Mortality in people diagnosed with type 2 diabetes at an older age: a systematic review

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Abstract

Objectives: to review all published observational studies reporting on all-cause mortality in patients with type 2 diabetes to determine the degree of increased mortality when diagnosed at an older age.

Design: systematic literature search.

Setting: the review included studies carried out in populations from Germany, United Kingdom, United States, Japan, Italy, Western Australia, Netherlands and Sweden.

Measurements: Medline, CINAHL, EMBASE, National Research Register and Cochrane Reviews were systematically searched from 1975 to 2004. We identified observational studies that reported overall mortality for people diagnosed with type 2 diabetes when they were over the age of 60, compared with a non-diabetic population. Outcome measures were expressed as risk ratios or relative risks.

Results: among 14 eligible studies, one study reported reduced mortality for patients diagnosed with type 2 diabetes over the age of 60, whereas another found virtually no increased risk of mortality. However, 7 of the 14 studies reported increased mortality in all patients diagnosed when older, and 5 studies for certain subgroups only. A meta-analysis showed the combined relative risks (with 95% CI) of increased mortality for men diagnosed between the ages of 60 and 70 to be 1.38 (1.08–1.76) and 1.13 (0.88–1.45) for men diagnosed aged 70 years or older. A similar pattern was found for the same age groups for women, with combined relative risks of 1.40 (1.10–1.79) and 1.19 (0.93–1.52) respectively.

Conclusion: increased mortality associated with a diagnosis of type 2 diabetes at an older age is lower than that reported for the general older diabetic population.

Keywords: type 2 diabetes, mortality, older people

Introduction

The incidence and prevalence of diabetes is increasing, with the worldwide prevalence estimated to almost double by 2030 [1]. Type 2 diabetes accounts for 85–90% of the diabetic population and is more commonly associated with older people [2]. The prevalence of diabetes is highest in people over 65 years of age, with the highest incidence also occurring in this age group [1, 3, 4]. The burden of diabetes in the older population is set to increase even further because of demographic change, the rising incidence of diabetes in all age groups [1] and the longer survival of people who are diagnosed at a younger age [5].

Older people with type 2 diabetes may have needs different from younger diabetic people, so both age and life expectancy should influence management, as well as any co-morbidities they may suffer from [6]. Older people with diabetes are under-represented in clinical trials and as a result are often treated according to guidelines based on expert opinion and the dubious extrapolation of results from clinical trials in younger people [7]. It is rarely acknowledged that older people with type 2 diabetes are a heterogeneous group consisting of patients with newly or recently diagnosed diabetes and patients who may have had diabetes for many years [8, 9].
People diagnosed with type 2 diabetes at an older age account for approximately half of all new cases. In the Poole Diabetes Study, just over half of all new cases (51%) were diagnosed in people over the age of 65 [10], and a similar proportion of 47% was found more recently for the equivalent age group in Tayside, Scotland [11]. Yet research in this particular group is almost non-existent. We know that diabetes affects mortality, with numerous studies highlighting the reduced life expectancy associated with a diagnosis of diabetes [12–14], with mortality found to be increased almost 4-fold [14] and even as high as 9-fold [12] in older diabetic people compared with non-diabetic people. However, it is not clear how diabetes affects mortality when the diagnosis is made at an older age. Therefore, the aim of this study was to review all published observational studies reporting on all-cause mortality for people diagnosed with type 2 diabetes at an older age to evaluate the degree of increased mortality compared with the non-diabetic population.

Methods

Search strategy

A systematic literature search was conducted using Medline covering the period from January 1975 to December 2004. ‘Type 2’ diabetes mellitus was not mentioned separately from ‘diabetes mellitus’ before 1983; so, two separate searches were conducted. The terms under which each search was carried out are as follows: Search 1: Type 2 Diabetes (Explode), Mesh Heading ‘Mortality’, Year 1983–2004

Search 2: Diabetes (Focus), Mesh Heading ‘Mortality’, Year 1975–1982

Both searches were limited to ‘Humans’, and only studies in English were considered.

Search 1 resulted in 403 papers and Search 2 in 41 papers, with a final total of 440 papers (4 papers were included in both). The abstract of each paper was checked to see if it met the criteria for this review. If insufficient information was available in the abstract, the full paper was retrieved. The reference lists from the eligible papers were also checked, and any paper considered relevant, but not included in the original Medline search, was added. The same search strategy and methodology was then used in the following additional databases: The National Research Register (59 papers), CINAHL (48 papers), EMBASE (54 papers) and the Cochrane Library (18 papers).

Selection criteria

Papers had to meet the following criteria to be included in this review. The study had to be observational and report overall mortality, describe type 2 diabetes alone (rather than type 2 and type 1 combined) and report overall mortality statistics specifically for a group of patients whose first diagnosis of type 2 diabetes had occurred after the age of 60. There also had to be a comparison (general) population. All papers considered a cohort of type 2 diabetic patients followed over time prospectively or retrospectively.

Statistical analysis

A summary (forest) plot was produced displaying the relative risk with 95% CI for each of the studies that provided the required figures. The point estimates and standard errors were computed using logarithmic transformation. Relative risks for different age groups at diagnosis were compared by testing for homogeneity using Q (chi-square) statistics. We calculated pooled averages using weights inversely proportional to the variants.

Results

Fourteen studies met our selection criteria [15–28] (Table 1), of which 11 were found in the original Medline search and 3 from the reference sections of these papers. Seven of the studies were carried out prospectively using historical information [15, 16, 19, 22, 23, 27, 28], and seven were prospective cohort studies [17, 18, 20, 21, 24–26]. The studies included populations from Germany [16], United Kingdom [19, 21, 27, 28], United States [15, 26], Japan [17, 18], Italy [23], Western Australia [20], Netherlands [22], Denmark [25] and Sweden [24] from 1975 to 2004. One study reported a reduced mortality for patients diagnosed with type 2 diabetes over the age of 60 [17], whereas another found virtually no increased risk of mortality [18]. However, of the 14 studies reported increased mortality in all patients diagnosed when older [15, 19, 21, 22, 24, 26, 27]. One study showed increased mortality for those diagnosed before the age of 70 but not thereafter [20], and in four other studies, increased mortality was found when diagnosed before the age of 75, but this was not replicated for certain age/sex groups over 75 years [16, 23, 28]. Another study found no increased mortality in patients over 80 years of age [25]. A summary of the results from the studies that provided a figure for increased risk of mortality is shown in Figure 1. The relative risks (with 95% CI) are displayed for patients diagnosed aged 60 years or older. Because of the evidence for an age effect, a meta-analysis was conducted using studies that reported separately for age groups and sex (Figures 2 and 3). These showed the combined relative risks (with 95% CI) of increased mortality for men diagnosed between the ages of 60 and 70 to be 1.38 (1.08–1.76), and 1.13 (0.88–1.45) for men diagnosed aged 70 years or older. A similar pattern was found for the same age groups for women, with combined relative risks of 1.40 (1.10–1.79) and 1.19 (0.93–1.52), respectively.

Discussion

This review indicates that people who are diagnosed with type 2 diabetes at an older age have slightly increased mortality compared with the general population. Although one Japanese study found that people diagnosed with type 2 diabetes over the age of 60 actually had lower mortality than the general population over a 4-year follow-up and another found only a very modest increase [17, 18], the values obtained were not statistically significant (P<0.5). It seems that the mortality rate from diabetes in Japan is known to be lower than that in western countries [29], and it is difficult to
Table 1. A summary of all 14 studies included in the review

<table>
<thead>
<tr>
<th>First author</th>
<th>Follow-up (yrs)</th>
<th>Males</th>
<th>Females</th>
<th>Setting</th>
<th>Diagnostic method</th>
<th>Measure of increased mortalitya</th>
<th>Age at diagnosis (yrs)</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>137</td>
<td>322</td>
<td></td>
<td></td>
<td></td>
<td>60–64</td>
<td>1.35 (1.49)</td>
<td>1.90 (1.48)</td>
<td></td>
</tr>
<tr>
<td>Panzar (1981) [16]</td>
<td>1 (10)b</td>
<td>93</td>
<td>220</td>
<td>Germany</td>
<td>General population</td>
<td>Blood glucose tests, WHO 1965 recommendations</td>
<td>70–74</td>
<td>1.37 (1.21)</td>
<td>1.34 (1.26)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>75–79</td>
<td>1.66 (0.96)</td>
<td>0.95 (1.04)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mihara (1983) [17]</td>
<td>4</td>
<td>291 (50)</td>
<td>112</td>
<td>Japan</td>
<td>General population</td>
<td>Diagnostic criteria recommended by Japan Diabetic Society</td>
<td>60+</td>
<td>0.64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sasaki (1989) [18]</td>
<td>9.4</td>
<td>–(89)</td>
<td></td>
<td>Japan</td>
<td>General population</td>
<td>GTT</td>
<td>65+</td>
<td>1.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duncan (1992) [19]</td>
<td>9</td>
<td></td>
<td></td>
<td>United Kingdom</td>
<td>General population</td>
<td>Random and fasting blood glucose tests</td>
<td>60+</td>
<td>Survival curves show excess mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knuiman (1992) [20]</td>
<td>6.7</td>
<td>60 (19)</td>
<td>61 (12)</td>
<td>Western</td>
<td>General population</td>
<td>Self reported</td>
<td>60–69</td>
<td>1.48 (1.06–1.90)</td>
<td>1.79 (1.24–2.34)</td>
<td></td>
</tr>
<tr>
<td>Crosson (1994) [21]</td>
<td>4.5</td>
<td>39 (24)</td>
<td>36 (11)</td>
<td>Australia</td>
<td>Normal glucose</td>
<td>Diabetes register, GTT, interpreted using 1985 WHO criteria</td>
<td>70+</td>
<td>1.42 (0.97–1.87)</td>
<td>0.92 (0.54–1.30)</td>
<td></td>
</tr>
<tr>
<td>Grauw (1995) [22]</td>
<td>6.8</td>
<td>19 (7)</td>
<td></td>
<td>United Kingdom</td>
<td>Tolerant subjects</td>
<td>Patient files that were in agreement with WHO criteria</td>
<td>65–74</td>
<td>3.0 (1.3–6.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muggge (1995) [23]</td>
<td>5</td>
<td></td>
<td></td>
<td>Italy</td>
<td>Non-diabetic population</td>
<td>Family physicians where diagnosis was based on National Diabetes Data Group criteria, diabetes clinics, prescriptions (two of above used)</td>
<td>65–74</td>
<td>1.23 (1.02–1.47)</td>
<td>1.34 (1.16–1.54)</td>
<td>1.30 (1.16–1.45)</td>
</tr>
<tr>
<td>Tibbin (1996) [24]</td>
<td>13</td>
<td>35</td>
<td></td>
<td>Sweden</td>
<td>Non-diabetic population</td>
<td>Screening based on WHO criteria</td>
<td>67–80</td>
<td>1.10 (0.73–1.59)</td>
<td>1.52 (1.20–1.90)</td>
<td>1.38 (0.73–1.59)</td>
</tr>
<tr>
<td>de Fine Olivarius (1997) [25]</td>
<td>6</td>
<td>375 (112)</td>
<td>371 (76)</td>
<td>Denmark</td>
<td>Danish population</td>
<td>Fasting whole blood glucose 7 mmol/L or over or fasting plasma glucose 8 mmol/L or over</td>
<td>60–79</td>
<td>1.14 (1.02–1.29)</td>
<td>1.22 (1.09–1.35)</td>
<td></td>
</tr>
<tr>
<td>Roper (2000) [26]</td>
<td>6.4</td>
<td>405</td>
<td></td>
<td>United States</td>
<td>Non-diabetic population</td>
<td>Blood sample and 2 hour glucose challenge or fasting blood glucose levels based on WHO criteria</td>
<td>65+</td>
<td>1.36 (1.06–1.73)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roper (2001) [27]</td>
<td>6</td>
<td></td>
<td></td>
<td>United Kingdom</td>
<td>Non-diabetic population</td>
<td>Diabetes Register, no more information given</td>
<td>65+</td>
<td>1.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tan (2004) [28]</td>
<td>4.6</td>
<td>3,594 (909)</td>
<td></td>
<td>United Kingdom</td>
<td>Comparators from general population</td>
<td>Diabetes Register, based on WHO criteria</td>
<td>75–84</td>
<td>1.47 (1.21–1.78)</td>
<td>1.15 (0.97–1.38)</td>
<td></td>
</tr>
</tbody>
</table>

For example, standardised mortality ratio and relative risks.

aPanzram (1981)—this study was followed up after both first and tenth year. Numbers contained within () refer to the 10-year follow-up.

bInformation not available.
judge whether the different health-care context in Japan 20 years ago makes these results incomparable. For example, diabetic people referred to in the Japanese studies were identified in hospital clinic or a diabetes centre, but no details are provided as to whether some may have been treated in primary care. Note though that we did not require a standardised diagnosis of type 2 diabetes as a selection criterion for studies in this review; therefore, this limitation is a general one.

Most of the studies reported an increased mortality in patients with type 2 diabetes, but this was relatively modest and much less than that reported for older diabetic patients in general [12, 14, 30]. Only two studies reported risk ratios of more than two, that is, suggesting that older patients diagnosed with
Type 2 diabetes have at least double the risk of mortality compared with the general population [15, 21]. However, one of these was an actuarial analysis carried out in the United States where the comparison population was 'Standard Lives', the unspecified nature of this comparison group making interpretation difficult [15]. Also, the diabetic population consisted of only patients who applied for life insurance and therefore is unlikely to be representative of the general diabetic population. The second was a large study of over 800 patients carried out in the United Kingdom but with only 19 patients newly diagnosed within our age group of interest (60+), with 4½ years of follow-up [21]. This small sample size is reflected by the presence of wide confidence intervals.

The results of the remaining studies were consistent in finding that the increased mortality associated with a diagnosis of type 2 diabetes is less than 1½-fold for men and only very slightly higher for women for follow-up periods of 5–10 years [20, 23, 28]. This consistency is notable, given the differences in methodology between the studies, in terms of setting, comparison population, time of the study and diagnostic criteria for diabetes (summarised in Table 1), especially as WHO criteria for diabetes have changed over time. We took a pragmatic approach in our review and did not impose stringent methodological criteria for inclusion, nor indeed did we require a standardised diagnosis of diabetes, as this would have greatly reduced the studies available for review, but we recognise this as a limitation. However, there is no indication that studies with less stringent criteria for diagnosis of diabetes (e.g. by self-report) have lower mortality differentials. Similarly, although some of the studies are relatively old (there are four studies over 15 years old), the mortality differential between diabetic and non-diabetic people does not seem to have lessened in recent years as a result of more modern interventions. We believe that the consistency between studies with very different methodologies reinforces the overall conclusion.

For studies reporting men and women together, again increased mortality is never greater than 1½-fold [24, 26, 28]. Another consistent finding was that the degree of increased mortality reduces as age at diagnosis increases [16, 19, 20, 22, 23, 27, 28], with diagnoses over the age of 70 [20] and 75 [16, 23] conferring no increased mortality at all in men [16, 20, 23] and women [16, 20]. Given the similarity in results from the studies, we judged that a meta-analysis was appropriate, which indicated that patients diagnosed over the age of 70 had a lower relative risk of mortality compared with patients diagnosed between the ages of 60 and 70. Very little difference was found between males and females, with females having only a marginally higher combined relative risk of mortality.

Four studies that displayed their data graphically in the form of survival curves also showed a reduced survival rate in older onset patients (over 60 years) compared with non-diabetic people, but this becomes less as age at diagnosis increases [19, 22, 25, 27]. For example, a diagnosis at the age of 60 showed a reduction in life expectancy of 4 and 6 years for men and women, respectively, reducing to around 2 and 4 years when diagnosis occurred over the age of 70 [27]. The only study to look separately at patients diagnosed over

In summary, while it is perhaps not surprising that a diagnosis of type 2 diabetes made at an older age has less impact on mortality, probably because there is less time for the detrimental effects of diabetes to manifest themselves, this review challenges the assumption that it has no effect at all (as reported in a previous study for older newly diagnosed men [28]). However, the increased mortality associated with a diagnosis of type 2 diabetes at an older age is relatively low, and older newly diagnosed patients can therefore be reassured that their increased mortality compared with non-diabetic people is substantially less than that reported for the older diabetic population in general.

Key points
• The mortality of older diabetic people may be up to four times higher than that of older non-diabetic people.
• People diagnosed with type 2 diabetes at an older age account for approximately half of all new cases of type 2 diabetes.
• In a systematic review, we investigated increased mortality in this particular subgroup of diabetic people and found that their risk of mortality was only slightly higher than that of non-diabetic people.

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The Chief Scientist Office funded the study but was independent of the study design, execution, analysis and write-up.

Conflicts of interest/financial disclosure
None to declare.

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