PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The future burden of obesity-related diseases in the 53 WHO European Region countries and the impact of effective interventions: A modelling study
AUTHORS	Webber, Laura; Divajeva, Diana; Marsh, Tim; McPherson, Klim; Brown, Martin; Galea, Gauden; Breda, Joao

VERSION 1 – REVIEW

REVIEWER	Justin Trogdon Associate Professor Health Policy and Management Gillings School of Global Public Health University of North Carolina at Chapel Hill United States
REVIEW RETURNED	27-Feb-2014

GENERAL COMMENTS	This paper extrapolates obesity trends for WHO European countries and explores the implications for obesity-attributable chronic disease prevalence in Europe. The methods are based on an earlier paper for the UK with this study extending the approach to other European countries. The results indicate continued increases in obesity rates and associated chronic diseases, with potential for large public health gains if interventions and policies can be developed to slow the growth in obesity. Major Comments Despite a very thorough and extensive attempt to extrapolate obesity and chronic disease trends, I am not convinced that the study contributes much to the policy debate. We already know that obesity trends are increasing (although slowing in the U.S.) and that this will increase rates of associated diseases like diabetes. For example, this analysis was not needed to write the concluding paragraph of the paper. While the study provides more precise numbers for the magnitude of the increase, are those numbers necessary to motivate policymakers to address obesity in these countries? The authors must make the case that having more precise numbers for the magnitude of the increase is pivotal in promoting policies and interventions. Even then, the study does not provide any evidence for specific policies or interventions. The state of the art right now would not provide anything close to a 1% or 5% decrease in population obesity. From a methodological standpoint, I wonder if the study is overly

	ambitious given the state of the data. For example, nearly 1/3 of the countries only had BMI data for 1 or 2 time periods (I'm not sure how trends were determined for countries with 1 BMI data point). A number of countries required proxies for disease rates. The authors should summarize in the main text how many of the countries required a proxy. Finally, the relative risk of disease from obesity was assumed to be constant across ages and countries. If the main contribution of the paper is more precise numbers for the increase in obesity and comorbidities, it severely limits the usefulness of the results if a large proportion (33%?) of the countries are based on assumed trends or proxy data. I also had several questions regarding the model. Based on the first part of Appendix 2, it appears the authors computed BMI distributions for most (all?) countries using data on mean BMI. How do the actual BMI distributions look for countries with good, national surveys? Were they generally lognormal as assumed? For countries where the actual BMI distribution can be measured, do you use the actual data or the lognormal assumptions described in Appendix 2? Are the extrapolations of BMI growth based on estimations using actual data on BMI distributions or modeled distributions as described on pp. 30-38? I assume these are done separately by country? Were the decreases in obesity applied to the obese equally? What if the heaviest (i.e., obese 3) were the target of the interventions? The authors are commended for compiling the mathematical assumptions in the Appendices. However, the reader needs a roadmap to explain the goals of the assumptions and major steps of the modeling process. For example, what is the goal of the first part of the "Sample sizes, probabilities and variances" section (p. 31)? Minor Comments p. 3, line 30: There is no mention of cancer results in the abstract. p. 4, line 9: Strengths and Limitations mentions forecasts of healthcare costs and cost-effectiveness, but they are not reported in the abstract or the paper. Please remove the mention of costs and cost-effectiveness from the Strengths and Limitations. p. 4, line 24: Define NCD at first use in the beginning of the Background section. p. 5, line 55: Reference to WHO database is incomplete. p. 6, line 21: Can the authors provide any intuition for how the conversion from prevalence to incidence was done in DISMOD II? p. 6, line 25: Should "rate" be "rare"? p. 6, line 34: How were the diabetes rates adjusted for different population BMI-distributions?

	p. 10, line 8: Add citation for under-reporting of weight in surveys or interviews. p. 30, line 22: Define HSE. p. 31, line 18: Is there a citation to support the approximation of the Beta distribution with a Normal distribution? p. 34, line 21: What does “should be recorded” mean? How is this statistic used in the analysis/model? p. 39, line 56: Drop last period on the page, after the colon. p. 40, line 9: Are “b” and “b’” supposed to be betas? p. 40, line 21: Please fix the reference called out by the “Error!” message.

REVIEWER	Timothy Dall IHS Global Inc., USA
REVIEW RETURNED	03-Mar-2014

GENERAL COMMENTS	This study represents an ambitious effort to quantify the future burden of obesity-related diseases in 53 European countries. The authors attempt to apply a standardized methodology to each country, while taking into account differences across countries in data availability and definitions/metrics used to quantify population characteristics and disease prevalence or incidence. Study findings provide valuable information for comparing outcomes across countries—but more importantly can be used to inform national and international initiatives to reduce disease burden. The authors provide an appendix with a thorough discussion of data sources, methods, and assumptions. The manuscript and accompanying appendix shows that the authors invested substantial time and thought into their analysis. I find no major problems with the study methods and manuscript write-up. The following are minor suggestions, and I leave it to the authors’ discretion to make any revisions accordingly. 1. The authors might consider a simple diagram that shows how their model works. To understand the model one needs to wade through large amounts of text and mathematical equations. 2. Figures 2 and 4 contain multiple diseases for each country, and are very difficult to read. Part of the difficulty reading these charts is that disease prevalence and incidence percentages differ widely by disease type, but are all put on the same scale. The authors might consider separate charts for each disease. 3. Appendix, Page 40, line 22. There is an “Error! Reference source not found” message in the text. 4. Page 60, in the BMI chart for Monaco the numbers appear to be truncated for females. The same applies to San Marino on page 72.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name Justin Trogdon
Institution and Country Associate Professor
Health Policy and Management
Gillings School of Global Public Health University of North Carolina at Chapel Hill United States
Please state any competing interests or state 'None declared': None declared.

This paper extrapolates obesity trends for WHO European countries and explores the implications for obesity-attributable chronic disease prevalence in Europe. The methods are based on an earlier paper for the UK with this study extending the approach to other European countries. The results indicate continued increases in obesity rates and associated chronic diseases, with potential for large public health gains if interventions and policies can be developed to slow the growth in obesity.

Major Comments

Despite a very thorough and extensive attempt to extrapolate obesity and chronic disease trends, I am not convinced that the study contributes much to the policy debate. We already know that obesity trends are increasing (although slowing in the U.S.) and that this will increase rates of associated diseases like diabetes. For example, this analysis was not needed to write the concluding paragraph of the paper.

Many thanks for this comment. We have altered the final paragraph so that it connects directly with the results of the study:

'This study provides a picture of the future with projections, and observes a worsening situation with increasing incidence of obesity-related disease. As a result, these findings call for governments to plan ahead and initiate change that effectively reduces key risk factors like obesity through preventative measures such as food tax, industry pledges and reduced junk food marketing'.

While the study provides more precise numbers for the magnitude of the increase, are those numbers necessary to motivate policymakers to address obesity in these countries? The authors must make the case that having more precise numbers for the magnitude of the increase is pivotal in promoting policies and interventions. Even then, the study does not provide any evidence for specific policies or interventions. The state of the art right now would not provide anything close to a 1% or 5% decrease in population obesity.

Thank you for this useful comment. To our knowledge this is the first study to provide future projections of obesity-related disease using all of the available data in each WHO-Euro country. Our dynamic microsimulation takes account of past and current trends and projects forward providing governments with evidence of the extent to which prevalence of disease will change, not just that it will. It is for governments to then use these projected figures to implement policies that are effective. Our previous work has tested the impact of real interventions (Hollingworth et al., 2012; NICE, 2013), however it was beyond the scope of this study to include real intervention data for each country. Should a country want this then we can easily update the simulation. We have included this in the limitations of the study:

'This study tested hypothetical, and largely aspirational scenarios. However, it acts to demonstrate the value of modelling to quantify the estimated future health burden of risk factors. If data are available the model can test the long term effectiveness of real policy interventions and future work aims to do this (econdaproject.eu).' on page 13, lines 20-23.

From a methodological standpoint, I wonder if the study is overly ambitious given the state of the data. For example, nearly 1/3 of the countries only had BMI data for 1 or 2 time periods (I'm not sure how trends were determined for countries with 1 BMI data point). A number of countries required proxies for disease rates. The authors should summarize in the main text how many of the countries required a proxy. Finally, the relative risk of disease from obesity was assumed to be constant across ages and countries. If the main contribution of the paper is more precise numbers for the increase in obesity and comorbidities, it severely limits the usefulness of the results if a large proportion (33%?) of the countries are based on assumed trends or proxy data.

Thank you for this comment. Appendix 2b) of the supplementary information now states how BMI was calculated from one data point:
'Bosnia and Herzegovina, Montenegro and Uzbekistan had only one BMI data point. For these countries 2008 estimates were used based on an analysis by Finucane and colleagues (The Lancet, 2011, 377, p557 – 567). This extrapolates from their estimated mean. The BMI-distribution is assumed to have the form [p,(1-p)/2,(1-p/2)] where p is the prevalence of normal weight, p is then determined from the known mean'.
We agree that a number of countries required proxy data of some sort, mostly survival data. However we believe this is still a useful exercise to highlight firstly where more data are needed, secondly as a demonstration of the utility of the model, and thirdly that we have a model for each of these countries that can easily be adapted when new data become available. Lines 21-22, p8 now state that 'Only Belarus, Denmark, Finland, Ireland, Norway, Russian Federation and the UK had full sets of disease data. Furthermore, many countries required a proxy for survival data'.

We have used relative risks from the International Obesity Task Force which applicable to populations across Europe. We are aware that for largely Asian populations for instance the relative risks would differ, therefore for work in these countries we would need to apply different risks.

I also had several questions regarding the model. Based on the first part of Appendix 2, it appears the authors computed BMI distributions for most (all?) countries using data on mean BMI. How do the actual BMI distributions look for countries with good, national surveys? Were they generally lognormal as assumed? For countries where the actual BMI distribution can be measured, do you use the actual data or the lognormal assumptions described in Appendix 2? Are the extrapolations of BMI growth based on estimations using actual data on BMI distributions or modeled distributions as described on pp. 30-38? I assume these are done separately by country?

Thank you for this useful comment. Where distribution data existed for a country we used this to extrapolate future trends. We have made our methods clearer in the supplementary information - Appendix 2a refers to projection made by using existing BMI prevalence data, 2b refers to computing BMI distribution from a single data point and 2c refers to computing BMI distribution from mean data. Where no data exist we extrapolated distributions from mean data.

Were the decreases in obesity applied to the obese equally? What if the heaviest (i.e., obese 3) were the target of the interventions?

The interventions tested a 1% and 5% reduction in population BMI rather than % change to the obesity group specifically. This has been amended in lines27-29 page 9.

The authors are commended for compiling the mathematical assumptions in the Appendices. However, the reader needs a roadmap to explain the goals of the assumptions and major steps of the modeling process. For example, what is the goal of the first part of the "Sample sizes, probabilities

and variances" section (p. 31)?

Many thanks for this comment. We have reorganised Appendix 2 to make the two stage modelling process clearer.

Minor Comments

p. 3, line 30: There is no mention of cancer results in the abstract.

Thank you for noting this, we have entered cancer results into the abstract.

p. 4, line 9: Strengths and Limitations mentions forecasts of healthcare costs and cost-effectiveness, but they are not reported in the abstract or the paper. Please remove the mention of costs and cost-effectiveness from the Strengths and Limitations.

Many thanks for this comment. We have noted in the limitations that these results do not present the cost impact of obesity-related disease burden, however that our model is capable of doing this should the right data be provided. We have removed this paragraph from the discussion.

p. 4, line 24: Define NCD at first use in the beginning of the Background section.

This has been added.

p. 5, line 55: Reference to WHO database is incomplete.

This has been added.

p. 6, line 21: Can the authors provide any intuition for how the conversion from prevalence to incidence was done in DISMOD II?

This has been added.

p. 6, line 25: Should "rate" be "rare"?

Yes, this has been changed.

p. 6, line 34: How were the diabetes rates adjusted for different population BMI-distributions?

Each individual in the microsimulation is on a certain BMI percentile – and this is determined by the BMI distribution given in module 1. A relative risk of disease connects an individuals BMI percentile to their risk of contracting a certain disease. Every individual has a probability of contracting, surviving and dying from a disease in any given year. Where proxy country data were used for a disease, the BMI distribution in the target country would enable the impact of obesity on diabetes to vary relative to the proxy country. Population statistics are also entered into each country model, therefore projections vary depending upon individual country demographics. Page 8, lines 25-28 now state: 'For example, if country x had diabetes data and these were used a proxy for country y where no data exist, then country y's BMI distribution would determine the future burden of type 2 diabetes via the relative risk'.

p. 10, line 8: Add citation for under-reporting of weight in surveys or interviews.

This has been added.

p. 30, line 22: Define HSE.
This has been defined.

p. 31, line 18: Is there a citation to support the approximation of the Beta distribution with a Normal distribution?

We have added a reference by Patel and Read (1996) to support this statement.

p. 34, line 21: What does “should be recorded” mean? How is this statistic used in the analysis/model?

Thank you for the comment. We have made the statement clearer by adding ‘and’ before the formula and ‘in order to perform the analyses after the formula. The sentence reads, ‘The value of the zero mean, unit variance residual statistic and $(m_1-m_2)/\sqrt{(\sigma_1^2\pm\sigma_2^2}$) should be recorded in order to perform the analyses.’

p. 39, line 56: Drop last period on the page, after the colon.

This has been deleted.

p. 40, line 9: Are “b” and “b’” supposed to be betas?

Thank you for noting this. Lines25-27on page 39 of the previously submitted manuscript explain that β has been taken as an arbitrary symbol to describe the distribution. In particular, they state: ‘Let β denote BMI in the continuous scale and let f(β|A,S,t) be the probability density function of β for age group A and sex S at time t’. For consistency b and b’ have now been replaced with β and β’.

p. 40, line 21: Please fix the reference called out by the“Error!” message.

This has been fixed.

References

Hollingworth, W., Hawkins, J., Lawlor, D. a, Brown, M., Marsh, T., & Kipping, R. R. (2012). Economic evaluation of lifestyle interventions to treat overweight or obesity in children. International journal of obesity (2005), 36(4), 559–66. doi:10.1038/ijo.2011.272

NICE. (2013). Overweight and obese children and young people - lifestyle weight management services. Retrieved from http://guidance.nice.org.uk/PHG/75

Reviewer: 2
Reviewer Name Timothy Dall
Institution and Country IHS Global Inc., USA
Please state any competing interests or state ‘None declared’: None declared

This study represents an ambitious effort to quantify the future burden of obesity-related diseases in 53 European countries. The authors attempt to apply a standardized methodology to each country, while taking into account differences across countries in data availability and definitions/metrics used to quantify population characteristics and disease prevalence or incidence. Study findings provide valuable information for comparing outcomes across countries—but more importantly can be used to inform national and international initiatives to reduce disease burden. The authors provide an appendix with a thorough discussion of data sources, methods, and assumptions.
The manuscript and accompanying appendix shows that the authors invested substantial time and thought into their analysis. I find no major problems with the study methods and manuscript write-up. The following are minor suggestions, and I leave it to the authors' discretion to make any revisions accordingly.
The authors might consider a simple diagram that shows how their model works. To understand the model one needs to wade through large amounts of text and mathematical equations.

Many thanks for this comment. We have now inserted a diagram and brief summary of the model at the end of technical appendix 2 d:

'The following diagram is a schematic of the microsimualtion model:
This illustrates the different modules involved in the microsimulation. A population of individuals are simulated based on known population statistics. An individual can be born and die in the model and has a specific risk (based on the risk distribution entered) of contracting, surviving and dying from a particular disease. An individual may be subject to a particular intervention in any given year that will change their risk trajectory'.

Figures 2 and 4 contain multiple diseases for each country, and are very difficult to read. Part of the difficulty reading these charts is that disease prevalence and incidence percentages differ widely by disease type, but are all put on the same scale. The authors might consider separate charts for each disease.

The new stack charts have been added to improve the reading of the data.

Appendix, Page 40, line 22. There is an "Error! Reference source not found" message in the text.

Thank you for this comment, this error has been deleted.

4. Page 60, in the BMI chart for Monaco the numbers appear to be truncated for females. The same applies to San Marino on page 72.

These diagrams relate to the population distribution within these countries rather than the BMI distribution. The populations in these countries are small and limited data exist on the age profile of these countries.

VERSION 2 – REVIEW

REVIEWER	Justin Trogdon Associate Professor Health Policy and Management Gillings School of Global Public Health University of North Carolina at Chapel Hill United States
REVIEW RETURNED	16-May-2014

GENERAL COMMENTS	The authors have addressed most of my earlier questions and concerns with the paper. I still feel that the main policy conclusions (i.e., more should be done to reverse obesity trends) could be made without a microsimulation model, but policymakers will hopefully respond to numbers targeted to their respective countries. The model also has promise as an evaluation tool for public health interventions to reduce obesity.

REVIEWER	Timothy Dall IHS Global Inc., USA
REVIEW RETURNED	19-May-2014

GENERAL COMMENTS	The authors have adequately addressed my previous comments.