Evaluation of the potential health benefits and cost savings of a point-of-care analyser for individuals with prediabetes

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Abstract

Objective: The main question addressed in this paper is whether a point-of-care analyser measuring insulin levels (developed by BioVolt) is effective in individuals with prediabetes in preventing or delaying them from getting diabetes and whether it leads to a cost reduction compared to usual care. Usual care in this case means there is no POC-analyser (thus insulin is not measured) available, indicating that only the regular care, as provided by the general practitioner, is available.

Background: Diabetes type 2 is an increasing concern in healthcare. A large part of the healthcare budgets are being spend on it. However, it is possible to prevent people from getting diabetes. This can be done for individuals with prediabetes. Prediabetes is the stage before diabetes in which it is possible to get healthy again.

Methods: A Markov model was developed to determine the difference in costs and the number of people progressing to diabetes in a situation in which the novel POC-analyser would be used compared to usual care. This model included the health states healthy, prediabetes, diabetes type 2, stroke, myocardial infarction and dementia. Death is the absorbing state in this model.

Results: The model shows a discounted cost reduction per individual of 2.8% for men, which is 676.46 Euro. The cost reduction achieved for women is larger at 5.1% or 1,244.66 Euro. In addition, due to using the point-of-care analyser. individuals spend (on average) more time in the "healthy" state (i.e. 13,28 months for men and 15,42 months for women). Besides this, there is also a substantial reduction in time spend in the diabetes state in the model, with a reduction of 12,81 months for men and 17,40 for women.

Conclusion: The point-of-care analyser would lead to increased quality of life and a cost reduction compared to the usual care. However further research will be needed to get a better insight on the real life effects of the POC-analyser on the probabilities since the model only gives an estimation on the effectiveness of such a device and the costs associated with it.

Introduction

Diabetes is becoming an increasingly challenging problem in health care. In 1980 a total of 108 million people worldwide had diabetes, this has increased to 442 million in 2014. The number of individuals suffering from diabetes is expected to rise to 642 million in 2040 (IDF, 2015). This means a rise of 4.7% to 8.5% of the global adult population. Diabetes also accounted for 1.5 million deaths in 2012 (WHO, 2016a). Most people suffering from diabetes have type 2, type 2 is accountable for 91% of the cases (IDF, 2015), which means their body does not react to insulin as it is supposed to (WHO, 2016a). The worldwide costs associated with diabetes were estimated to range between 673 billion and 1,197 billion US Dollars in 2015. This means that 12% of the global healthcare budget is being spend on diabetes (IDF, 2015). Even though the treatment is expensive, it is important to treat diabetes

appropriately, because when this does not happen it increases the probability of multiple different complications with higher associated costs. Stroke, heart diseases and dementia are among these complications. The occurrence of these complications often leads to a long revalidation process, a life with increased medical attention (or a combination of both), or even death. Also, the costs associated with these conditions can be rather high due to the long term treatment. Thus reducing the amount of people getting diabetes yields substantial health benefits and may save health care costs.

A large group of individuals is at risk of developing diabetes type 2. One of the main indicators of being at risk is a high body mass index (BMI). There are 1.9 billion adults with overweight and 600 million people being obese, indicating that a large part of the world population is at risk of developing diabetes (WHO, 2016b). Another way of identifying the individuals at risk is by measuring their fasting glucose to determine whether they have prediabetes. Prediabetes is a state before progressing to diabetes in which the individual has an impaired glucose tolerance (IGT) or impaired fasting glucose (IFG). The cut-off value for healthy individuals is less than 140 mg/dl for the oral glucose tolerance test and individuals with a value of 200 mg/dl or higher are defined as having diabetes (ADA, 2014; Lee & Derr, 2017). The group with values in between is defined as the prediabetes group. The lifetime risk of people progressing from prediabetes to diabetes is as high as 70% according to the American Diabetes Organisation (ADA) (Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). Reducing body weight in individuals with high BMI will effectively reduce their probability of progressing from prediabetes to diabetes type 2, since individuals with prediabetes often have a higher BMI. Several studies suggest a positive impact of lifestyle modifications (diet changes and increase of physical activity) in prediabetes patients on the risk of progression to diabetes (Diabetes Prevention Program Research, 2002; Li et al., 2008; Ramachandran et al., 2006). These show risk reductions of 28.5% [20.5%-37.3%] (Ramachandran et al., 2006) up to 58% [48-66%] (Diabetes Prevention Program Research, 2002). This can also lead to the individual reverting back to a normal glucose blood level.

To date, however, little attention has been devoted to developing devices which can be used by individuals with prediabetes or diabetes in order to measure their own insulin levels. More specifically, especially the group of prediabetes patients are often left out of interventions aimed at the prevention of diabetes. This happens because they are not always diagnosed and prediabetes also lacks a proper treatment plan (Stalenhoef, 2009). This is however arguably the group that could benefit most, and can halt the increase of diabetes type 2 patients. The lack of insulin testing is mainly caused by the more complicated process compared to measuring glucose levels. Measuring insulin levels currently requires hospital laboratory testing whereas the glucose test can be done at home by the individuals themselves (Pritchard, 2017). That is why BioVolt is developing a point-of-care (POC) analyser that can be used to measure the insulin levels of individuals at home. The company managed to create this by further developing existing techniques into a device with an accuracy which is expected to be close to the equivalent central laboratory tests. These techniques are enzyme-linked

immunosorbent assay (ELISA) and lateral flow analyses (LFA). This POC-analyser will provide the user with instant feedback and test results on their insulin levels. Following this, the individual will receive recommendations regarding food intake or the increase of physical activity through an internet portal. The advantage of instant feedback is that the user instantly knows whether he or she is effectively improving their lifestyle in order to reduce the risk of progressing to diabetes. This timely feedback will be more motivational than having to wait for the result of a blood test conducted by the laboratory of the hospital. Besides that, positive feedback can lead to a higher intrinsic motivation (Vallerand & Reid, 1988), and may thereby result in higher adherence to the advices given via the portal compared to a situation without feedback.

The main question addressed in this paper is whether this novel POC-analyser is effective in delaying or preventing the progression to diabetes and whether it leads to a cost reduction compared to usual care. Usual care in this case means there is no POC-analyser (thus insulin is not measured) available, indicating that only the regular care, as provided by the general practitioner, is available. This information is of interest to health insurance companies when deciding on reimbursement of the device, as well as to BioVolt when deciding how to continue development and how to set a price for the device.

Methods

The analyser will be available for individuals with prediabetes to measure their insulin levels. The individuals can see whether they are on their way to reach their predetermined goal. This goal is an insulin level, determined by a specialist. Based on the measured insulin level and relevant risk indicators the internet portal that comes with the analyser will give personalized lifestyle advice in the form of dietary tips and physical activity. This advice will be given through an internet portal (BioVolt, 2017).

Model

A Markov model was developed to determine the difference in costs and the number of people progressing to diabetes in a situation in which the novel POC-analyser would be used compared to usual care. Markov models can be used to get insight into the amount of time individuals spend in certain health states and thus offer a way to assess the cost associated with these states (Boyd & Lau, 1998). It also makes it possible to get a better view on how the time spend in each of the states changes due to the intervention. The time frame used in this Markov model is fifty years. This time frame was chosen in order to capture the long term effects of mainly prediabetes and diabetes on developing more severe complications, such as stroke, myocardial infarction and dementia. Besides, this also gives a better insight on the long term costs associated with the different complications. As the transitions between healthy, prediabetes and diabetes occur slowly (Tuso, 2014), the cycle duration was set at one year, in order to allow to see noticeable changes between the amount of individuals in

the states. The starting age was set at fifty years, as from this age onwards the probabilities of developing either of the included conditions is noticeable. At lower ages these probabilities are too small to actually have a substantial impact on the results. In every cycle of the model, each individual has a certain probability of moving to another health state. This probability depends on the health state they are in and, for the health state prediabetes, on whether the POC-analyser is being used or not. As men and women have different risk of complications when they are in the Healthy, Prediabetes and Diabetes health states, the analyses were performed separately for men and women. The possibility of reverting back to prediabetes from diabetes has not been included due to the lack of the evidence of this possibility. Individuals can move to dead from every other state.

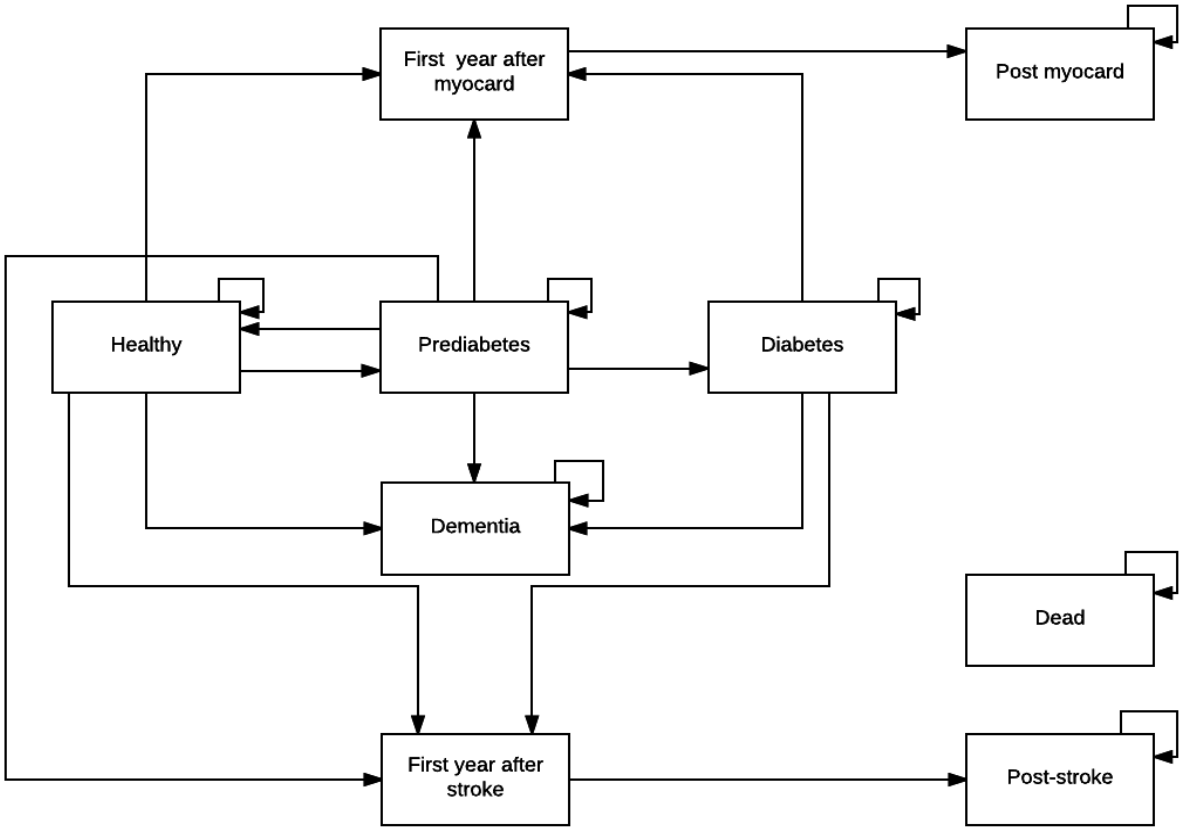

Figure 1 Graphical presentation of the model

The states being used in the model (see figure 1) are the following ones:

1. *Healthy*. This is the state in which all individuals are in at the beginning of the model. It is thus assumed that all the other conditions are absent in these individuals.
2. *Prediabetes*. Prediabetes is a state where the individuals can either return back to healthy, develop diabetes type 2 or remain in the prediabetes state. Individuals with this condition suffer from increased probabilities to progress to stroke, myocardial infarction, dementia and death.
3. *Diabetes (type 2)*. Individuals in this state cannot revert to prediabetes or healthy once this state is reached. Like for prediabetes, the probabilities on stroke, myocardial infarction, dementia and death are increased. However, those probabilities are higher in diabetes patients compared to prediabetes patients.
4. *First year after a stroke*. This is a state in which patients who recently suffered from a stroke stay for a year. This is a separate state in the Markov model, because of the increased risk of complications and the higher costs occurring in the first year after a stroke.
5. *Post-stroke*. After one year the patients in "the first year after a stroke" state progress to this state.
6. *First year after a myocardial infarction*. Similar to the first year after a stroke patient who suffered recently from a myocardial infarction move into this state. Individuals in this state have increased complications and cost associated with them compared with subsequent years. As mentioned individuals with prediabetes and diabetes have an increased probability of moving to this state.
7. *Post myocardial infarction*. Individuals who had a myocardial infarction end up in this state after one year in the first year after a myocardial infarction state.
8. *Dementia*. When individuals are diagnosed with dementia they move to this state.
9. *Death*. Individuals from all the other states can move to this state.

Prediabetes

There are three transition probabilities involved with prediabetes. These are from healthy to prediabetes, prediabetes to healthy and prediabetes to diabetes. The first has a yearly probability of 1.9% (Anjana et al., 2015), the second one of 7.5% (Tabák et al., 2012) and the last one of 8.4% (Anjana et al., 2015).

Mortality

The data on mortality risks were retrieved from the site of *Statistics Netherlands.* Statistics Netherlands is an autonomous national agency with the mandate to collect and process data. The data concerning the mortality risks are collected for men and women separately and for every age up to an

age of 99 years (CBS, 2015). The mortality rates published for 2015 were the most recent ones, thus these were used in the model.

Stroke

Data on the risk of getting a stroke have been previously published, as incidence rates defined per ten years of age and separately for men and women (Hollander et al., 2003), using the age categories 55-64, 65-74, 75-84 and 85 plus (see appendix 2). However, data for the individuals aged 50-54 years were not available from this study, thus in the model it is assumed that these incidence rates are similar to those for the age category of 55-64. A moving average including the past three years was applied to avoid large differences between the start of a new age category and the previous one. Both individuals with prediabetes and diabetes have a higher probability of suffering from a stroke compared to healthy individuals. In case of prediabetes there is a relative risk of 1.06 [1.01-1.11] according to the standards used by the American Diabetes Association (ADA) (Huang, Cai, Mai, Li, & Hu, 2016). The relative risk for individuals with diabetes to suffer from a stroke is 1.36 [1.10-1.68] compared to healthy individuals (O'Donnell et al., 2010). To distinguish the short term health consequences and costs of stroke from the long term health consequences and costs, two stroke health states were defined, one representing the first year following stroke and one representing all years after this first year. All surviving individuals in the "First year after Stroke" state automatically move to the "Post Stroke" state the next year. Of all individuals with non-fatal strokes, 72.0% also survive the first year after stroke (Wu et al., 2014). The probability that an individual does not survive the stroke was set to seven percent based on literature (NHG, 2013). The excess mortality rate for individuals surviving the first year following a stroke compared to healthy individuals was identified from literature as 2.0 [1.1-2.9] (Brønnum-Hansen, Davidsen, & Thorvaldsen, 2001).

Myocardial infarction

The impact and consequences of a myocardial infarction, in terms of health states and transitions, is modelled similarly as for stroke. However, the transition probabilities are different. The study, from which the data are taken, uses intervals of ten years and makes a separation between men and women. The age categories used in this study are 50-59, 60-69, 70-79, 80-89 and 90 plus (Koek et al., 2007). In this case a moving average over the past three years is used as well. Also both prediabetes and diabetes have a higher probability of suffering from a myocardial infarction compared to healthy individuals (see appendix 3). Although the relative risk for individuals with prediabetes to suffer from a myocardial infarction could not be retrieved from literature, this relative risk was estimated to be 1.33 in prediabetes patients which is based on the ratio between the risk of a stroke with prediabetes and diabetes. The incidence rate of getting a myocardial infarction when having diabetes is 1.7 [1.6-1.8] (Lindhardsen et al., 2011). Myocardial infarction is also split up in a first year after the infarction and a state in which people end up after they have spent a year in the aforementioned state. This has been done for the same reasons as for the individuals with a stroke. In this case it gives a better view

on the long term consequences of the costs. Both states do have the same probabilities to die. After one cycle in the first year after myocardial infarction they move on to the post myocardial infarction state.

Dementia

According to the Rotterdam study (Ott et al., 1999) the risk of suffering from dementia when having diabetes type 2 is 1.9 [1.3-2.8] times higher than in healthy individuals. The increased risk for someone with prediabetes to suffer from dementia is 1.18 [1.04-1.33] (Crane et al., 2013). The incidence rates for dementia are also used from the Rotterdam study (Ott, Breteler, Harskamp, Stijnen, & Hofman, 1998). In this case the provided incidence rates are also divided into different age categories (see appendix 4). The 95+ category for men had an incidence rate of 0 due to the low number of individuals in this group, this is however not expected in a larger population than used in the Rotterdam study. This has been overcome by using the increase in incidence rate between 85-89 (0.0286) and 90-94 (0.0296) as an estimate of the increase in incidence rate after 95 years of age, resulting in an incidence rate 0.0306.

Intervention

The POC-analyser will be available for individuals with prediabetes. This way they can measure their own insulin levels in order to increase the probability they revert back to healthy and reduce the risk that they progress to diabetes. A relative reduction of 58% [48%-66%] (Diabetes Prevention Program Research, 2002) in diabetes incidence has been used in the model. This study's lifestyle goals consisted of at least a weight loss of 7 percent and 150 minutes per week of physical activity. The mean age of the population was 51 years. Besides this, as there was a lack of studies reporting this increase, the probability to return to healthy from prediabetes was assumed to increase with the same percentage. Although multiple studies were found that reported on this probability. The included study used a population of 3234 non diabetic persons with elevated fasting and post-load plasma glucose concentrations. This sample size was substantially larger than the 577 in another study on this topic (Li et al., 2008). Besides the included study was conducted in the United States, while the other one took place in China. This led to the conclusion that next to the larger sample size, the population from the United States is expected to be better comparable to the Dutch population. The percentages from this study are therefore used to calculate the transitions rates from prediabetes to healthy and from prediabetes to diabetes when the POC-analyser is used. This results in a yearly probability of reverting from prediabetes to healthy of 11.9% and a 3.5% probability to progress from prediabetes to diabetes.

The yearly price for the POC-analyser is 500 Euros. This has been determined by BioVolt after conducting a marketing research regarding the price people are willing to pay for such a service. The service includes all costs associated with the device, including the device itself, the test strips and a subscription to the online data portal.

Costs

Because of the one-year cycles, the costs used in the model are yearly costs. The cost of prediabetes is based on two control visits at the general practice assistant per year (ZorgcoöperatieKatwijkaandeRijn, 2009), assuming that 50% of the individuals with prediabetes are diagnosed as such (Heianza et al., 2013). This means the other 50% of the individuals do not use such control visits since they are not aware of their prediabetes. The cost for the treatment of diabetes, dementia and post stroke are collected from "Volksgezondheidenzorg". This is a site (https://www.volksgezondheidenzorg.info) that uses data acquired from the National Institute for Public Health and the Environment (RIVM, 2011).

The cost for the "post myocardial infarction" state were calculated by using the standard care given to individuals with such an infarction (NHG, 2012). This resulted in a list of medicines that are administered to these individuals. Besides a yearly general practitioner consult of 18,47 Euros was included as well (NHG, 2012). The costs occurring immediately after suffering from a myocardial infarction were 5021 Euros (Soekhlal, Burgers, Redekop, & Tan, 2013). However these were for the treatment immediately after the infarction, that is why the yearly medicine cost were added to this. This resulted in a total cost of €5707.42. The combination of medication that those patients were assumed to receive was the following one:

Table 1. Cost of myocardial infarction medication

Medicines	Dose (Daily mg)	Cost (Euros)
Acetylsalicylic acid (Aspirin)	80	0,46
Simvastatin	40	0,27
Metoprolol	200	0,60
Lisinopril (elderly)	5	0,50
Lisinopril	20	0,16

The costs for these specific medicines were acquired from the website (https://www.medicijnkosten.nl) of Care Institute Netherlands (ZorginstituutNederland, 2017).

Table 2. Costs included in the model

Condition	Yearly cost (Euros)	Source
Prediabetes	7.39	(Independer, 2017; ZorgcoöperatieKatwijkaandeRijn, 2009)
Diabetes	1,530.15	(Volksgezondheidenzorg, 2017)
Dementia	46,153.85	(Volksgezondheidenzorg, 2017)
Post stroke men	4,411.10	(Volksgezondheidenzorg, 2017)
Post stroke women	5,985.27	(Volksgezondheidenzorg, 2017)
First year after a stroke	29,484.00	(van Eeden et al., 2015)
First year after a myocardial infarction	5,707.42	(NHG, 2012; Soekhlal et al., 2013; ZorginstituutNederland, 2017)
Post myocardial infarction	686.42	(NHG, 2012; ZorginstituutNederland, 2017)
Point-of-care analyser	500.00	

Discount rate

As the time horizon of the model exceeds one year, a discount rate of 4% has been used for all costs according to the Dutch Guideline for economic evaluations in healthcare (ZorginstituutNederland, 2016).

Analysis

A one way sensitivity analysis will be performed to give an indication on the impact of the different parameters on the cost reduction of the intervention compared with the usual care. In this analysis, one parameter at a time is changed, while leaving the other parameters unaffected. The different values that are inserted in the model involve the average probabilities, a lower limit (LL) and a upper limit (UL). In most cases, transition probabilities have been determined by the confidence interval reported in the corresponding studies. For costs these limits have been determined by a LL of 25% less cost than the average value, and an UL of 25% more than the average value. See appendix 1 for the values used.

In addition a two way sensitivity analysis will be performed on these probabilities because of the large uncertainty around the transition rates concerning prediabetes. As mentioned before the transition from prediabetes to healthy could not be obtained in any study. In this analysis the transition probabilities for prediabetes to diabetes and prediabetes to healthy are varied independently. Ranging from 1% to 9% in case of prediabetes to diabetes and 5% to 15% in case of prediabetes to healthy. This gives the opportunity to see which values should (at least) be achieved in the intervention group to reach a cost-neutral outcome compared to the usual care.

Results

The model shows a discounted cost reduction per individual of 2.8% for men, which is 676.46 Euro. The cost reduction achieved for women is larger at 5.1% or 1,244.66 Euro. In addition to the estimated cost savings the intervention also results in a difference in time spend in the different health states. Table 3 and 4 show the time spent in each state for both men and women in usual care and when POC-analyser is used. The last column shows the difference between usual care and the intervention. The amount of time spent in healthy and prediabetes increases with the use of the POC-analyser. These increases are 13.28 and 1.63 months respectively for men and 15.42 and 1.89 for women. On the other hand, the amount of time individuals spend in the health states diabetes, dementia, stroke and myocardial infarction decreases. Mainly the time spend in the diabetes state per person shows a large reduction of 12.81 months for men and 17.40 for women.

Table 3. Time spent in each state (months) for men

	Usual care	Intervention	Difference
Healthy	253.33	266.61	13.28
Prediabetes	23.66	25.28	1.63
Diabetes	22.90	10.09	-12.81
Dementia	11.55	11.19	-0.36
Stroke*	13.32	13.21	-0.11
Myocardial infarction*	42.94	42.04	-0.90
Total	367.70	368.42	-0.72

**Both states combined with first year after stroke/myocardial infarction*

Table 4. Time spent in each state (months) for women

	Usual care	Intervention	Difference
Healthy	290.44	305.86	15.42
Prediabetes	28.24	30.13	1.89
Diabetes	30.77	13.37	-17.40
Dementia	16.49	15.42	-1.07
Stroke*	12.87	13.61	-0.74
Myocardial infarction*	22.79	23.59	-0.80
Total	401.60	401.98	-0.38

**Both states combined with first year after stroke/myocardial infarction*

One way sensitivity analysis

The one way sensitivity analysis shows that in most cases the difference in cost between the usual care and intervention barely changes when model input parameters are set to their lower or upper limit (figure 2 and 3). The parameters “intervention prediabetes to healthy” up to “diabetes to dementia” all differ noticeably from the average cost reduction, with “diabetes to dementia” being the most influential parameter. The parameter “diabetes to dementia” ranges from 314.89 Euros when the LL input is used, to 1,175.25 Euros when the UL input value is used for men, and a LL of 577.82 Euros to an UL of 2,120.28 Euros for women. The parameter “intervention prediabetes to healthy” ranges from a LL of 626.22 Euros to an UL of 714.75 Euros for men and a LL of 1,172.77 Euros to an UL of

1,299.26 Euros for women. The parameters concerning cost with largest impact on the outcome are mainly the cost of diabetes and dementia. This is the case for both men and women. The order of importance of the parameters differs a bit between these subgroups.

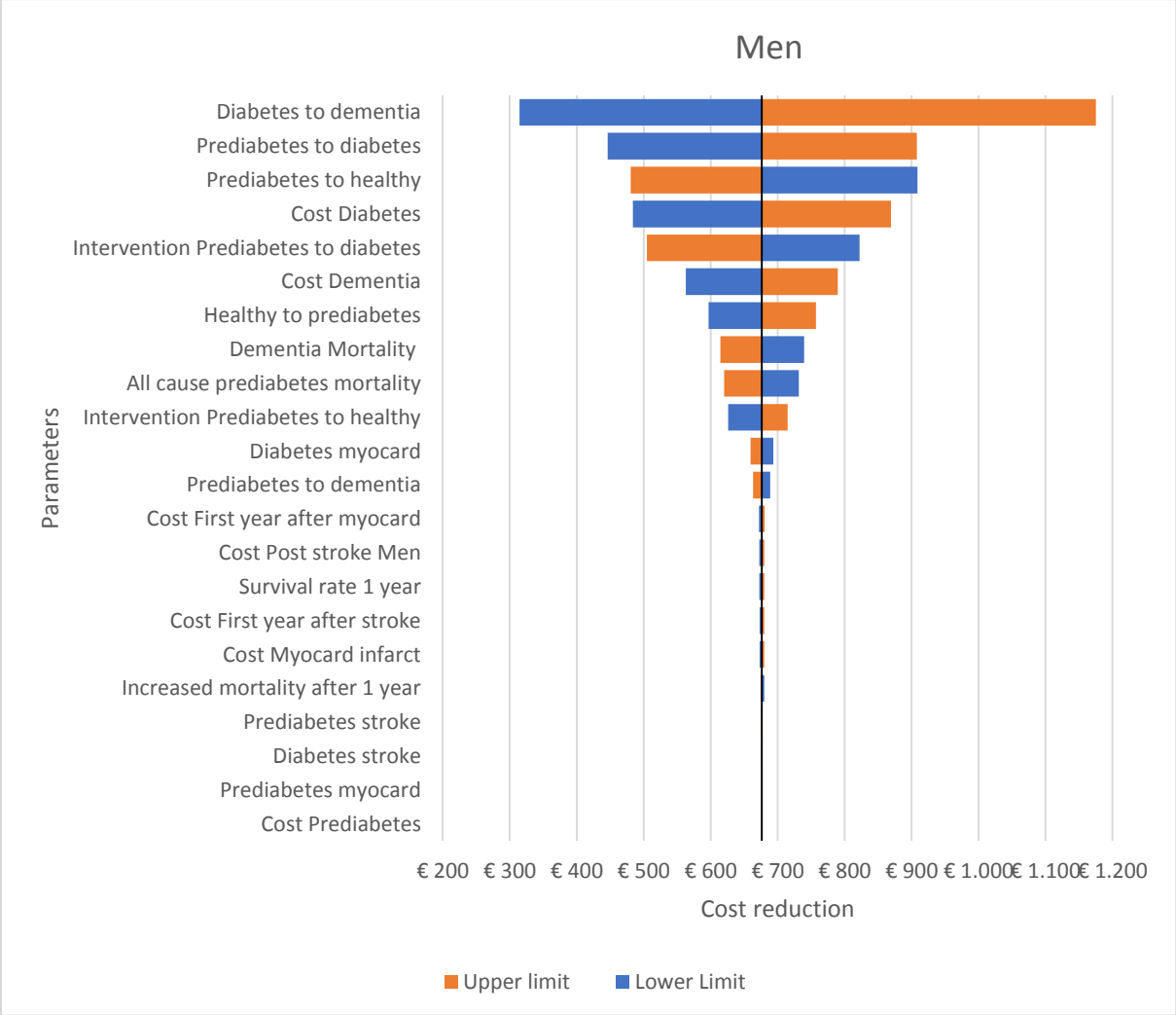

Figure 2 Tornado diagram men (one-way sensitivity analysis)

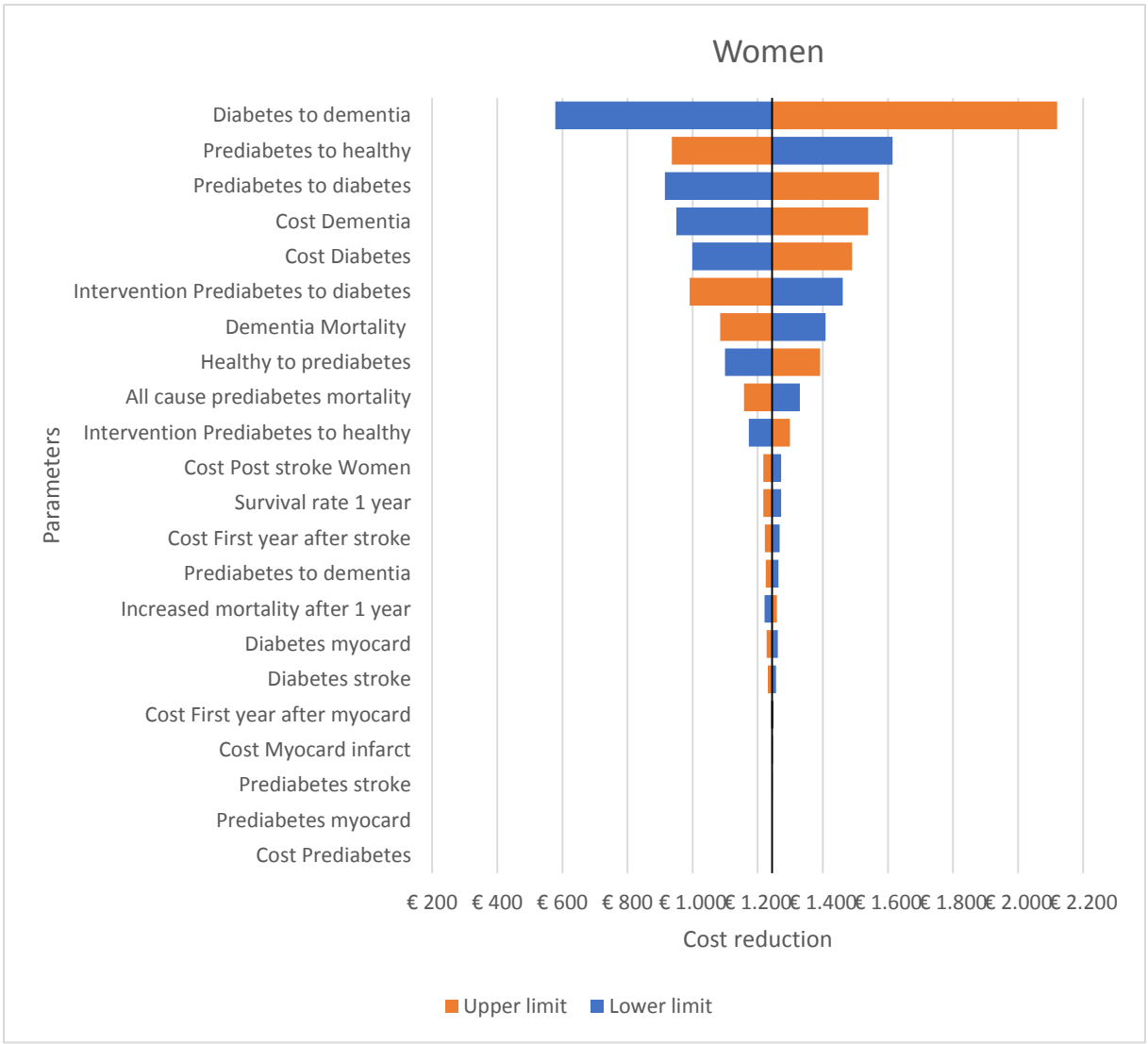

Figure 3 Tornado diagram women (one-way sensitivity analysis)

Two way sensitivity analysis

The two way sensitivity analysis performed on the effects of the lifestyle modifications shows a predictable pattern. More individuals reverting to healthy from prediabetes results in a larger cost reduction per person. In the opposite situation more individuals progress to diabetes, resulting in a smaller cost reduction. The probability that the intervention reduces costs is larger in women than in men. Both figure 4 and 5 show that in most of the evaluated scenarios a cost reduction will be achieved. However the transition probability for prediabetes to diabetes for men should not be higher than 8%. This probability can be 9% for women, but a transition probability for prediabetes to healthy of at least 13% needs to be achieved in this case. To achieve a cost saving in at least half of the cases a yearly transition probability for prediabetes to diabetes below 6% should be reached for both men and women. Concerning the transition from prediabetes to healthy, this probability is 10% for men and 7% for women. The blue lines in the figures show the transition probabilities without the use of the POC-analyser.

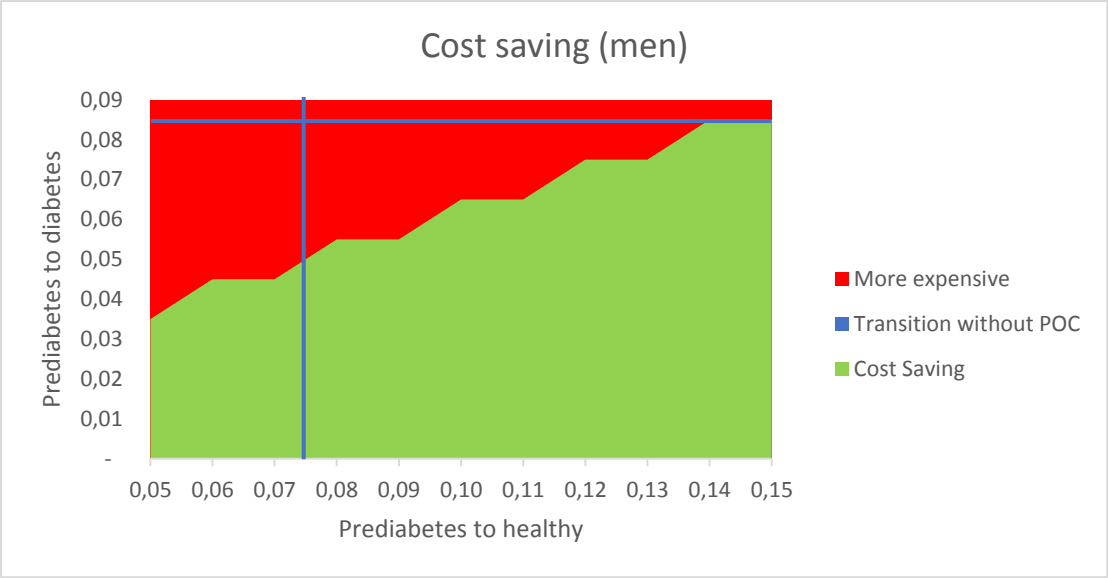

Figure 4 Transition probabilities of the intervention and their possible outcomes (two-way sensitivity analysis men)

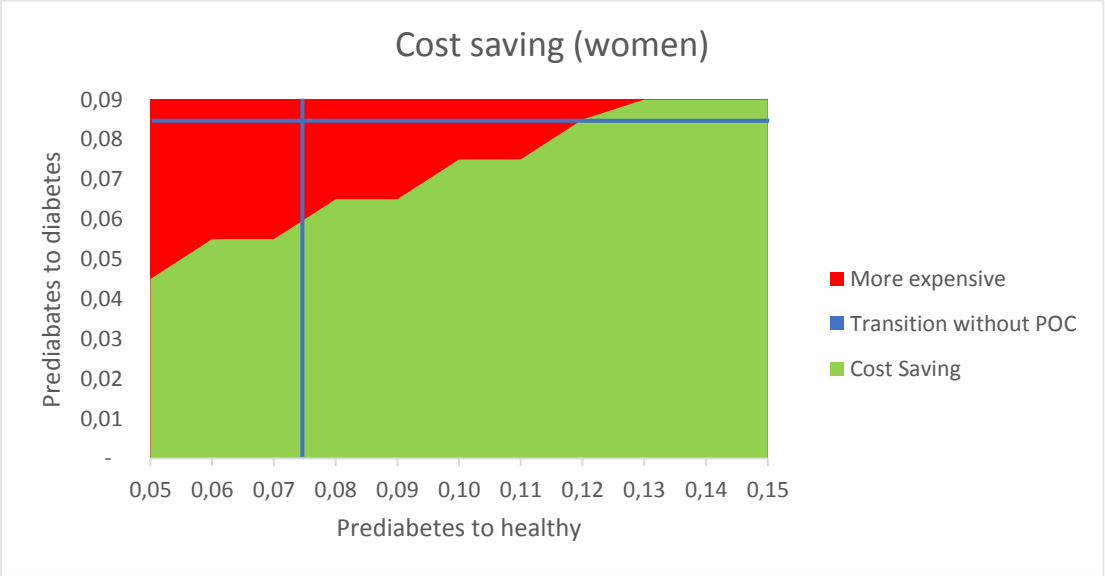

Figure 5 Transition probabilities of the intervention and their possible outcomes (two-way sensitivity analysis women)

Discussion

In this paper we assessed whether the use of a novel POC-analyser to measure insulin levels is effective in delaying or preventing the progression to diabetes and would lead to a cost reduction compared to usual care (no such POC device available).

Results

The POC-analyser is expected to lead to a reduction in the progression from prediabetes to diabetes while simultaneously increasing the amount of individuals reverting from prediabetes to healthy. This however is completely dependent on the adherence of the individuals to the use of the POC-analyser

and the lifestyle advises. With a progression rate of 6% from prediabetes to diabetes and a regression rate of 10% for men and 7% for women from prediabetes to healthy, a cost reduction will be achieved in most cases in the group using the POC-analyser. The effect of the intervention is more noticeable for women, as a larger cost reduction can be achieved in this group (i.e. 2.8% for men and 5.1% for women). An explanation for this difference might be that women live longer than men, resulting in a longer period in which the intervention reduces healthcare costs. The total annual cost for diabetes (both type 1 and type 2) in the Netherlands is 1.7 billion Euros (Volksgezondheidenzorg, 2017). As the number of women and men is about the same in the Netherlands (CBS, 2017). This would result in an expected cost reduction of about 4.0%, which is the average of the cost reductions achieved in men and women. This could lead to a potential saving of approximately 34.0 million a year with the POC-analyser when it is taken into account that 50% of the individuals with prediabetes are diagnosed. These costs are still the combined one for both types of diabetes, thus the real value would be lower due to the large cost associated with type 1 compared to type 2. Besides cost savings there are also health benefits. As shown in table 3 and 4, the amount of time individuals spend in the “healthy” state increases and the time spend in “diabetes” decreases. On the other hand individuals stay slightly longer in the prediabetes state, this increase is just a little over a month per individual. However prediabetes itself does not lead to a significant reduction in quality of life, unless it progresses to another condition (for example stroke, dementia or myocardial infarction). This increase in the time spend in prediabetes is just a small fraction compared to the increase in months in the healthy state (13.28 months for men and 15.40 for women) and the reduction of time spend in the diabetes state (12.81 months for men and 17.40 for women). The differences in time spent in dementia, stroke and myocardial infarction are small, suggesting that the POC-analyser would mainly lead to an increase in healthy life years. This can also be seen in the small difference between the total amount of time spent alive in the group with usual care and the group using the POC-analyser.

Based on our results it appears that, the probability that the analyser will lead to an increase in quality of life and a decrease in cost is rather substantial. The exact numbers can however only be verified when the analyser is available for testing. At the moment the outcomes are rough estimations of what the impact potentially can be.

Analysis (one-way, two-way)

The only parameter not included in the one way analysis was the one concerning whether a stroke is fatal or not, this has been done because of the certainty around this parameter due to it being derived from governmental statistics. On the other hand the two way analysis was needed because it is rather unclear how much effect a lifestyle intervention may have on the regression from prediabetes to healthy and the progression from prediabetes to diabetes. The large variety in results between the different studies concerning lifestyle modification in individuals at risk lead to this conclusion (Diabetes Prevention Program Research, 2002; Li et al., 2008). Besides this, it is not yet possible to

say how well the adherence to such lifestyle modifications of the individuals will be. Both analyses gave a clear view of the reversion and progression rates that should be achieved with the device and which parameters are the most influential ones.

Limitations

One of the assumptions of the model is that every individual first has to progress through prediabetes before they can progress to diabetes. Thus healthy to prediabetes to diabetes, which means going from healthy to diabetes without the prediabetes step is impossible. Also, individuals can only experience one event concerning stroke, dementia and myocardial infarction. This means that an individual with stroke will never end up in the "dementia" or "myocardial infarction" states. In reality however this is of course possible. When this is taken into account it will probably lead to more cost savings since more people in the group without the POC-analyser are at risk. This means the probability of someone suffering from more than one of these complications in the usual care group is larger than in the group using the POC-analyser.

Another assumption is that every individual will actually use the POC-analyser when it is available to them. In reality this will probably not be the case and thus the results differ compared to real life. A lower amount of individuals using the analyser results in more individuals progressing to diabetes and thus decreasing the cost savings compared to this study. However it is also possible that due to the availability of a POC-analyser more individuals will be aware of their prediabetes, which could lead to a reduction in the number of individuals progressing to diabetes.

One of the weaknesses of the model is that a large amount of complications also caused by diabetes are not included. This choice was made because of the limited available time and in certain cases the lack of evidence. Mainly evidence on the subject of prediabetes is scarce. However, this model included the most costly and most common complications, which means that the results should give a good indication of the overall effects.

Secondly, the cost of diabetes type 2 might be overestimated. The included cost is the combined one for both diabetes type 1 and 2. Generally the costs associated with type 1 are higher than those of type 2, which means that in this case the included cost should probably be lower. However, as 91% of individuals with diabetes have type 2 (IDF, 2015), the effect of this overestimation is likely to be limited.

Thirdly, the mortality rates used includes all types of mortality, thus also from complications included in the model. This might result in a larger amount of deaths than observed in practice. Besides, the mortality rate used for individuals with dementia is for individuals aged 77 years and older, also resulting in a larger amount of individuals dying from dementia compared to the general population.

Lastly, dementia has a substantial influence on the results. Mainly the transition probability from diabetes to dementia has a lot of influence on the cost reduction. The rather high yearly cost associated with dementia is one of the main reasons of this relation. This is also shown by the parameter cost

dementia, which also has a large effect on the cost reduction. Another reason why dementia has such a large influence on the outcomes is the uncertainty in the study where the data is acquired from. This resulted in a big difference between the lower and upper limits used in the one way sensitivity analysis.

Recommendations

This research used quite a few parameters of which it was not completely sure what these would exactly be in a real life situation with the POC-analyser. One of the things that has to be done in a potential next evaluation of the POC-analyser is testing how well the adherence of the individuals is and to what extent the progression rates change. The population of the study used for the transition probabilities in this model had a mean age of 51 years. Since the starting age is 50 in the model, the adherence at first will be similar to this study. However later on the adherence may differ from the one assumed in the model. Further research will be needed to get a better insight on the real life effects of the POC-analyser on the probabilities since the model only gives an estimation on the effectiveness of such a device and the costs associated with it.

Appendix 1: Transitions and costs with corresponding lower and upper limit

		Value	Lower limit	Upper limit	Source
Transitions	HeaPre*	0.019	0.017	0.022	(Anjana et al., 2015)
	PreDia*	0.084	0.072	0.098	(Anjana et al., 2015)
	PreHea	0.075	0.050	0.100	(Tabák et al., 2012)
Stroke	StrokePre	1.060	1.010	1.110	(Huang et al., 2016)
	StrokeDia	1.360	1.100	1.680	(O'Donnell et al., 2010)
	Increases mortality after one year	2.000	1.100	2.900	(Brønnum-Hansen et al., 2001)
	Survival rate 1 year	0.720	0.540	0.901	(Wu et al., 2014)
Dementia	Prediabetes	1.180	1.040	1.330	(Crane et al., 2013)
	Diabetes	1.900	1.300	2.800	(Ott et al., 1999)
	Mortality	2.000	1.500	2.700	(Agüero-Torres, Fratiglioni, Guo, Viitanen, & Winblad, 1999)
Myocardial infarction	Diabetes	1.700	1.600	1.800	(Lindhardsen et al., 2011)
	Prediabetes**	1.325	1.247	1.403	(NHG, 2013)
Mortality	All-cause mortality prediabetes	1.130	1.020	1.250	(Huang et al., 2016)
Intervention	PreHea***	0.119	0.111	0.125	(Diabetes Prevention Program Research, 2002)
	PreDia***	0.035	0.029	0.044	(Diabetes Prevention Program Research, 2002)
Costs (Euros)					
	Prediabetes	18.47	13.85	23.09	(Independer, 2017; ZorgcoöperatieKatwijkaandeRijn, 2009)
	Diabetes	1,530.15	1,147.61	1,912.69	(Volksgezondheidenzorg, 2017)
	Dementia	46,153.85	34,615.38	57,692.31	(Volksgezondheidenzorg, 2017)
	Post stroke Men	4,411.10	3,308.32	5,513.87	(Volksgezondheidenzorg, 2017)
	Post stroke Women	5,985.27	4,488.95	7,481.58	(Volksgezondheidenzorg, 2017)
	First year after stroke	29,484.00	22,113.00	36,855.00	(van Eeden et al., 2015)
	Myocardial infarction	5,707.42	4,280.57	7,134.28	(Soekhlal et al., 2013)
	First year after myocardial infarction	686.42	514.82	858.03	(NHG, 2012; ZorginstituutNederland, 2017)

**Hea means healthy, pre means prediabetes and dia means diabetes*

***Calculated by using the ratio between the risk ratios of diabetes/prediabetes to stroke, due to no available data on this subject*

****Calculated by using the transition probabilities without the intervention and the percentages from the study*

Appendix 2: Stroke

(Hollander et al., 2003)			Moving average	
Age	**Men**	**Women**	**Men**	**Women**
50	0.0017	0.0012	0.0017	0.0012
51	0.0017	0.0012	0.0017	0.0012
52	0.0017	0.0012	0.0017	0.0012
53	0.0017	0.0012	0.0017	0.0012
54	0.0017	0.0012	0.0017	0.0012
55	0.0017	0.0012	0.0017	0.0012
56	0.0017	0.0012	0.0017	0.0012
57	0.0017	0.0012	0.0017	0.0012
58	0.0017	0.0012	0.0017	0.0012
59	0.0017	0.0012	0.0017	0.0012
60	0.0023	0.0021	0.0019	0.0015
61	0.0023	0.0021	0.0021	0.0018
62	0.0023	0.0021	0.0023	0.0021
63	0.0023	0.0021	0.0023	0.0021
64	0.0023	0.0021	0.0023	0.0021
65	0.0076	0.0031	0.0041	0.0024
66	0.0076	0.0031	0.0058	0.0028
67	0.0076	0.0031	0.0076	0.0031
68	0.0076	0.0031	0.0076	0.0031
69	0.0076	0.0031	0.0076	0.0031
70	0.0090	0.0057	0.0081	0.0040
71	0.0090	0.0057	0.0085	0.0048
72	0.0090	0.0057	0.0090	0.0057
73	0.0090	0.0057	0.0090	0.0057
74	0.0090	0.0057	0.0090	0.0057
75	0.0181	0.0143	0.0120	0.0086
76	0.0181	0.0143	0.0151	0.0114
77	0.0181	0.0143	0.0181	0.0143
78	0.0181	0.0143	0.0181	0.0143
79	0.0181	0.0143	0.0181	0.0143
80	0.0199	0.0117	0.0187	0.0134
81	0.0199	0.0117	0.0193	0.0126
82	0.0199	0.0117	0.0199	0.0117
83	0.0199	0.0117	0.0199	0.0117
84	0.0199	0.0117	0.0199	0.0117
85	0.0255	0.0206	0.0218	0.0147
86	0.0255	0.0206	0.0236	0.0176
87	0.0255	0.0206	0.0255	0.0206
88	0.0255	0.0206	0.0255	0.0206
89	0.0255	0.0206	0.0255	0.0206
90	0.0334	0.0265	0.0281	0.0226
91	0.0334	0.0265	0.0308	0.0245
92	0.0334	0.0265	0.0334	0.0265
93	0.0334	0.0265	0.0334	0.0265
94	0.0334	0.0265	0.0334	0.0265
95	0.0698	0.0331	0.0455	0.0287
96	0.0698	0.0331	0.0577	0.0309
97	0.0698	0.0331	0.0698	0.0331
98	0.0698	0.0331	0.0698	0.0331
99	0.0698	0.0331	0.0698	0.0331

Appendix 3: Myocardial infarction

(Koek et al., 2007)			Moving average	
Age	**Men**	**Women**	**Men**	**Women**
50	0.00426	0.00101	0.00426	0.00101
51	0.00426	0.00101	0.00426	0.00101
52	0.00426	0.00101	0.00426	0.00101
53	0.00426	0.00101	0.00426	0.00101
54	0.00426	0.00101	0.00426	0.00101
55	0.00426	0.00101	0.00426	0.00101
56	0.00426	0.00101	0.00426	0.00101
57	0.00426	0.00101	0.00426	0.00101
58	0.00426	0.00101	0.00426	0.00101
59	0.00426	0.00101	0.00426	0.00101
60	0.00778	0.00282	0.00543	0.00161
61	0.00778	0.00282	0.00661	0.00222
62	0.00778	0.00282	0.00778	0.00282
63	0.00778	0.00282	0.00778	0.00282
64	0.00778	0.00282	0.00778	0.00282
65	0.00778	0.00282	0.00778	0.00282
66	0.00778	0.00282	0.00778	0.00282
67	0.00778	0.00282	0.00778	0.00282
68	0.00778	0.00282	0.00778	0.00282
69	0.00778	0.00282	0.00778	0.00282
70	0.01371	0.00685	0.00976	0.00416
71	0.01371	0.00685	0.01173	0.00551
72	0.01371	0.00685	0.01371	0.00685
73	0.01371	0.00685	0.01371	0.00685
74	0.01371	0.00685	0.01371	0.00685
75	0.01371	0.00685	0.01371	0.00685
76	0.01371	0.00685	0.01371	0.00685
77	0.01371	0.00685	0.01371	0.00685
78	0.01371	0.00685	0.01371	0.00685
79	0.01371	0.00685	0.01371	0.00685
80	0.02171	0.01359	0.01638	0.00910
81	0.02171	0.01359	0.01904	0.01134
82	0.02171	0.01359	0.02171	0.01359
83	0.02171	0.01359	0.02171	0.01359
84	0.02171	0.01359	0.02171	0.01359
85	0.02171	0.01359	0.02171	0.01359
86	0.02171	0.01359	0.02171	0.01359
87	0.02171	0.01359	0.02171	0.01359
88	0.02171	0.01359	0.02171	0.01359
89	0.02171	0.01359	0.02171	0.01359
90	0.02996	0.02226	0.02446	0.01648
91	0.02996	0.02226	0.02721	0.01937
92	0.02996	0.02226	0.02996	0.02226
93	0.02996	0.02226	0.02996	0.02226
94	0.02996	0.02226	0.02996	0.02226
95	0.02996	0.02226	0.02996	0.02226
96	0.02996	0.02226	0.02996	0.02226
97	0.02996	0.02226	0.02996	0.02226
98	0.02996	0.02226	0.02996	0.02226
99	0.02996	0.02226	0.02996	0.02226
100	0.02996	0.02226	0.02996	0.02226

Appendix 4: Dementia

(Ott et al., 1998)			Moving average	
Age	**Men**	**Women**	**Men**	**Women**
50	0.0014	0.0000	0.0014	0.0000
51	0.0014	0.0000	0.0014	0.0000
52	0.0014	0.0000	0.0014	0.0000
53	0.0014	0.0000	0.0014	0.0000
54	0.0014	0.0000	0.0014	0.0000
55	0.0014	0.0000	0.0014	0.0000
56	0.0014	0.0000	0.0014	0.0000
57	0.0014	0.0000	0.0014	0.0000
58	0.0014	0.0000	0.0014	0.0000
59	0.0014	0.0000	0.0014	0.0000
60	0.0009	0.0012	0.0012	0.0004
61	0.0009	0.0012	0.0011	0.0008
62	0.0009	0.0012	0.0009	0.0012
63	0.0009	0.0012	0.0009	0.0012
64	0.0009	0.0012	0.0009	0.0012
65	0.0008	0.0019	0.0009	0.0014
66	0.0008	0.0019	0.0008	0.0017
67	0.0008	0.0019	0.0008	0.0019
68	0.0008	0.0019	0.0008	0.0019
69	0.0008	0.0019	0.0008	0.0019
70	0.0045	0.0036	0.0020	0.0025
71	0.0045	0.0036	0.0033	0.0030
72	0.0045	0.0036	0.0045	0.0036
73	0.0045	0.0036	0.0045	0.0036
74	0.0045	0.0036	0.0045	0.0036
75	0.0148	0.0178	0.0079	0.0083
76	0.0148	0.0178	0.0114	0.0131
77	0.0148	0.0178	0.0148	0.0178
78	0.0148	0.0178	0.0148	0.0178
79	0.0148	0.0178	0.0148	0.0178
80	0.0251	0.0252	0.0182	0.0203
81	0.0251	0.0252	0.0217	0.0227
82	0.0251	0.0252	0.0251	0.0252
83	0.0251	0.0252	0.0251	0.0252
84	0.0251	0.0252	0.0251	0.0252
85	0.0286	0.0504	0.0263	0.0336
86	0.0286	0.0504	0.0274	0.0420
87	0.0286	0.0504	0.0286	0.0504
88	0.0286	0.0504	0.0286	0.0504
89	0.0286	0.0504	0.0286	0.0504
90	0.0296	0.0683	0.0289	0.0564
91	0.0296	0.0683	0.0293	0.0623
92	0.0296	0.0683	0.0296	0.0683
93	0.0296	0.0683	0.0296	0.0683
94	0.0296	0.0683	0.0296	0.0683
95	0.0306	0.1115	0.0299	0.0827
96	0.0317	0.1115	0.0306	0.0971
97	0.0328	0.1115	0.0317	0.1115
98	0.0340	0.1115	0.0328	0.1115
99	0.0351	0.1115	0.0340	0.1115
100	0.0364	0.1115	0.0352	0.1115

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