Translating patient related outcome measures into practice—lessons to be learnt

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Provenance: This is an invited Editorial commissioned by Section Editor Qi-Nan Wu, MD, PhD (Associate Professor of Endocrinology Department, South West Hospital, Third Military Medical University, Diabetic Foot Diagnosis & Treatment Medical Center of Chongqing, Chongqing, China), and Guest Section Editor Xiaotian Lei [The First Hospital Affiliated to Army Medical University (Southwest Hospital), Chongqing, China].

Comment on: Bradley C, Eschwège E, de Pablos-Velasco P, *et al.* Predictors of Quality of Life and Other Patient-Reported Outcomes in the PANORAMA Multinational Study of People With Type 2 Diabetes. Diabetes Care 2018;41:267-76.

Submitted Feb 21, 2018. Accepted for publication Feb 28, 2018.

doi: 10.21037/atm.2018.03.11

View this article at: http://dx.doi.org/10.21037/atm.2018.03.11

The landscape of type 2 diabetes (T2D) therapy is continuously evolving. Recent therapeutic trials showing cardiovascular and mortality benefit have influenced its management in clinical practice (1,2). It is increasingly apparent that T2D is a heterogeneous entity (3). Hence, there is a need to emphasize patient-centred approaches to care (3). In current clinical practice, metabolic and biochemical targets remain the predominant drivers for diabetes management. Patient related outcome measures (PROMs) have been a topic of research interest, but its additional value in routine clinical practice remains uncertain. This editorial explores the findings from the recently published PANORAMA study and its clinical implications (4).

Study summary

The PANORAMA study evaluated factors that predict PROMs, such as quality of life and health status in people with T2D, by analyzing cross sectional data collected from nine countries. The study randomly or consecutively selected 5,813 people with T2D, from primary and secondary care. PROMs analysed included the Audit of Diabetes-Dependent Quality of Life (ADDQol), Diabetes Treatment Satisfaction Questionnaire (DTSQ), Hypoglycaemia Fear Survey-II subscale, and EuroQol-5 Dimension visual analog scale (EQ-VAS). The predictive factors analysed included patient characteristics, physician-reported adherence, complications and HbA1c (4).

In spite of the mean overall QoL score being rated as 'good', three quarters of the studied population reported that their diabetes-related QoL (DQoL) would have been 'better' without the disease. 'Freedom to eat as I wish' was the factor most adversely affecting QoL. Treatment escalation to three oral anti-diabetic agents (OADs) or insulin predicted worse QoL. Higher Diabetes treatment-related satisfaction Questionnaire (DTSQ) score was associated with lower HbA1c level and physician-reported treatment adherence. Although hypoglycaemia concern was generally low among this cohort, insulin therapy predicted an increase in the fear of hypoglycaemia.

The authors of the study used EQ-VAS to assess health status, to succinctly differentiate it from reported QoL. Depression was the strongest predictor of worse patient-perceived health status. Other predictors of worse health status were presence of microvascular and macrovascular disease, higher BMI and frequency of physician visits (4).

The strengths of the study included use of multiple, well-validated assessments of PROMs and recruitment of large multinational cohorts on varied therapeutic regimens including oral agents, GLP-1 agonists and insulin. This provides a broader insight into factors that may influence

patients' perspective of their condition (4). An important limitation is the baseline HbA1c of recruited participants (52 mmol/mol, 6.9%), which is lower than that reported from national audits in T2D (5), thus limiting the generalizability of the study. Other limitations include the small selection bias towards patients with microvascular disease and the method of recruitment (consecutive sampling) in countries where electronic health records were not established. The use of cross-sectional data also meant causal relationships could not be determined (4).

Implications for current management strategies

Dietary modification is an essential intervention in T2D, either on its own or in combination with other therapies (6). Its efficacy has been proven, particularly in studies adopting some level of carbohydrate reduction (7). Consensus on standardizing dietary approach, however, remains elusive. In the PANORAMA study, all participants were offered 'dietary and exercise advice'. It should be noted that the majority of patients enrolled were from primary care settings across many countries. The time constraints and resources available in this often busy clinical setting, may cast some doubt on the robustness and validity of this approach in reality. One could argue that this is broadly reflective of current, often suboptimal practice.

The recently published DiRECT study (8) may provide some interesting insight. People with T2D of less than 6 years duration on OADs only were recruited from primary care and underwent a 12-month intensive primary-care led weight management programme. The co-primary outcomes of 15 kg weight loss and diabetes remission reached statistical significance. QoL health status measures, as evaluated by the EuroQol 5 Dimension (EQ-5D) collected at 12 months, showed statistically significant improvements. The study is particularly relevant as the majority of people with T2D are managed in primary care. It is speculated that the reported improvement in health status was the consequence of improved health and well-being, and reduction in medication burden and associated side effects, psychological and physical complications of obesity and disease-related stigma. Lifestyle modification has been shown to be cost effective, and it is plausible that wider structured implementation in primary care could result in multiple benefits to patients and the health service (9). It is important to note that those with more complex co-morbidities were excluded and thus individualized approaches focusing on PROMs may be more appropriate in such cases (8,10).

The generic ADDQol and DQoL found that 'lack of freedom to eat as I wish' had the most negative impact on QoL. Unhealthy dietary patterns established over many years have been associated with increased rates of obesity (11) contributing significantly towards the epidemic of T2D currently seen (8). As most healthcare professionals would consider dietary alterations to be a positive clinical intervention for people with T2D, it is important to be aware this may be seen as restrictive and detrimental to their quality of life. This is in concordance with and may partly explain our own clinical experience, in which the rate of poor compliance with diet and lifestyle modification is highly prevalent. Therefore, better understanding of the link between PROMs and lifestyle modification strategies may help healthcare professionals adopt more suitable approaches to implement and support patients to achieve their goals (12).

In type 1 diabetes, structured education has been shown to be successful in improving QoL and diabetes-related outcomes. The dose adjustment for normal eating (DAFNE) study group evaluated the impact of structured education on HbA1c, hypoglycaemia and QoL (ADDQol). Significant improvements in HbA1c and QoL were observed. Notably, significant improvements to 'dietary freedom' were seen (13). The utility of structured education strategies for people with T2D however has remained controversial. The DESMOND study showed that a patient-centered education programme improved some diabetes-related outcomes in those newly diagnosed with T2D. It showed benefits in weight loss and smoking cessation, but no significant effect on HbA1c and QoL (14); this was further confirmed in a 3-year follow up study (15). Results from the PANORAMA study thus indicate that there may be a need to develop a bespoke, sustained approach to education in T2D, whilst focusing on improving PROMs to ensure adherence.

Treatment escalation is primarily driven by HbA1c targets. In asymptomatic patients in particular, such recommendations often involve challenging consultations especially when therapy results in side effects without improvement in PROMs. The PANORAMA study showed that lower treatment satisfaction was associated with higher HbA1c, combination therapy with insulin and OAD, physician-reported patient reluctance to intensify treatment, depression, weight gain and abdominal pain. Combination therapy with insulin and OAD or being on three OADs also adversely impacted on diabetes-related quality of life. Variable expertise in non-specialist care, such as in primary care settings,

may have led to suboptimal patient-education regarding mechanism of drug action, evidence of therapeutic value and side effects, to support patient expectations. Rise *et al.* performed a qualitative analysis of diabetes education on a series of lifestyle measures including diet, physical activity and perception of OADs. Patients were shown to have a more positive outlook of their therapy following education (16). It remains to be shown whether treatment de-escalation could lead to improvement in PROMs.

Insulin therapy is often perceived as a more invasive and unwanted treatment escalation. This is compounded by the need for more frequent blood glucose monitoring, risk of hypoglycaemia and undesirable weight gain. Known independent predictors for fear of hypoglycaemia include insulin use and a previous episode of hypoglycaemia, which is also associated with sulphonylurea use. Interestingly, higher HbA1c levels were associated with a reduced diabetes-related quality of life. This may be due to more frequent symptomatic dysglycaemia, the need for higher treatment intensity and associated adverse effects, and microvascular complications. The GUIDANCE study looked at PROMs in insulin-treated T2D, and found similar outcomes. Higher DTSQ scores were associated with having received diabetes education, macrovascular complications and better health status (17).

It is also important to examine the impact of other therapies on PROMs which form an essential part of T2D management, such as antihypertensive agents and statins. In PANORAMA, higher blood pressure was marginally associated with better QoL, possibly due to lesser tablet burden and side effects. The SPRINT research group compared PROMs in patients with intensive blood pressure control to standard treatment (18). Although the authors reported no difference between the groups, people with diabetes were excluded from the study and different QoL measurements were used (18). However, in PANORAMA, combination T2D therapy and consequently higher treatment burden was associated with worse PROMs (4). The impact of statin use on PROMs has not been specifically investigated, although from our own clinical experience and many others, a small but significant number of patients have reported experiencing side-effects with statins, adversely affecting their QoL.

PROMs in clinical practice—ready for prime time?

In a busy clinical setting, the focus is more often on quantifiable disease-related targets, rather than patient-related outcomes. QoL measurements in clinical practice may help focus the consultation on issues that matter the most to patients, promote shared decision making, gauge treatment response and adherence, and help identify hidden issues such as depression (19). Depression was a common factor adversely affecting a range of PROMs (4). Currently, PROMs are predominantly utilized as a research tool. This raises the question of transferability to routine clinical practice. Most research methodologies are designed for evaluation over a fixed time period, whereas the focus in clinical practice is to monitor disease status and treatment efficacy over years. Current PROMs scores also present results quantitatively as means or averages, and while this is of value in research, its relevance in clinical practice is less clear due to notable variability sometimes seen between individuals (19).

PANORAMA highlighted the number of validated PROMs available. Clearly, it is not feasible from a pragmatic or practical perspective to use them all in routine clinical practice. A range of factors influencing PROMs were identified across these platforms, emphasizing the need to develop a unified, standardized PROM which can be applied in a timely manner in a busy clinical practice. The format should be intuitive, accessible and possess an easy-to-understand scoring system to ensure optimal implementation by health care professionals. Integration with portable device technology, such as tablets or mobile phone apps, may improve uptake of PROMs.

Future considerations

It is increasingly apparent that multimodal and multidisciplinary management strategies in T2D are needed to achieve optimal outcomes. PROMs clearly have an important role in this context. Future considerations should include individualized management within a true multidisciplinary team including physicians, specialist nurses, dieticians, physiotherapists and psychologists (3,8,20). This approach has the potential to result in improved clinical and patient-related outcomes.

Physician-reported treatment adherence remains the strongest predictor for patient treatment satisfaction, which is also associated with better generic QoL (ADDQoL). Treatment adherence however is a complex area, and there is still a lack of evidence to help identify common characteristics in patients with and without good treatment adherence (19). Medication non-adherence imposes a

significant burden on the health service. Recent systematic and Cochrane reviews on the subject have failed to show convincing outcomes with interventions to improve treatment adherence (21,22). It remains to be seen if novel diabetes devices and technologies, such as flash glucose monitoring, will improve adherence and show QoL benefits especially in insulin-treated T2D (23,24).

There is an unmet need to identify patient-related factors influencing positive and negative adherence behaviours and develop effective strategies to address this issue. The PANOROMA study highlighted some interesting findings, suggesting that perhaps other non-clinical, as yet unidentified factors contribute towards adherence behaviour. Unfortunately in our experience, PROMs are still not routinely employed in treatment settings for diabetes management, and recommendations for their use are still absent from most national treatment guidelines (25). This suggests that more evidence of clinical benefit and validation across wider patient populations is needed, to convince healthcare professionals, payers and providers of its incremental value to patient care.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Majeed W, Thabit H. Translating patient related outcome measures into practice—lessons to be learnt. Ann Transl Med 2018;6(10):187. doi: 10.21037/atm.2018.03.11

