Can self-rated health be used for risk prediction in patients with type 2 diabetes?

Alison J. Hayes Ph.D, Philip M. Clarke Ph.D, Paul G. Glasziou Ph.D, R. John Simes FRACP, Paul L. Drury FRACP, Anthony C. Keech. FRACP

1. Public Health, University of Sydney, NSW Australia.  
2. Primary Care, University of Oxford, United Kingdom.  
3. NHMRC Clinical Trials Centre, University of Sydney, NSW, Australia.  

Running Title: Self-rating for risk prediction in type 2?

Corresponding Author:  
Dr Alison Hayes  
Public Health, University of Sydney,  
NSW 2006 Australia; alisonh@health.usyd.edu.au

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ABSTRACT

Objective: To investigate whether self-rated health using the EQ VAS is an independent predictor of vascular events and major complications in people with type 2 diabetes after controlling for standard clinical risk factors.

Research design and methods: The study is based on 7348 people with a mean follow-up of 2.4 years after completing the EQ-5D questionnaire. We used Cox proportional hazards modeling to estimate hazard ratios associated with EQ VAS scores after controlling for baseline covariates: age, sex, smoking status, diabetes duration, HbA1c, systolic blood pressure, body mass index, plasma lipids and prior clinical history.

Results: A 10 point higher EQ VAS score was associated with a 6% (95% CI:1,11) lower risk of vascular events, and a 22% (95% CI:15,28) lower risk of diabetic complications.

Conclusions: Self-rated health using the EQ VAS provides additional information on patient risk that is over and above that determined from clinical risk factors.
Several risk models are available for people with diabetes (1-3) based on clinical risk factors such as systolic blood pressure and HbA1c. These provide a means of identifying high risk patients to target the management of diabetes care (4) and can be used for economic evaluation of diabetes therapies (5). To date, little attention has been given to the role of subjective measures of health in risk assessment and few studies have considered outcomes other than mortality, which are particularly relevant to people with diabetes whose risk of cardiovascular and other complications is elevated (6).

Studies on self-rated health have consistently shown that people who report their health status as “poor” or “fair” have higher mortality than those reporting their health as “excellent” or “good” (7). Self-rated health may also be measured with a visual analogue scale (VAS), for example the EQ VAS from the EQ-5D (8) - a thermometer like scale with zero representing the worst, and 100 the best imaginable health state. In this study we examine whether self-rated health measured by the EQ VAS is an independent predictor of cardiovascular events and major diabetic complications in people with type 2 diabetes.

RESEARCH DESIGN AND METHODS

The study is based on Australian and New Zealand participants of the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study (9) who participated in a quality of life sub-study. We focused on two endpoints: cardiovascular events and other diabetes-related complications (see Table 1 and online appendix available at http://care.diabetesjournals.org).

Baseline values of clinical risk factors were calculated as an average of all available measures between trial randomisation and first administration of the EQ-5D questionnaire. Mean values from the whole sample were imputed for patients (<1% of the sample) with any missing baseline risk factors.

Log-rank methods without adjustment for covariates were used to test for significant differences in risk between patients categorised into approximate quartiles according to their EQ VAS scores.

We used Cox proportional hazards modeling to estimate hazard-ratios associated with EQ VAS scores after controlling for baseline covariates; age, sex, smoking status, diabetes duration, HbA1c, systolic blood pressure, body mass index (BMI), plasma lipids and prior clinical history. We investigated any heterogeneity in the hazard ratio of the VAS by an interaction term with prior events. Risk factors were dropped from the models through stepwise elimination if their hazard ratios were not significantly different from one (P>0.1). The proportional hazards assumption was tested using Schoenfeld residuals (10). Stata/SE version 9.1 was used for all statistical analyses (11).

RESULTS

A total of 7348 patients (87.5% of all Australian and New Zealand patients in the FIELD trial) consented and correctly answered a written EQ-5D questionnaire at an average of 2.9 years after trial randomisation, generating a mean follow-up of 2.4 years. The average (SD) patient age was 66 (6.9) years; 91.8% were white and 38% were female. The mean (SD) EQ VAS score reported was 77.8 (15.9); other baseline risk factors were similar to those reported in the FIELD trial (12).

The cumulative hazard of vascular events and complications was stratified by patients’ baseline EQ VAS score (p<0.001), with differences most pronounced for patients scoring below 70 (see online appendix).
After adjustment for other risk factors, EQ VAS scores remained significant independent predictors of cardiovascular events, with a 10 point increase in VAS score associated with a 6% (95% CI 1–11) decrease in the risk of a future event (Table 1). Patients with a history of any prior event were three times more likely to experience a vascular event.

A 10 point change in EQ VAS was associated with a 22% (95% CI 15–28) reduction in the risk of complications for patients with no known clinical history of prior events. For individuals with a history of prior events, the EQ VAS score was not significantly associated with future complications (p=0.054).

CONCLUSIONS
This study demonstrates that self-rated health reported on the EQ VAS provides additional information on the risk of vascular events and complications in people with type 2 diabetes that is over and above that determined from clinical history and established risk factors.

Possible reasons for patients with lower self-rated health having poorer outcomes are that self-rated health is a marker of disease severity, or that it could indicate diabetes-related complications at a sub-clinical stage. Interestingly, the increase in relative risk associated with the EQ VAS is less for acute events such as MI than for more chronic complications.

Self-rated health has received little attention in the literature on risk assessment for diabetes and was not listed in a recent editorial of emerging risk factors for cardiovascular disease (13), or in a statement on risk factors for cardiovascular disease in diabetes (14). One recent study indicated that measures of social-functioning were significant predictors of mortality and disability in people with diabetes (15) and the Wisconsin Epidemiologic Study of Diabetic Retinopathy showed that health-related quality of life can predict mortality in people with type 2 diabetes (16). Our study extends these findings by demonstrating that self-reported health can predict which patients are at a higher risk of major complications of diabetes, even after taking into account established risk factors.

The EQ VAS could potentially be used in a clinical setting to target primary prevention in diabetes patients. Our results suggest that a 10 point difference in VAS score stratifies risk of complications to a greater degree than a one unit change in the ratio of total cholesterol to HDL cholesterol, or 10 years longer duration of diabetes. A key feature of the VAS in this setting is its simplicity, as it only requires patients to indicate a score on a 0-100 scale to represent their current health status.

The models presented here focus on a single measure of self-rated health and demonstrate how variations in this measure across a population, affect subsequent outcomes. Whether change in health status at an individual level can also predict risk is unknown. Addressing this question would require repeated measures of EQ VAS on the same individual.

ACKNOWLEDGEMENTS
A list of acknowledgements is contained in the online appendix.
REFERENCES

### TABLE 1. Cox Proportional hazard models for fatal and non-fatal vascular events, and complications of diabetes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vascular events*</th>
<th>Diabetic complications†</th>
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</thead>
<tbody>
<tr>
<td>Number of Individuals</td>
<td>7348</td>
<td>7348</td>
</tr>
<tr>
<td>Number of patients with outcome</td>
<td>453</td>
<td>193</td>
</tr>
<tr>
<td>EQ VAS per 10 point increase</td>
<td>0.94</td>
<td>0.78</td>
</tr>
<tr>
<td>EQ VAS per 10 point increase (no prior events)</td>
<td>-</td>
<td>0.93</td>
</tr>
<tr>
<td>EQ VAS per 10 point increase (prior events)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>0.77</td>
<td>0.57</td>
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<tr>
<td>BMI</td>
<td>-</td>
<td>1.05</td>
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<tr>
<td>HbA1c per %</td>
<td>1.20</td>
<td>1.45</td>
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<tr>
<td>Age per 10 years</td>
<td>1.49</td>
<td>1.79</td>
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<tr>
<td>Diabetes duration per 10 years</td>
<td>-</td>
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<td>Current smoker</td>
<td>1.58</td>
<td>2.27</td>
</tr>
<tr>
<td>Systolic blood pressure (per 10mm Hg)</td>
<td>1.16</td>
<td>-</td>
</tr>
<tr>
<td>Total/ HDL cholesterol ratio</td>
<td>1.14</td>
<td>1.13</td>
</tr>
<tr>
<td>Prior events‡</td>
<td>3.31</td>
<td>-</td>
</tr>
</tbody>
</table>

* Vascular events included vascular death, MI, stroke and hospitalized angina. During follow-up, 453 patients had one or more vascular events, comprising: vascular deaths (89), MI (129), stroke (83), hospitalized angina (152).

† Diabetic complications included heart failure, lower extremity ulcers, amputation, renal dialysis. During follow up, 193 patients experienced diabetic complications, with the first complication being heart failure (95), ulcers (44), amputations (30), ulcer plus amputation (7) and renal dialysis (17).

‡ A total of 1454 patients had a history of any prior events (non-fatal vascular events or diabetic complications defined above) at the time of administration of the EQ-5D questionnaire.

A note in interpretation: A 10 point increase in EQ VAS is associated with a 6% (1-0.94) lower risk of vascular events and a 22% (1-0.78) lower risk of major complications (patients with no prior events). Separate hazard ratios are presented where there are significant differences in the terms for EQ VAS interacted by prior events.