

# HUMANISTIC BURDEN ASSOCIATED WITH DIABETIC RETINOPATHY: EVIDENCE FROM A LITERATURE REVIEW

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## BACKGROUND

- Diabetic Retinopathy (DR) is the most common microvascular complication of both Type-1 and Type-2 diabetes mellitus (T1DM and T2DM) that can lead to vision loss.<sup>(1)</sup>
- Globally, DR is the leading cause of blindness among working-age adults<sup>(1)</sup>. It is estimated that the number of people with vision threatening DR (VTDR) will increase to 56.3 million by 2030.<sup>(2,3)</sup>
- There are two primary types of DR: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). PDR is the more advanced form of the disease.<sup>(4)</sup>
- Diabetic macular oedema (DME) is the most common manifestation of DR leading to vision loss and can complicate any stage of DR.<sup>(5)</sup>
- Visual impairment may have serious consequences in diabetic patients, profoundly affecting health- and vision-related quality of life.<sup>(6)</sup>

## OBJECTIVE

- The aim of this review was to collate evidence pertaining to the humanistic burden associated with DR.

## METHODS

- MEDLINE®, EMBASE® and the Cochrane Library databases were searched using disease-specific search terms and keywords for outcomes of interest from database inception to January 2019.

### Selection of studies

- Abstracts of all identified studies were screened for relevance, followed by a full-text evaluation for inclusion based on predefined criteria presented in Table 1.

Table 1. Literature review methodology

| Sources                | Databases | MEDLINE® and Embase® via Embase.com<br>MEDLINE® In-process and Cochrane via OvidSP®  |
|------------------------|-----------|--|
| Population             |           | Patients with DR (proliferative and/or non-proliferative)  |
| Interventions          |           | Not applicable   |
| Comparator             |           | Not applicable   |
| Outcomes               |           | Humanistic burden of illness related to affected persons and carers <ul style="list-style-type: none"> <li>health related quality of life</li> <li>disabilities</li> <li>effects on activities of daily living</li> <li>utilities</li> </ul>     |
| Key inclusion criteria |           | <ul style="list-style-type: none"> <li>Systematic literature reviews</li> <li>Real-world prospective, retrospective, or cross-sectional observational studies</li> <li>Any other relevant study design capturing outcomes of interest</li> </ul> |
| Study design           |           |  |
| Language               |           | English  |
| Publication date       |           | Database inception to January 2019   |

Key: DR = Diabetic retinopathy

## RESULTS

- Diabetic retinopathy negatively impacts multiple domains leading to reduced quality of life and increased functional burden.
- A number of instruments have been used to measure patient-reported outcomes in patients with DR; the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) was the most frequently used instrument to assess vision related QoL (VRQoL).

### Health related quality of life

#### Impact on vision related quality of life

- The VRQoL assessed using the NEI VFQ-25 showed a relatively worse QoL in DR patients compared to controls<sup>(7-11)</sup> (Figure 1).
- According to the NEI VFQ-25, general health, general vision, near and distance activities, mental health, driving, and role limitations are the most commonly impacted domains in DR patients compared to controls.<sup>(12,13)</sup>
- Evidence also suggests that PDR patients have a worst NEI VFQ-25 score compared to mild and moderate NPDR patients<sup>(7,14)</sup> (Figure 1).

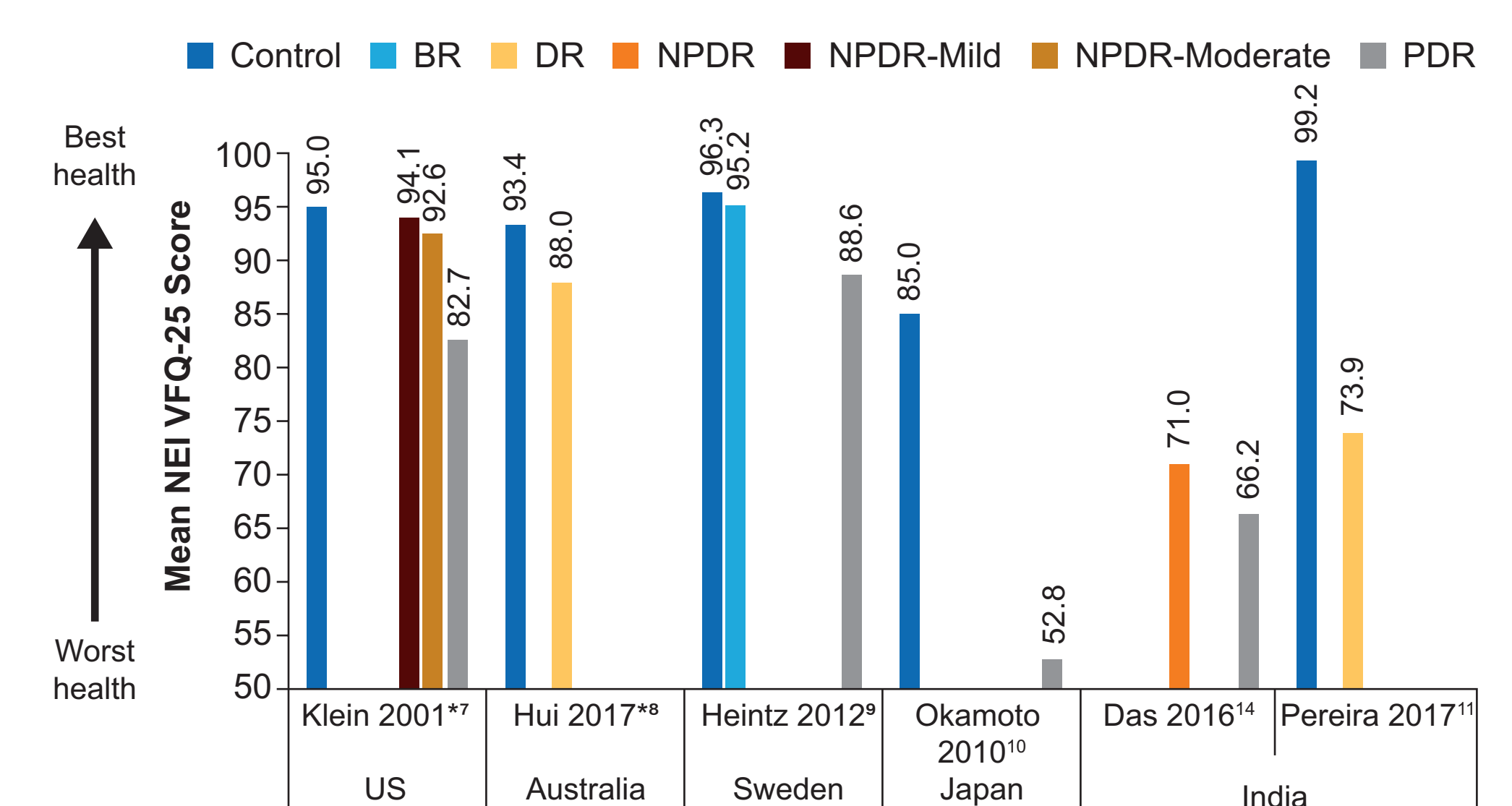


Figure 1. Mean summary score of NEI VFQ-25 in DR patients (including PDR) and controls without DR

Key: BR = Background retinopathy; DR = Diabetic retinopathy; NPDR = Non-proliferative diabetic retinopathy; PDR = Proliferative Diabetic retinopathy; \*Controls are healthy subjects  
Note: Two studies Okamoto 2010 and Heintz 2012 reported data for PDR without DME

#### Impact on general quality of life

- The impact on general quality of life was measured using the SF-12 and SF-36 instruments. These instruments consists of the physical and the mental component score (PCS and MCS), both ranging from 0-100 with a higher score indicating better health.
- A linear trend was observed between DR severity level and the SF-12 PCS and MCS scores i.e. an increase in DR severity was associated with lower SF-12 scores<sup>(15,16)</sup> (Figure 2).
- Whereas, in another study, only the PCS score was statistically significantly worse in sight threatening DR (STDR) patients compared to controls (P < 0.05).<sup>(17)</sup> Likewise, in studies conducted in the US<sup>(18)</sup> and Germany,<sup>(6)</sup> SF-12 PCS scores were lower than the MCS mean scores (Figure 2).

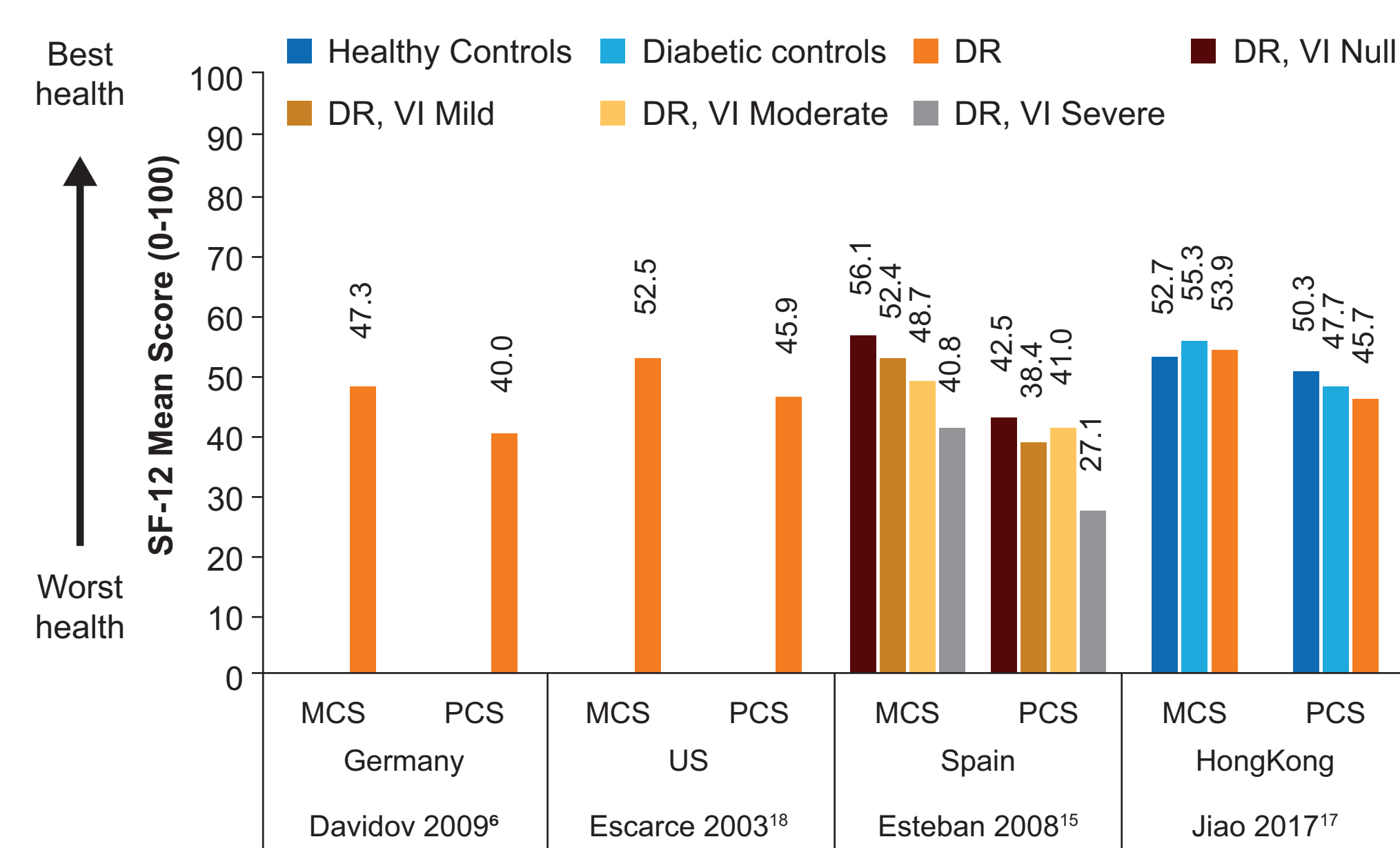


Figure 2. SF-12 PCS and MCS scores in DR patients across geographies

Key: Mild = Background retinopathy; Moderate = pre-proliferative retinopathy; Severe = maculopathy or proliferative retinopathy; PCS = physical component score; MCS = mental component score; SF 12 = short form -12 score; VI = visual impairment

- SF-36 scores in all dimensions were lower in the PDR group compared to their respective controls.<sup>(19)</sup>

#### Impact on depression and emotional well-being

- The presence of DR was associated with statistically significantly higher rates of depression assessed using the Patient Health Questionnaire-9 compared to patients without DR (35% vs. 21.1%, P < 0.001) and an increased trend was observed between depression and disease severity (NPDR: 33%; PDR: 39.1%, P value for trend = 0.002).<sup>(20)</sup>
- Similarly, severe NPDR or PDR was associated with higher levels of depressive symptoms whereas no association was found between DR and anxiety symptoms<sup>(21)</sup> (Figure 3).

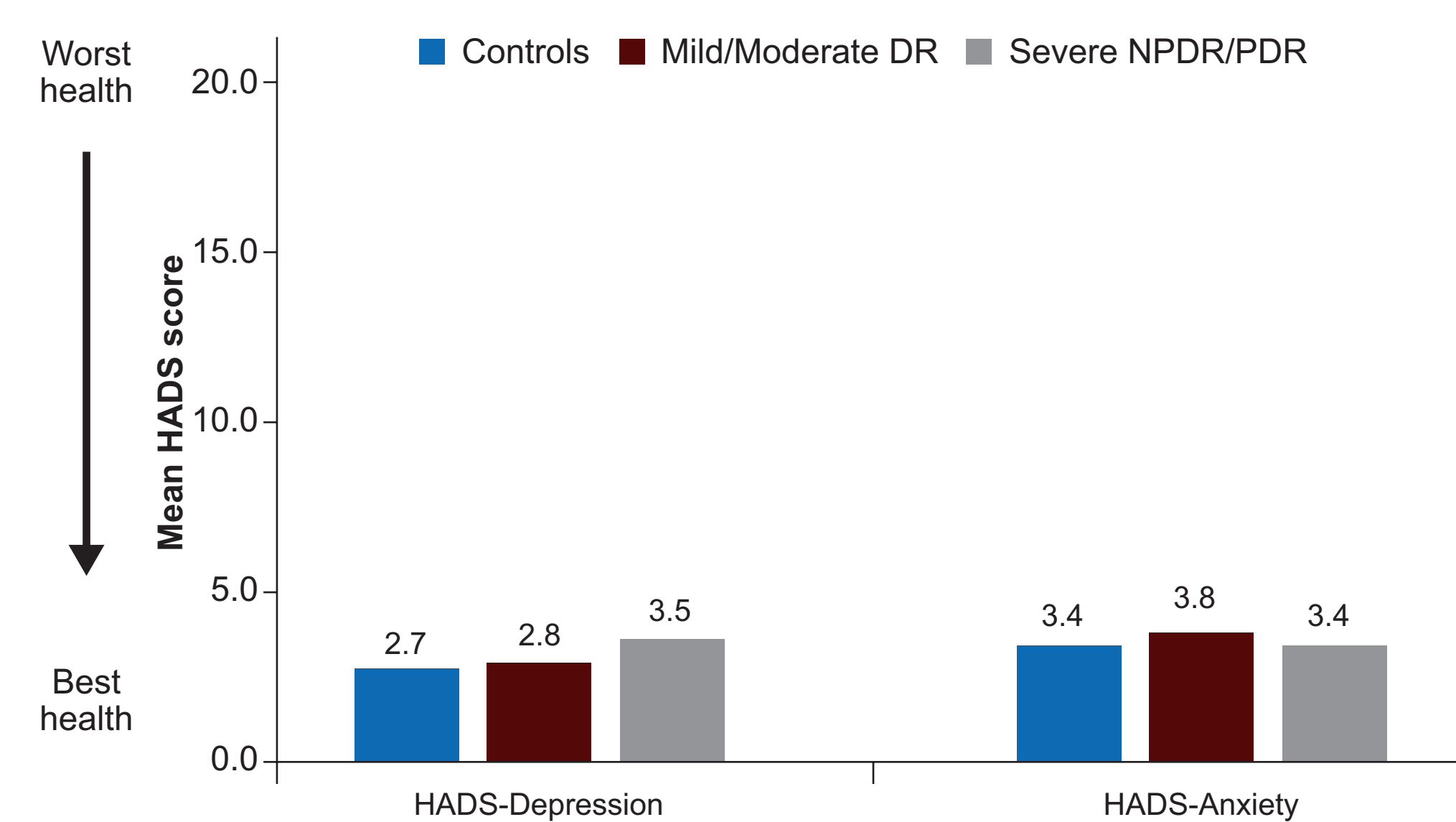


Figure 3. Mean HADS score in patients with DR (including PDR) and control subjects without DR

Key: HADS = Hospital Anxiety and Depression scale; NPDR = Non-proliferative diabetic retinopathy; PDR = Proliferative diabetic retinopathy

#### Health utilities

- Using the EQ-5D, utility values were relatively lower in DR patients compared to controls<sup>(22-24)</sup> (Figure 4).

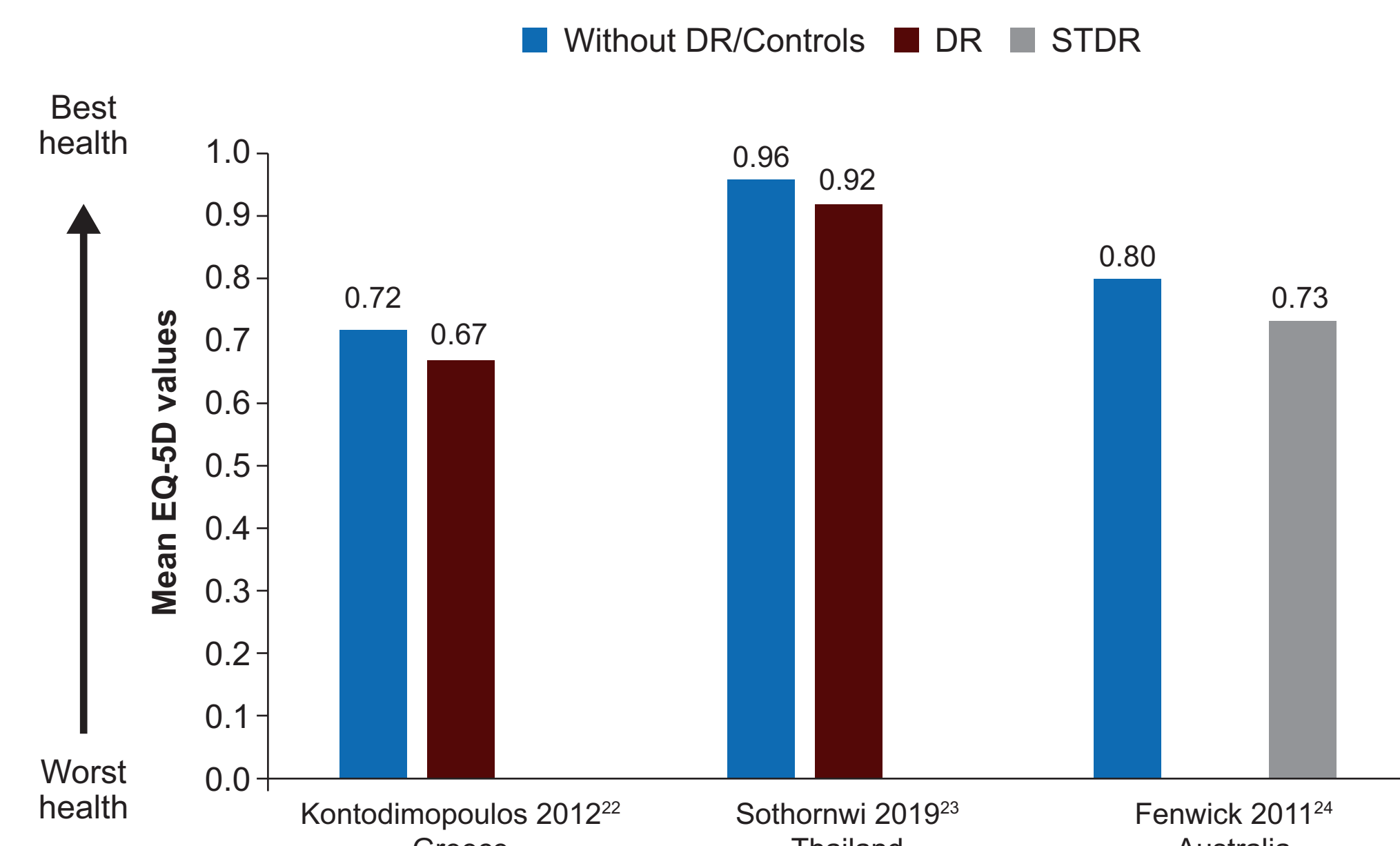


Figure 4. Mean EQ-5D scores among patients with diabetes retinopathy

Key: DR = Diabetic Retinopathy; EQ-5D = EuroQoL-Five Dimensions; STDR = Sight Threatening Diabetes Retinopathy

- The EQ-5D scores further decreased with increased disease severity<sup>(25,26)</sup> (Figure 5). Similar results were observed using the TTO, SG, and VAT analysis.

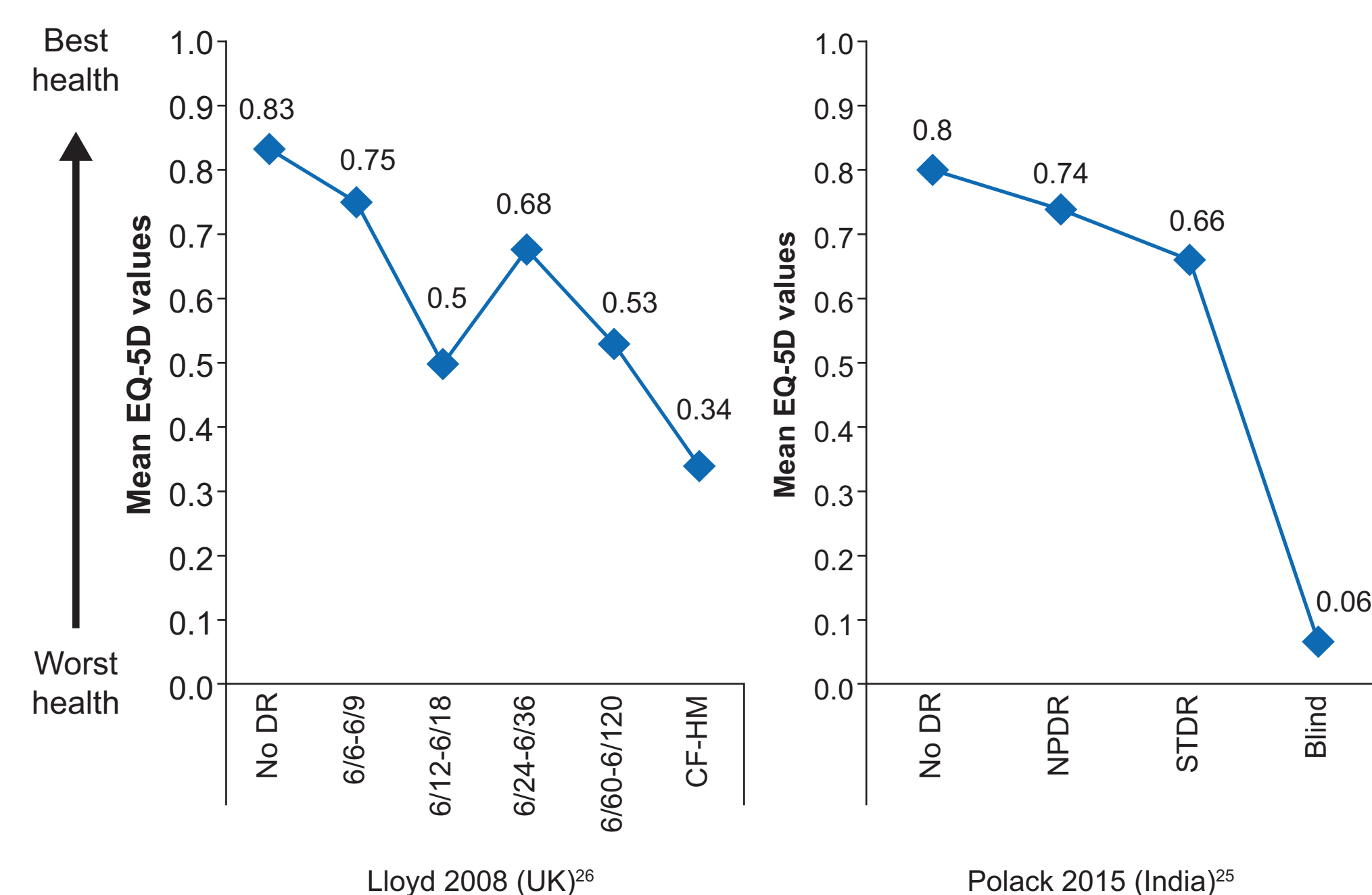


Figure 5. EQ-5D single index values among patients with DR according to VA level

Key: DR = Diabetic Retinopathy; NPDR = Non-proliferative diabetic retinopathy; STDR = Sight Threatening Diabetes Retinopathy; EQ-5D = EuroQoL-Five Dimensions; VA = Visual acuity; CF = Counting Fingers; HM = Hand Motion

- When using the SF-6D, slightly lower preference scores were reported among patients with DR compared to those without DR and decreased with increased disease severity.<sup>(17,22)</sup>

#### Activities of daily living

- A statistically significant decrease in the overall mobility and impairment (M&I) score vision specific items was observed in patients with DR compared to controls with no eye problems (P < 0.001)<sup>(27)</sup> (Figure 6).

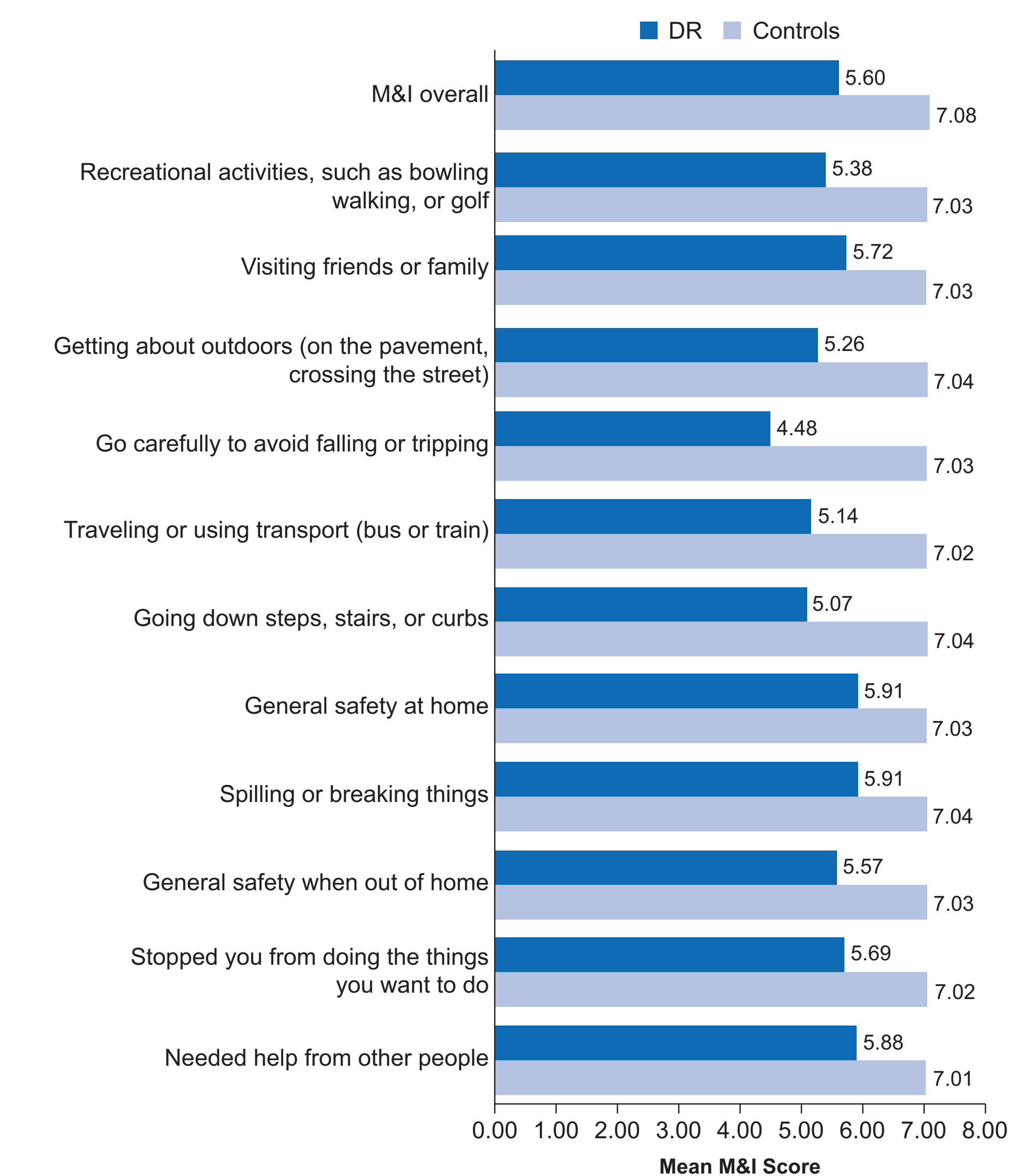


Figure 6. Mean overall and individual item scores on the M&I Scale in DR patients compared to controls

Key: DR = Diabetes Retinopathy; M&I = Mobility and impairment

- According to disease severity, vision related functional burden (>40 years old) was higher in severe NPDR or PDR (48.5%) compared to mild/moderate NPDR (20.4%) and no DR (20.2%).<sup>(28)</sup>
- Patients with VTDR and PDR were 6 to 12 times more likely to report lower participation in daily living activities compared to those with less severe DR.<sup>(29)</sup>

#### Caregiver Burden

- While it is expected that there is a substantial caregiver burden, no studies were identified to substantiate this in caregivers of DR patients.
- However, for DME patients, it was reported that almost half of patients (44%) need caregiver support to perform the daily activities<sup>(30)</sup> which further leads to productivity loss.

## CONCLUSIONS

- Available evidence suggests that the presence of DR and visual impairment lead to significant impairment of VRQoL, physical components of HRQoL, daily living activities and emotional well-being.
- Evidence also suggested that QoL decreases with increased disease severity i.e. among all DR patients, PDR patients have worst QoL compared to mild and moderate NPDR patients.
- As DR is a progressive disease, treatments that delay disease progression are warranted to limit impairment.

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#### Disclosures

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