potential health and productivity benefits resulting from improved control of risk factors. Improvements in risk factor control in all scenarios were assumed to be permanent throughout the models' time horizons. Detailed descriptions of model inputs and data sources are provided in Supplementary material online, *Tables S1 to S7*.

Intervention scenarios of improved risk factors control (i.e. all effects of risk factor modifications applied in this study were performed via the PCE-ASCVD algorithm, except for the scenario involving the incidence of diabetes):

- Cohort 1 (scenario 1): Using the PCE-ASCVD algorithm, the model assumed a 17% reduction in SBP based on a meta-analysis of randomized clinical trials (RCTs) conducted by Aggarwal et al. in 2018.[19] The study demonstrated that intensive SBP-lowering significantly lowered the rate of CVD outcomes. The reduction in SBP was applied to individuals whose original levels were above the guideline-recommended threshold (>130/80 mmHg).[20] This simulated intervention effect is larger than that achieved through lifestyle interventions,[21] representing a realistic change that could be achieved across the treatment cascade. Acknowledging that the threshold for SBP can vary between countries and change over time, and driven by the guideline recommendation for the thresholds,[20] our models used the thresholds of SBP ≤130 mmHg. For example, if an individual's SBP level was initially 150 mmHg (>130 mmHg, guideline threshold), it was adjusted to 124.5 mmHg (i.e. 17% reduction). On the other hand, a person with an SBP of 129 mmHg (≤130 mmHg, guideline threshold) was assumed to be unaffected by the intervention. Further description of Aggarwal *et al.* in 2018 is provided in Supplementary material online, *Table S6*.
- Cohort 2 (scenario 2): Using the PCE-ASCVD algorithm, the model assumed a 19% reduction in the number of smokers. This reduction was based on findings from a retrospective analysis of prospectively collected data from 8770 individuals without CVD in the Framingham Heart Study.[22] The study highlighted that among heavy smokers, quitting smoking was associated with a significantly lower risk of CVD within 5 years compared to current smokers (see Supplementary material online, *Table S6*).
- Cohort 3 (scenario 3): The model assumed a 58% reduction in the incidence of T2D, based on an RCT conducted by Knowler *et al.* in 2002 in a cohort receiving a lifestyle modification program.[23] This large study was chosen because it was conducted among ethnically and culturally diverse populations. Furthermore, unlike a previous study that did not demonstrate the effectiveness of diabetes medications for prevention,[24] Knowler et al. reported that metformin was effective in preventing diabetes, although to a lesser extent than the lifestyle intervention. In the model, 58% of individuals who did not develop incident diabetes were replaced by healthy individuals. To account for the higher productivity observed in the healthy population, productivity indices were increased accordingly.[25,26] It is important to note that the incidence of T2D is not a parameter of the PCE-ASCVD algorithm, but it was added to each year in our dynamic model to account for new cases of diabetes[13] (see Supplementary material online, *Table S6*).
- Cohort 4 (scenario 4):

Using the PCE-ASCVD algorithm, the model assumed a 39 mg/dL reduction in total cholesterol, based on a meta-analysis that estimated the efficacy of statin therapies in 18 686 individuals with diabetes at high risk of vascular events.[27] The study included 14 RCTs by the Cholesterol Treatment

Trialists' (CTT) Collaborators over a follow-up period of 4.3 years. The study demonstrated that there was a significant 21% proportional reduction in major vascular events per mmol/L reduction in LDL cholesterol in people with diabetes. This study was selected as it was identified as the best meta-analysis of all available data, providing more reliable information about the effects of statins on vascular outcomes in people with diabetes (see Supplementary material online, *Table S6*).

Outcomes

The key outcomes were to (i) quantify the burden of CVD in people with T2D in terms of PALYs experienced and (ii) estimate the potential productivity benefits that could be achieved by improving CVD risk factor control over 10 years from 2023 to 2032. These outcomes reflected differences in the years of life lived, differences in PALYs gained through improved CVD risk factor control in hypothetical scenarios, and costs of PALYs in terms of GDP. All results were presented as discounted values, with an annual discount rate of 5%, following the recommendation of the Australian guidelines.[28]

Productivity indices

To calculate the productivity indices for all generated cohort groups, the total number of working days missed in a year, including absenteeism, presenteeism, and workforce dropouts, was determined as a percentage of the maximum working days in a year for individuals aged 40 to 69 years. PALYs were then estimated by multiplying the years of life lived by the productivity indices. The productivity index ranges from 0 (indicating no productivity) to 1 (indicating full productivity) and considers the reduced work productivity resulting from absenteeism, workforce dropouts, and presenteeism.

Absenteeism

The number of days absent from work per year due to MI and stroke in individuals with T2D was obtained from Sørensen J and Jon Ploug.[29] In the first year, people with T2D experienced 92 absent days from work due to MI, and in the subsequent years, they experienced 56 days. In relation to stroke, they experienced 125 absent days in the first year and 71 days in the following years. In comparison, individuals without MI or stroke had 38 absent days in both the first and subsequent years.

Presenteeism

The number of days of unproductive time at work in people with T2D with and without CVD was obtained from Goetzel et al.[25] Individuals with T2D and CVD experienced an average of 7 days of unproductive time at work per year. It is important to note that Goetzel et al. reported the unproductive time separately for people with CVD and T2D. Therefore, the average of both diseases was considered in this study.

Workforce dropout

The model assumed that 9% and 38% do not return to work after MI and stroke events, respectively. In addition, the mean time to return to work after an MI was 60.34 days[30] and 61 days after a stroke.[31] As data on early retirement for people with T2D were not available, it was assumed to be similar to the general Australian population.

In the current models, labor force participation was considered to adjust the total number of PALYs. This included employed and unemployed individuals, and those not in the labor force (see Supplementary material online, *Table S7*). The total number of working days per year for a full-time worker was assumed to be 240, considering that full-time workers typically work five days a week (40 h per week) and take four weeks of annual leave each year. Therefore, the productivity index was calculated by subtracting the days absent from work or unproductive time at work from the number of days worked in a year (i.e. 240 days), divided by the number of days worked in a year (i.e. 240 days). PALYs were calculated by multiplying the years of life lived by the productivity indices and then adjusted based on workforce participation in different age groups and sexes.

To determine the total economic value, the PALYs generated in each year of the models were multiplied by the GDP for a full-time worker for that particular year. To predict the future GDP per hour worked, we used trend data from the Australian Bureau of Statistics for GDP per hour worked from 1975 to 2018.[32] GDP per full-time worker was then calculated by multiplying GDP by the number of working hours in a year for a full-time worker (i.e. 40 h multiplied by 48 weeks).[33] Using labor force participation data and the mean hours worked by age and sex, we estimated the proportional number of equivalent full-time (EFT) workers in each age group and sex category, assuming that full-time workers work 40 h per week. The value of PALY ranged from AU$204 167 (€124 542) in 2023 to AU$224 892 (€137 184) in 2032.

Sensitivity analyses

Probabilistic sensitivity analyses (PSA) to further explore the uncertainty around base-case key model inputs were conducted. The PSA involved modifying the parameter values to the lower and upper bounds of their confidence intervals (CIs), using 10 000 iterations of a Monte Carlo simulation. For parameters where CIs were not available, we assumed a 10% standard error around the mean. We assigned uncertainty ranges to the base-case values of the proportions of CVD events for the T2D populations with and without prior CVD, the transition probabilities for recurrent events in T2D, and the productivity indices. The PSA was performed using the @Risk-7.5® software (Palisade Corporation, NY, US). The key input parameters and their respective probability distributions are detailed in Supplementary material online, *Table S8*. In addition, sensitivity analyses, in terms of scenario analyses, were conducted to explore the impact of key input data on years of life lived, PALYs, and associated costs. These analyses included using the upper bound estimate for absent days reported by Sørensen J and Jon Ploug,[29] assuming a constant GDP over time, reducing the annual discount rate to 3% applied to costs and outcomes as recommended by the World Health Organization,[34] and reducing the incidence of T2D by 29%.[35] The 29% reduction in T2D incidence was based on a meta-analysis of real-world diabetes prevention programs, which estimated the effect of a wide-scale lifestyle modification program on diabetes incidence in people with prediabetes or diabetes risk factors. The 29% of people who did not develop incident diabetes were replaced by healthy people, and consequently, higher productivity indices were considered.[25,26]

Model validation and calibration

The model was validated to ensure that assumptions and inputs were consistent with the current literature and that results were robust to variation in key parameters. The validity of the model was examined using the Assessment of the Validation Status of Health-Economic decision models (AdViSHE) and TECHnical VERification (TECH-VER) validation tools.[36,37] Independent checks were also performed in the Excel sheet to detect any modelling errors to emphasize the face validity of the modelling approach and data sources. We also calibrated the dynamic model using incidence rates of fatal and non-fatal cardiovascular events in the Australian population. Data on the incidence rates of non-fatal MI and non-fatal stroke in Australians with T2D were obtained from Morton et al.[38] Data on the incidence rates of CVD death for T2D were based on the 2021 Australian Bureau of Statistics.[39] Calibration ratios were then applied to the model.

Results

Years of life lived

In the base case, between 2023 and 2032, the projected total years of life lived in the population with T2D with first and recurrent CVD were 4 998 019 (95%CI (4 944 693–5 050 731). The predicted years of life

Table 1 Total years of life lived in an Australian cohort with type 2 diabetes with first and recurrent CVD and the impact of improved risk factor control (estimates for the total population)

Year	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	Sum (2023–32)
Base-case[a]	605 766	583 281	559 722	533 958	509 251	484 473	461 276	440 261	419 876	400 155	4 998 019
Cohort 1 (scenario 1)	605 766	584 033	561 109	535 778	511 464	486 881	465 980	446 709	425 554	405 254	5 028 528
Difference (cohorts base-case and 1)	—	751	1387	1820	2213	2408	4703	6448	5678	5099	30 508
Cohort 2 (scenario 2)	618 134	595 442	571 017	545 108	520 104	495 141	471 537	450 221	429 658	408 533	5 104 896
Difference (cohorts base-case and 2)	12 368	12 161	11 295	11 150	10 853	10 669	10 260	9960	9782	8378	106 877
Cohort 3 (scenario 3)	623 679	589 298	564 846	538 516	513 481	488 412	464 951	443 703	423 123	391 776	5 041 786
Difference (cohorts base-case and 3)	17 913	6017	5123	4558	4230	3940	3675	3442	3247	(8378)[b]	43 767
Cohort 4 (scenario 4)	606 121	584 578	562 609	539 250	516 534	494 086	472 625	452 111	432 039	412 523	5 072 475
Difference (cohorts base-case and 4)	355	1297	2887	5292	7282	9614	11 348	11 850	12 162	12 368	74 455

Cohort 1 (scenario 1): the model assumed a 17% reduction in systolic blood pressure (SBP).
Cohort 2 (scenario 2): the model assumed a 19% reduction in the number of smokers.
Cohort 3 (scenario 3): the model assumed a 58% reduction in the incidence of type 2 diabetes.
Cohort 4 (scenario 4): the model assumed a 39 mg/dL reduction in the total cholesterol.
[a]Base-case: original model with original estimates from the National Health Survey without any adjustment in risk factors.
[b]Numbers between brackets represent negative findings.

lived were higher in males (2 797 332) than in females (2 200 688). Within a 10-year time horizon, implementing a 17% reduction in SBP and a 19% reduction in number of smokers resulted in gains of 30 508 and 106 877 years of life lived, respectively. When considering a 58% reduction in the incidence of T2D, the model projected a gain of 43 767 years of life lived. Also, when considering a 39 mg/dL reduction in total cholesterol, the model predicted an additional year of life lived of 74 455. *Table 1* summarizes the total years of life lived over ten years in all cohort groups.

PALYs and GDP

In the base case, the estimated total PALYs lost were 1.21 million (95% CI (1.10–1.29 million), contributing to an AU$258.93 (€157.94) billion (95%CI (AU$258.73–261.69 (€157.83–159.63) billion) lost in the country's GDP. The estimates were also higher in males than females, with 797 768 PALYs vs. 414 073 PALYs. If there were a 17% reduction in SBP and a 19% reduction in smoking numbers, there would be gains of 7889 and 28 971 PALYs, respectively. These reductions would also result in economic gains of AU$1.72 (€1.05) billion and AU$6.21 (€3.79) billion, respectively. Additionally, reducing the incidence of T2D by 58% would project gains of 320 124 PALYs, accompanied by economic gains of AU$68.34 (€41.69) billion. Also, when considering a 39 mg/dL reduction in total cholesterol, the model predicted an additional PALYs of 7117 with additional economics of AU$1.55 billion (€947.33 million).

Tables 2 and *3* summarize the PALYs and the broader economic costs for the Australian population over the next decade in all cohort scenarios.

Granular results in people with first CVD, recurrent CVD, and total population (first and recurrent), stratified by sex, are provided in Supplementary material online, *Tables S9* to *S17*.

Sensitivity analysis

Detailed results of PSA are provided in *Table 4*.

Compared to the base-case, increasing the number of absent days in line with the upper bound value of absent days reported by Sørensen J and Jon Ploug (35) resulted in a loss of 786 322 PALYs and AU$168 billion in GDP (i.e. 65%). When no temporal growth in GDP was considered, there was a decrease of AU$25 (€15) billion in GDP compared to the base-case (i.e. 10%). Conversely, when the annual discount rate was reduced to 3%, there was an increase of AU$22 (€13) billion in GDP compared to the base case (i.e. 9%). Also, when assuming reducing incidence of T2D by 29%, there was an increase of 152 127 PALYs and AU$32 (€20) billion in GDP compared to the base-case (i.e. 11%). The results of the scenario analyses are summarized in *Table 5*.

Model validation and calibration

External validation suggests the model may overestimate the burden of CVD in T2D in Australia. The authors compared the model's findings to national results reported by the Australian Institute of Health and Welfare,[40] Morton *et al.*[38] and Marquina *et al.*[41] This comparison indicated the model overestimated non-fatal MI, non-fatal stroke, and CVD death in people with diabetes at risk and with CVD. The detailed results of calibration were previously published.[13] Validation of model checklists are presented in Supplementary material online, *Table S18*.

Discussion

To our knowledge, this is the first study to predict long-term productivity and economic consequences in terms of PALYs in people with CVD and T2D. The findings of our study highlight the impact on productivity attributable to T2D with first and recurrent CVD in Australia, as well as the potential gains attainable from improved control of risk

Table 2 Total productivity-adjusted life-years in an Australian cohort with type 2 diabetes with first and recurrent CVD and the impact of improved risk factor control (estimates for the total population)

Year	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	Sum (2023–32)
Base-case[a]	146 705	141 053	135 295	129 173	123 303	117 445	111 964	107 023	102 251	97 627	1 211 841
Cohort 1 (scenario 1)	146 746	141 276	135 748	129 789	124 049	118 254	113 100	108 409	103 530	98 830	1 219 731
Difference (cohorts base-case and 1)	41	222	453	616	745	809	1135	1386	1279	1204	7889
Cohort 2 (scenario 2)	149 678	144 013	138 199	132 154	126 291	120 420	114 875	109 870	105 050	100 263	1 240 812
Difference (cohorts base-case and 2)	2973	2960	2903	2980	2987	2975	2910	2847	2798	2636	28 971
Cohort 3 (scenario 3)	189 506	178 467	170 855	162 963	155 425	147 977	140 995	134 632	128 511	122 634	1 531 965
Difference (cohorts base-case and 3)	42 800	37 414	35 560	33 789	32 122	30 533	29 030	27 609	26 259	25 007	320 124
Cohort 4 (scenario 4)	146 762	141 155	135 543	129 692	124 023	118 437	113 134	108 168	103 357	98 687	1 218 958
Difference (cohorts base-case and 4)	57	102	248	518	719	992	1170	1145	1105	1061	7117

Cohort 1 (scenario 1): the model assumed a 17% reduction in systolic blood pressure (SBP).
Cohort 2 (scenario 2): the model assumed a 19% reduction in the number of smokers.
Cohort 3 (scenario 3): the model assumed a 58% reduction in the incidence of type 2 diabetes.
Cohort 4 (scenario 4): the model assumed a 39 mg/dL reduction in the total cholesterol.
[a]Base-case: original model with original estimates from the National Health Survey without any adjustment in risk factors.

factors. During a 10-year analysis among Australians aged 40 to 69 years, the projected total years of life lived in the population with T2D with first and recurrent CVD (i.e. the base-case) were 4 998 019. This resulted in 1.21 million PALYs lost, contributing to an AU$258.93 (€157.94) billion decline in the country's GDP. Our findings also revealed that if there were reductions in SBP, number of smokers, total cholesterol, and incidence of T2D, there would be gains of 7,889, 28,971, 7,117, and 320 124 PALYs, respectively. These improvements would also result in economic gains of AU$1.72 (€1.05) billion, AU$6.21 (€3.79) billion, AU$1.55 billion (€947.33 million), and AU$68.34 (€41.69) billion, respectively. These results highlight the need for increased primary preventive efforts at the population level.

While there are no directly comparable studies to ours, our findings align with several other studies conducted by our group assessing the impact of overall diabetes on productivity using the PALY, including Australia,[5,10] India,[8] Bangladesh,[6] China,[7] and South Africa,[9] noting the variations in the age structures of populations with CVD due to diabetes among countries.

In Australia, using a dynamic model, it was projected that preventing diabetes led to Australians achieving 87 million PALYs, amounting to AU$18.0 trillion to the country's GDP over the next decade.[10] In another study, it was projected that diabetes would reduce PALYs lived by working-age Australians by 791 428 (or 11.1%), contributing to an AU$80 billion decline in GDP.[5] However, neither study measured the productivity burden of CVD with T2D, or explored hypothetical scenarios focusing on the potential gains from improved control of CVD risk factors.

Compared to the published study by Magliano *et al.*, the current study has several key differences and advantages. First, the current study used a dynamic model that accounted for the future incidence of diabetes, migration, and mortality cases each year, reflecting a more realistic picture of the burden of CVD in T2D In contrast, the Magliano *et al.* study used a life-table model with fixed cohort populations. Second, the current study incorporated a 5% discount rate for long-term outcomes, while Magliano *et al.* did not report results using discounting rates as per Australian guidelines. This is important to ensure that models reflect the true value of future outcomes over time. The current model also accounted for differences in workforce dropout, which were not considered in the Magliano *et al.* study. Excluding early exit from the workforce may have led to an underestimation of the true burden of diabetes in the previous study. Furthermore, the current study used temporal GDP per EFT worker projections for Australia ranging from AU$204 167 (€124 542) in 2023 to AU$224 892 (€137 184) in 2032, whereas Magliano *et al.* used a constant GDP of AU$100,000, which may have also underestimated the true burden of diabetes. Additionally, the Magliano *et al.* study estimated the burden of diabetes using baseline data for 2011, while the current study projected the burden from 2023 to 2032. This difference in timeframe provides further insights into the evolving productivity burden of CVD among Australians with T2D.

Among the Chinese population (i.e. 20–49 years in females and 20–59 years in males), individuals with diabetes were predicted to experience a loss of 75.8 million PALYs, resulting in a US$2.6 trillion decline in GDP.[7] These results are not comparable to ours due to a non-dynamic closed cohort model that focuses on Australians aged 40 to 69 years only. However, like our current study, the absolute number of PALYs lost was higher in males, reflecting higher prevalence of diabetes and higher retirement age in China.

In a similar study, by Banker et al., the productivity of the Indian population, with diabetes, aged 20–59 years, was examined.[8] Having diabetes was projected to lead to a loss of 89 million PALYs, equivalent to US$2.6 trillion in lost GDP. Results are not comparable to ours given a broader retirement age range (working lifespan of 20–59 years) and an assumed constant GDP over time. In addition, like in the China study, the use of a non-dynamic model prevented the ability to account for variations in the population over time, including deaths, migration, and incident T2D.

Table 3 Total cost of productivity-adjusted life-years in (AUS$)[a] in an Australian cohort with type 2 diabetes with first and recurrent CVD and the impact of improved risk factor control (estimates for the total population)

Year	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	Sum (2023–32)
Base-case[b]	$29 952 353 104	$29 123 247 882	$28 245 929 938	$27 265 313 163	$26 310 245 100	$25 330 569 717	$24 406 388 142	$23 575 704 524	$22 760 027 210	$21 955 414 699	$258 925 193 480
Cohort 1 (scenario 1)	$29 960 660 331	$29 169 151 253	$28 340 502 963	$27 395 283 954	$26 469 234 222	$25 505 042 474	$24 653 861 617	$23 881 056 380	$23 044 624 045	$22 226 090 883	$260 645 508 121
Difference (cohorts base-case and 1)	$8 307 227	$45 903 370	$94 573 024	$129 970 791	$158 989 122	$174 472 757	$247 473 475	$305 351 856	$284 596 835	$270 676 185	$1 720 314 641
Cohort 2 (scenario 2)	$30 559 329 109	$29 734 370 285	$28 852 091 690	$27 894 387 011	$26 947 648 389	$25 972 309 829	$25 040 748 565	$24 202 865 665	$23 382 885 799	$22 548 317 682	$265 134 954 026
Difference (cohorts base-case and 2)	$606 976 005	$611 122 403	$606 161 752	$629 073 848	$637 403 289	$641 740 112	$634 360 423	$627 161 141	$622 858 589	$592 902 984	$6 209 760 546
Cohort 3 (scenario 3)	$38 690 794 160	$36 848 044 005	$35 669 906 161	$34 397 392 485	$33 164 273 562	$31 915 846 913	$30 734 536 122	$29 657 658 067	$28 605 073 262	$27 579 351 239	$327 262 875 975
Difference (cohorts base-case and 3)	$8 738 441 056	$7 724 796 122	$7 423 976 223	$7 132 079 322	$6 854 028 462	$6 585 277 196	$6 328 147 980	$6 081 953 543	$5 845 046 052	$5 623 936 541	$68 337 682 496
Cohort 4 (scenario 4)	$29 964 020 660	$29 144 338 947	$28 297 621 282	$27 374 705 488	$26 463 671 961	$25 544 567 449	$24 661 391 743	$23 827 881 554	$23 006 028 898	$22 193 968 187	$260 478 196 169
Difference (cohorts base-case and 4)	$11 667 556	$21 091 065	$51 691 344	$109 392 325	$153 426 861	$213 997 731	$255 003 601	$252 177 031	$246 001 688	$238 553 488	$1 553 002 690

Cohort 1 (scenario 1): the model assumed a 17% reduction in systolic blood pressure (SBP).
Cohort 2 (scenario 2): the model assumed a 19% reduction in the number of smokers.
Cohort 3 (scenario 3): the model assumed a 58% reduction in the incidence of type 2 diabetes.
Cohort 4 (scenario 4): the model assumed a 39 mg/dL reduction in the total cholesterol.
[a]The 2024AU$/€ exchange rate is AU$1 = €0.61.
[b]Base-case: original model with original estimates from the National Health Survey without any adjustment in risk factors.

Afroz et al.[6] for the Bangladeshi population of working age (20–59 years) with diabetes, reported in their study a loss of 9.2 million PALYs attributable to diabetes, corresponding to a total of US$97.4 billion in lost GDP. Again, these results are not comparable to ours due to the longer working lifespan and that the Afroz *et al.* model was non-dynamic and assumes that people with complications due to diabetes are as productive as those without diabetes.

From South Africa, Hellebo *et al.*[9] have recently estimated a 13 million lost PALYs with T2D. Here, similar to other studies,[5–8] the generalizability of results is limited by the use of a non-dynamic model and a retirement age range that is different.

Another study, from Germany, projected that by 2040, 5.5 million Germans with T2D will experience a loss of 15.4 million PALYs until the retirement age of 69.[42] This, however, also included the working-age population of 20 to 40 years, which was not accounted for in our model, and it did not incorporate the discounting of future outcomes.

Despite evidence indicating that females experienced a higher proportion of productivity losses due to labour force participation drop-outs (70.4% vs. 40.0%) and presenteeism (3.7% vs. 2.8%) compared with males,[43] our model shows that males experienced greater PALYs burden over their working lifetime compared to females (were 797 768 vs. 414 073). This difference may be attributed to the higher prevalence of CVD due to diabetes and the higher labour force participation with males in Australia, added to the dynamic nature of our model, which demonstrates a decrease in the size of the Australian population with T2D and CVD in females compared to males over time.

Clinicians have expressed some concerns about the performance of the 2013 PCE-ASCVD risk algorithm for the population with T2D with no prior CVD. This is because the algorithm was only validated in adults aged 40–79 years, and its calibration may be suboptimal for those aged 80 or older, potentially resulting in overestimation of risk in this group.[44] However, the 2013 PCE-ASCVD has been validated in Australians with T2D and demonstrated better performance compared to the 1991 Framingham, 2008 Framingham, and 2008 office-based Framingham risk models. It has been recommended for use in clinical practice to guide primary prevention strategies for ASCVD in this population.

The authors' own calibration results[13] further indicated the PCE-ASCVD performed well against Australian mortality and incidence data. The authors chose not to use the Fremantle diabetes-specific CVD risk equation, as it was only validated for 5-year risk prediction and was based on a regional Western Australian population. Additionally, the Fremantle equation did not include important risk factors such as smoking, status of hypertension treatment, and systolic blood pressure. In contrast, the PCE-ASCVD validation was based on the national, longitudinal AusDiab study population across several Australian states and territories, with 10-year follow-up. For the first stage microsimulation model, the authors also used data from the Australian NHS, which provided a nationally representative sample of 313 Australians with T2D aged 40–90 years. Note, while there is more recent 2022 NHS data,[45] it did not collect blood biomarkers, making it unsuitable for our study.

Using PALYs as a measure of productivity is a significant strength of our study. PALYs consider individual health conditions and the societal impact by linking health states to productivity levels. To reflect the economic cost associated with each PALY, we utilized country-specific GDP per EFT worker. GDP provides a comprehensive societal perspective and is widely used to assess a country's economic well-being from a human capital approach. Another strength of our study lies in the dynamic nature of our model, which allowed for a more realistic

Table 4 Results of probabilistic sensitivity analyses for the base-case model for the total population (type 2 diabetes with and without CVD populations over 10 years)

Outcome	Total, Mean (LL and UL of uncertainty range)
Years of life lived	4 997 829 (4 944 693–5 050 731)
Productivity-adjusted life-year	1 209 930 (1 102 266–1 289 943)
Cost of productivity-adjusted life-year (AU$)[a]	259 154 991 008 (258 729 946 010–261 689 490 592)

LL, lower limit; UL, upper limit.
[a]The 2024AU$/€ exchange rate is AU$1 = €0.61.

Table 5 Scenario analyses in total population over 10 years

	Years of life lived	Productivity-adjusted life-years	Cost of productivity-adjusted life-years (AU$)[a]
Base-case[b]			
Base-case	4 998 019	1 211 841	258 925 193 480
Using the upper bound estimate for absent days			
Base-case	4 998 019	425 519	90 917 528 000
Assuming a constant GDP over time			
Base-case	4 998 019	1 211 841	233 465 292 773
Reducing the annual discount rate to 3%			
Base-case	5 417 932	1 313 841	281 194 621 240
Reducing the incidence of T2D by 29%			
Base-case	4 966 454	1 363 968	$291 394 312 870

[a]The 2024AU$/€ exchange rate is AU$1 = €0.61.
[b]Base-case: original model with original estimates from the Australian National Health Survey without any adjustment in risk factors, GDP: gross domestic product T2D: type 2 diabetes.

projection of CVD in people with T2D. Furthermore, our study benefited from the robustness of the data sources used, which are Australian age- and sex-specific. Additionally, we parameterized the model using data from large RCTs and real-world population-based studies.

However, our study has several limitations that need to be acknowledged. The data sources used in our analysis were not specific to the Australian population. The reductions in SBP, number of smokers, total cholesterol, and incidence of T2D were based on evidence from international studies, as these were identified as the best available evidence for estimating the effect of interventions on diabetes and CVD events. This is due to the lack of high-quality Australian RCTs on these risk factors among people with T2D. Despite using the best available evidence, there is a need for future Australian-focused research to validate and build upon our estimates. This would help ensure the study results are more directly applicable to the Australian setting. The results of our study may be underestimated since the model only considered Australians aged 40 to 69 years with T2D. However, the model was adapted from a previously published model, which started at 40 to 89 years, assuming that at age 40, CVD risk increases. Also, the Australian NHS data we used only included individuals aged 40 and above, making it difficult to incorporate those aged 20 to 39 years. In addition, T2D and CVD are both relatively uncommon in people under the age of 40. As a result, the overall impact or burden of these conditions within the younger adult population is likely to be minimal.[46] Also, the models assumed and simulated sustained improvements in risk factor control throughout the model time horizon. This assumption may oversimplify the reality, as sustained improvements may be unrealistic for some individuals due to factors such as genetic predisposition and environmental factors. Another limitation is that we did not stratify our cohorts based on level of education and income level due to the small population size included in the microsimulation phase of the published model.[13] Moreover, exercise levels are not incorporated as a part of the PCE equation. Additionally, data in relation to these factors were not available from the NHS. However, our previous work has shown that CVD is expected to have the greatest impact on individuals in the lowest socioeconomic group in Australia.[47] Also, while lowering body mass index may reduce CVD risk through improved glucose control, we did not have access to data on overweight status and its management from the NHS dataset used in our analysis. As such, we were unable to incorporate the potential impact of overweight management on CVD outcomes in our current model. In addition, the mean population levels of SBP, HDL-cholesterol, and smoking status, obtained from the NHS, may have changed since 2012. Another limitation is that the model did not account for potential adverse outcomes. Intensive reduction in SBP, for example, may lead to adverse complications such as hypotension. However, we assumed that the proportion of individuals experiencing such complications would be low and that this would only marginally affect our findings. Furthermore, the PALY metric, and the resulting cost calculations, can be sensitive to the method used. Indeed, there is no single universally accepted valuation method for estimating productivity, and different approaches may yield different PALY values.[48] Our model utilized the human capital approach, which estimates the cost of PALYs based on GDP per full-time worker. This approach is relatively straightforward given the availability of GDP and workforce participation data, and it is a comprehensive method that captures the overall economic performance of a country. Moreover, it is a well-established and standardized method across countries, allowing for international comparisons, and many decision-makers are familiar with this approach. However, it has its own limitations as GDP is generated through various means beyond just human labour. There are alternative methods, such as using salary estimates to reflect both personal income and tax revenue, which could also be considered. We recommend reporting PALYs as absolute values, rather than in ratio calculations, to avoid the potential for double counting of costs.[4] Additionally, other productivity estimation approaches, such as the friction cost and the Washington Panel methods, have their own limitations. The friction cost approach only considers productivity losses during the 'friction period', which is the time it takes to replace a worker who is absent or unable to work due to illness. This method does not account for the long-term productivity losses that may occur beyond the friction period. As a result, the friction cost approach may lead to an underestimation of the true productivity costs associated with disease. The Washington Panel approach incorporates productivity losses into quality of life measures, rather than as a separate cost.

Despite evidence showing that remission from T2D is possible with specific interventions, our model assumed that remission was not possible.[49] Also, T2D results in multiple complications, not only CVD; thus, our productivity burden will be an underestimate relative to the total burden of diabetes. However, we have focused on CVD as a complication of T2D, which is a major outcome of T2D. Furthermore, our study did not modify HDL levels. The model also did not consider the resources and costs required to achieve the interventional improvements, as this was beyond the scope of the study's objective. It is crucial to acknowledge that real-world risk factor improvement strategies come with associated costs. Moreover, absenteeism and presenteeism data were obtained from historical studies conducted in the US and Europe, which may not accurately reflect current situation in Australia. Further studies are needed to refine our model estimates. Also, our model assumed no change in productivity over the time horizon. However, projecting changes in productivity over the next ten years is challenging due to the lack of age- and sex-specific data and information related to job types. The durations of T2D and CVD, undiagnosed diabetes, and ethnicity were not accounted for in our model. This was because the data we obtained from the NHS did not include information on these factors, despite their known influence on productivity in terms of presenteeism, absenteeism, early retirement, premature death, and reduced workforce participation.[50,51] Finally, our projections of GDP were based solely on productivity-related factors such as absenteeism, presenteeism, and workforce dropout. They did not consider the direct medical costs of managing CVD, which are significant as shown in our previous publication.[13]

The impact of CVD on productivity in T2D patients has global and Australian implications. CVD significantly affects morbidity and mortality among working-age Australians, where the long-term impact of reduced income persists due to ineffective prevention strategies. Our assessment highlights the impact of disease on productivity and underscores the importance of interventions for prevention, treatment, and control of CVD in T2D.

In conclusion, our results suggest that CVD in people with T2D could have a significant impact on PALYs in the Australian population over the next 10 years. However, improved control of risk factors has the potential to mitigate the impact of this condition, not only on the productivity of affected individuals, but also on the overall Australian economy.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

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Author contributions

D.A. was involved in the study design, data acquisition, development of the model, data analysis and interpretation, and wrote the first draft of the manuscript. D.A.-B. contributed to analysis and interpretation of data. C.M., J.M., M.L., E.Z., S.T., and D.L. contributed to interpretation of data. ZA led the study conception and design and contributed to data analysis and interpretation. All authors contributed to revising and approving the manuscript. D.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Data availability

All data analysed during this work are included in this published article and its supplementary files, and in the relevant references. Any additional data are available on request from authors.

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