PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The costs of diabetes amongst Australians aged 45-64 years from 2015 to 2030: projections of lost Productive Life Years (PLYs), lost personal income, lost taxation revenue, extra welfare payments and lost Gross Domestic Product from Health&WealthMOD2030
AUTHORS	Schofield, Deborah; Shrestha, Rupendra; Cunich, Michelle; Passey, Megan; Veerman, Lennert; Tanton, Robert; Kelly, Simon

VERSION 1 - REVIEW

REVIEWER	David Cavan International Diabetes Federation Belgium
REVIEW RETURNED	19-Jul-2016

GENERAL COMMENTS	General comment This paper provides an innovative approach to estimate the economic burden of diabetes. The methodology is sound, and results are presented clearly. In the introduction section, some of the data sources mentioned are not the most recent estimates on the topic. Elsewhere, some of the assumptions made need to be justified. Specific comments • Page 6, line 7 - More recently the International Diabetes Federation estimates there were 415 million people with diabetes in 2015. http://www.diabetesatlas.org • Page 6, line 11 – “and complications (such as stroke, blindness, heart attack, kidney failure, amputation, and poor psychological wellbeing” I would rewrite these lines as “and complications which can ultimately lead to stroke, blindness, heart attack, kidney failure, lower limb amputation, and poor psychological wellbeing” • Page 6, line 25/26 - “The Global Burden of Disease Study 2010 reports that there were 1.3 million deaths due to diabetes worldwide in 2010” - More recently the International Diabetes Federation estimates there were 5 million deaths associated with diabetes in 2015. http://www.diabetesatlas.org • Page 9, line 28 – “the chronic conditions trends were for the period from 2003 to 2023, with prevalence rates assumed to stabilise

	afterwards." – what is the rationale for the assumption? • Page 11 line 5 – "One of the options was 'own ill-health or disability'. All respondents were asked whether they have a main long-term health condition" – Did the authors consider to ask about those not working because of the need to provide informal care to a person with diabetes or another long term condition? If not this should be mentioned in the discussion on limitations. • Page 13 line 9-10 - "are employed part-time with diabetes; 1,464,800 (20.54%)" – shouldn't it be full-time? • Page 13 Line 43-44 - "This increase was largely due to the real increase in wages over the projection period" – how is this statement justified? • Page 14 line 33-39 – add reference. ? • Page 16 line 4-5 – prevention of diabetes, could the authors please further develop this idea by explaining what type of prevention they have in mind, and what could be done in terms of prevention efforts to achieve the mentioned goals?

REVIEWER	Mark Danese Outcomes Insights, Inc.
REVIEW RETURNED	02-Oct-2016

GENERAL COMMENTS	This is a study estimating the economic impact of diabetes on economic outcomes in Australia, including labor force participation, lost wages and taxes, and the GDP. It is a very detailed study, and the authors are clear about the data sources used. The major limitation to this paper is that it is unclear whether it is a simulation model or an analysis of economic data. The design states that it is simulation model, but the STROBE statement is for an observational study. There is no figure to show how the data sources are combined and how data flows through the model. I realize that this model has been published before, but something in supplementary materials, or even just for reviewers would be immensely helpful. The authors claim that they are presenting 95% confidence intervals. However, it also appears as if they are combining data across different surveys in the context of their model. If so, they are simply propagating uncertainty, and the intervals are not true 95% confidence intervals. They are uncertainty intervals. The authors are not clear about their methods, so it is hard for readers/reviewers to evaluate this point properly. The introduction is very long. Much of the introduction could be moved to the discussion. I think it would be more appropriate to comment on the Australian results and how they compare to those of other countries in the discussion. It would be helpful to use figures to display the data. Table 3 is a

	good example, but even some of the data from Table 1 would be better presented graphically. Table 1 is a very dense table and readers can't see any trends over time.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: David Cavan
Institution and Country: International Diabetes Federation, Belgium Please state any competing interests or state 'None declared': none declared

Please leave your comments for the authors below General comment This paper provides an innovative approach to estimate the economic burden of diabetes. The methodology is sound, and results are presented clearly. In the introduction section, some of the data sources mentioned are not the most recent estimates on the topic. Elsewhere, some of the assumptions made need to be justified.

Authors' response:
We have addressed the concerns of Reviewer 1 with regard to updating relevant estimates for the topic e.g. updating the estimated prevalence of diabetes in the world using the International Diabetes Federation (2015) (see opening paragraph on page 6). We have also provided a further rationale for the assumptions e.g. revisions in Methods section (page 9).

Specific comments

• Page 6, line 7 - More recently the International Diabetes Federation estimates there were 415 million people with diabetes in 2015. http://www.diabetesatlas.org

Authors' response: We have updated the estimates as suggested.
• Page 6, line 11 – "and complications (such as stroke, blindness, heart attack, kidney failure, amputation, and poor psychological wellbeing"

I would rewrite these lines as

"and complications which can ultimately lead to stroke, blindness, heart attack, kidney failure, lower limb amputation, and poor psychological wellbeing"

Authors' response:
We made adjustments to the text as follows:

"The disability burden of diabetes is associated with a range of symptoms (such as fatigue, increased thirst, frequent urination, blurred vision) and complications which can eventually lead to stroke, blindness, heart attack, kidney failure, amputation, and poor psychological well-being – all of which can result in serious impairment, activity limitations and participation restriction." (p. 6)

• Page 6, line 25/26 - "The Global Burden of Disease Study 2010 reports that there were 1.3 million deaths due to diabetes worldwide in 2010" - More recently the International Diabetes Federation estimates there were 5 million deaths associated with diabetes in 2015. http://www.diabetesatlas.org

Authors' response: We have updated the estimates as suggested. The text reads as follows:

"Diabetes is a leading cause of deaths each year, with the International Diabetes Federation (2015)

reporting that there were 5 million deaths from diabetes worldwide in 2015.[1]"

• Page 9, line 28 – "the chronic conditions trends were for the period from 2003 to 2023, with prevalence rates assumed to stabilise afterwards." – what is the rationale for the assumption?

Authors' response:
The trend estimates were based on the 2003 Australian Burden of Disease study. In that study and later related work, it was assumed reasonable to apply the trends in the short term, but also recognized that extrapolation of linear trends into the indefinite future would lead to unlikely low and high rates for some diseases. The further into the future, the greater the uncertainty. The decision to apply the trend for 20 years is arbitrary (as data on future rates are not available), but was deemed reasonable in view of the stability in the trend prior to 2003.

We have made it clearer in the revised manuscript that the assumption about chronic disease trends is from the 2003 Australian Burden of Disease and Injury Study (page 9):

"For trend sin chronic conditions, we applied the age and sex specific trends in chronic conditions estimated in the 2003 Australian Burden of Disease and Injury Study,[22] which estimated trends for the period from 2003 to 2023 and assumed that prevalence rates would stabilise afterwards."

• Page 11 line 5 – "One of the options was 'own ill-health or disability'. All respondents were asked whether they have a main long-term health condition" – Did the authors consider to ask about those not working because of the need to provide informal care to a person with diabetes or another long term condition? If not this should be mentioned in the discussion on limitations.

Authors' response:
The focus of this study is on the economic impacts for people with diabetes such as their labour force participation and income; and how the lost productivity of those with the disease translates into costs to government in the way of lost income tax revenue, extra welfare payments and lost GDP.
We did not seek to measure and quantify the additional indirect costs (such as carer costs) in this study; however, we have clarified this in the Discussion and noted some of our previous work on the lost labour force participation of informal carers due to caring for someone with a chronic condition (including diabetes) which suggests that the total indirect costs of diabetes are even larger. See text below (page 15):

"The focus of this study was on the economic impacts of diabetes on individuals (such as lost labour force participation and lost income) and how their lost productivity translates into costs to government (lost income tax revenue, extra welfare payments) and society (lost GDP). Whilst quantifying these indirect costs addresses some of the research gap, there are other costs that could also be considered such as informal carer costs. We did not seek to measure these additional costs in the present study; however, we note that our previous work on the lost labour force participation of people caring for someone with a chronic condition in Australia showed that 60% of primary carers caring for someone with endocrine/nutritional and metabolic disorders (i.e. thyroid, diabetes and high blood pressure) were not in the labour force, which placed this disease group as the fifth top work-limiting conditions for caregivers.[38] Thus the indirect costs of diabetes are likely to be even larger after taking more of these type of costs into account."

Reference 38:
Schofield D, Cunich M, Shrestha R, Passey M, L V: The impact of chronic conditions of care recipients on the labour force participation of informal carers in Australia: which conditions are associated with higher rates of non-participation in the labour force? BMC Public Health 2014, 14(561).

• Page 13 line 9-10 - “are employed part-time with diabetes; 1,464,800 (20.54%)” – shouldn’t it be full-time?
Authors’ response: Yes – corrected.

• Page 13 Line 43-44 - “This increase was largely due to the real increase in wages over the projection period” – how is this statement justified?
Authors’ response:
We have added the basis of projected growth in wages (and no project growth in welfare payments for those out of the labour force due to diabetes) into the paper on page 13:
“This increase was largely due to projected real growth in wages over the period, whilst no projected real growth in welfare payments for those not in the labour force due to diabetes. Historically earnings in Australia grow at a rate that is one per cent above inflation.[28, 29]”

• Page 14 line 33-39 – add reference. ?
Authors’ response: Yes – added reference 10: Australian Institute of Health and Welfare. Diabetes expenditure in Australia 2008-09, Cat. no. CVD 62. Canberra: AIHW, 2013.

• Page 16 line 4-5 – prevention of diabetes, could the authors please further develop this idea by explaining what type of prevention they have in mind, and what could be done in terms of prevention efforts to achieve the mentioned goals?

Authors’ response:
The type of prevention of diabetes that is assessed in the referenced studies (references 39-41) is early pharmacological (metformin) and lifestyle interventions to prevent type 2 diabetes in adults with impaired glucose tolerance, some of whom were part of a screening trial (reference 41). We have made this clearer in the text as follows (page 16):

“Several randomised controlled trials have demonstrated that lifestyle and pharmacological (metformin) interventions can prevent or delay type 2 diabetes in high-risk individuals,[39-41]…”

In terms of prevention of diabetes to improve labour force participation, Passey et al (2012) (reference 42) built upon the findings of Bertram et al. (2010) to estimate the impact on labour force participation and personal income of a diabetes prevention intervention using screening and treatment (metformin or a lifestyle intervention targeting diet and exercise) in pre-diabetic Australians aged 45-64 years. We have elaborated on this point in the Discussion below, making the linkages clearer too:

“Several randomised controlled trials have demonstrated that lifestyle and pharmacological (metformin) interventions are effective in preventing or delaying type 2 diabetes in high-risk individuals (i.e. people with impaired fasting glucose or impaired glucose tolerance).[39-41] Bertram et al (2010) assessed both the health effects and direct (medical) costs of a number of interventions to prevent diabetes. The authors concluded that screening to identify people with pre-diabetes, followed with treatment using metformin or diet and exercise for those at risk were the most cost-effective interventions in preventing or delaying the onset of the disease.[42] A recent Australian economic study has shown that diabetes prevention interventions using screening and treatment (metformin or a lifestyle intervention targeting diet and exercise) in pre-diabetic adults (aged 45-64 years) could increase labour force participation and reduce income losses.[43]”

Reviewer: 2
Reviewer Name: Mark Danese

Institution and Country: Outcomes Insights, Inc.
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below This is a study estimating the economic impact of diabetes on economic outcomes in Australia, including labor force participation, lost wages and taxes, and the GDP. It is a very detailed study, and the authors are clear about the data sources used.

The major limitation to this paper is that it is unclear whether it is a simulation model or an analysis of economic data. The design states that it is simulation model, but the STROBE statement is for an observational study. There is no figure to show how the data sources are combined and how data flows through the model. I realize that this model has been published before, but something in supplementary materials, or even just for reviewers would be immensely helpful.

Authors' response:
The study is based on cross-sectional data from the nationally representative Surveys of Disability, Ageing and Carers 2003 and 2009 conducted by the Australian Bureau of Statistics; output data from two established microsimulation models (STINMOD and APPSIM), Treasury's population and labour force projections, and chronic disease trends data for Australia. Using these data, the study was a simulation of how the number of people aged 45-64 years with diabetes increases over time (based on population growth, disease trend data) and sought to quantify the economic losses due to diabetes from the individual's perspective (lost labour force participation, lost income), and the governmental perspective (lost income tax, extra welfare payments, lost GDP). This required the development of Health&WealthMOD2030 (the model), which simulated cross-sectional snapshots of the health, labour force participation and economic outcomes of older workers in Australia at five-year time points from 2015 to 2030.

The STROBE available checklists do not have a specific statement for simulation studies. The "STROBE Statement checklist for cohort, case-control, and cross-sectional studies (combined)" with the title listed for "observational studies" (see http://www.strobe-statement.org/?id=available-checklists) was deemed to be the most appropriate from the STROBE available statements, given the nature of the data incorporated and analysed in our microsimulation model, Health&WealthMOD2030.The current study has analysed the simulated cross-sectional data at every five years from 2015 to 2030.

We have made the design of the simulation study clearer in the revised abstract (page 4):

"Design: A simulation study of how the number of people aged 45-64 years with diabetes increases over time (based on population growth and disease trend data) and the economic losses incurred by individuals and the government. Cross-sectional outputs of a microsimulation model (Health&WealthMOD2030) which used the Australian Bureau of Statistics' Survey of Disability, Ageing and Carers 2003 and 2009 as a base population and integrated outputs from two microsimulation models (STINMOD and APPSIM), Treasury's population and labour force projections, and chronic disease trends data."

We have included a flow diagram (Figure 1 below) showing how the data sources are combined and how data flows through the model.

See page 9 for reference to Figure 1: "How the data sources were combined and how data flows through the microsimulation model are illustrated in Figure 1."

The authors claim that they are presenting 95% confidence intervals. However, it also appears as if they are combining data across different surveys in the context of their model. If so, they are simply

propagating uncertainty, and the intervals are not true 95% confidence intervals. They are uncertainty intervals. The authors are not clear about their methods, so it is hard for readers/reviewers to evaluate this point properly.

Authors' response:
We have changed this in the paper so that we refer to 'uncertainty intervals (UIs)' now.

The introduction is very long. Much of the introduction could be moved to the discussion. I think it would be more appropriate to comment on the Australian results and how they compare to those of other countries in the discussion.

Authors' response:
The current version of the Introduction describes the rationale for the study, including the specific research questions that inspired the work. We have established how the disease burden (globally) is growing over time and the substantial and growing direct costs of the disease for Australia and elsewhere to then "set the scene" for why the indirect costs through lost productive life years due to diabetes were essential to quantify and then value using relevant measurements such as lost income for individuals, lost income taxation and extra welfare payments for the government, and lost GDP (which are also measurements translatable to policy). However, we have moved some of the text from the Introduction to the Discussion and doing so has enhanced the paper. The new paragraphs, which are better fits in the Discussion, are (page 15):

"With the health burden of the condition being so large, the total cost of diabetes (direct and indirect costs) for national governments is correspondingly significant and thus an issue requiring urgent policy attention.[3, 14] Consequently, several governments (such as The Fit for Work Europe Coalition) have put forward the case for counting labour productivity as a relevant outcome measure in health investment decisions, especially decisions involving patients with long-term health conditions.[37]

The ageing of the global population has also highlighted the need to focus on the retention older workers.[38] In Australia, 4.15% of people aged 45-64 years who have diabetes are not in the labour force, representing a pool of people who might have worked had they not had this condition.[39] Australia, like most other developed countries, will need to maximise the labour force participation of its older workers in order to have sufficient taxation revenue from which to fund the healthcare and services used by the ageing population.[40]"

It would be helpful to use figures to display the data. Table 3 is a good example, but even some of the data from Table 1 would be better presented graphically. Table 1 is a very dense table and readers can't see any trends over time.

Authors' response:
The information in Table 3 has been converted to three separate figures (i.e. Figures 2-4). And all references to these data have been appropriately adjusted in the text e.g. page 14; and the notes that were under old Table 3 are now under new Table 3 (i.e. definition of "missing or lost workers" and the estimated number of missing workers due to diabetes in each year).

VERSION 2 – REVIEW

REVIEWER	David Cavan International Diabetes Federation, Brussels, Belgium
REVIEW RETURNED	10-Nov-2016

GENERAL COMMENTS	I am happy with the revisions and recommend publication

REVIEWER	Mark Danese Outcomes Insights, Inc, United States
REVIEW RETURNED	13-Nov-2016

GENERAL COMMENTS	The revised manuscript has been revised appropriately. My only comment is that there is a typo on Figure 4 -- "income" is spelled "incoem".