

Putting the puzzle together: accessing raw quality of life data from clinical study reports for use in evidence synthesis

Background

Quality of life is a broad concept with its definition, left open to debate. It has been explained as a measure that incorporates all aspects of an individual, both their success in attaining certain pre-determined states or conditions and their sense of well-being and satisfaction with their current life conditions.¹ Mental health services have shifted from being based on a narrow notion of health and disease and being focused on reducing symptoms, to a more holistic approach which takes into consideration both well-being and functioning.^{1,2} For example, mental health services in UK now include the routine assessment of patient-reported outcomes in psychological services,² and they are increasingly being used to assess the efficacy and effectiveness of health care interventions.³ Health related quality of life (HRQoL) scales measure the subjective health and functional status of patients and their general well-being, as seen from their own perspective.⁴

The content of these measures, varies considerably and they can cover generic concepts of functioning (such as physical functioning), through to very specific symptoms that are disease specific (e.g. dyspnoea for respiratory disease, dexterity for arthritis etc.).³ Disease or condition specific instruments as their names suggests have been developed to provide information on the patient's perception of that specific disease or health problem. Generic health related quality of life (HRQoL) instruments measure the overall well-being of people as per their own perspective. Two of the most widely used of these are the Short-Form-36 (SF-36) and the preference-based utility measure EuroQol-5D (EQ-5D).

As only about half of all studies are subsequently published⁵ and a review of 101 trials found that HRQoL outcomes were the least reported on in journal publications⁶ and this was very much the case for antidepressant trials⁷ we undertook this study looking at clinical study reports (CSRs).

Objectives

The HRQoL assessments in industry sponsored antidepressant trials have almost universally been left unpublished and so we undertook an evidence synthesis of raw SF-36 and EQ-5D data from CSRs of these trials.

Methods

From the CSRs received,⁸ one researcher (TS) selected those that described double-blind placebo randomised controlled trials and then excluded those that did not contain any HRQoL outcomes or any patient-reported outcomes (PRO) at all. The types of measures used in these trials were mapped by one researcher (TS) and those trials that contained SF-36 and EQ-5D as outcome measures, were selected. These CSRs were converted to readable PDF and all relevant pages - with study information, protocols and the result tables for SF-36 and EQ-5D, were copied by one researcher (TS) for use in data extraction. The primary researcher (TS) and one of two second observers extracted data independently from the selected pages of all the CSRs. We contacted the concerned pharmaceutical companies Eli Lilly, Pfizer and GlaxoSmithKline (GSK) for the journal publications of these trials and for comparison and for the missing data

Results

Out of the 198 CSRs we received from the regulators we could include 15 trials that had SF-36 and EQ-5D as outcomes corresponding to 19,015 pages of data from eight trials of duloxetine, six trials of paroxetine and one trial of sertraline (see Figure 1). One other sertraline trial and four venlafaxine trials used unnamed HRQoL instruments and no results were available. Four of the duloxetine, two of the paroxetine and the sertraline trial from the included trials were either missing or had incomplete HRQoL results. This corresponded to 2 trials with no results data for SF-36 and one trial with no results data for EQ-5D and three trials with partial or unclear data for SF-36 and four trials with partial or unclear data for EQ-5D (see Figure 2). We did not receive all the missing data and results requested nor did all the trials have journal publications. The ones that did also suffered from selective reporting bias.

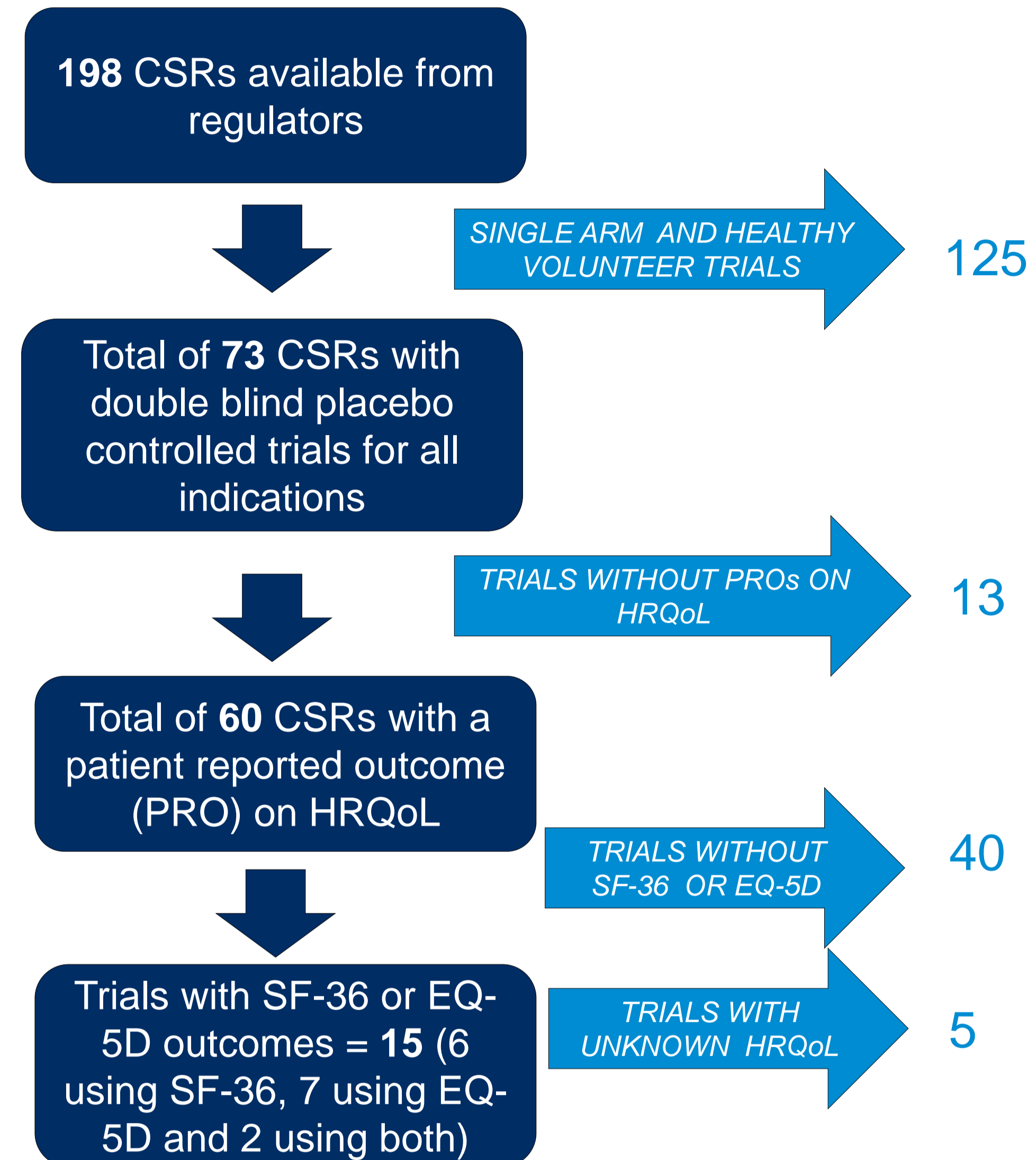


FIGURE 1 FLOW CHART OF SELECTION OF TRIALS

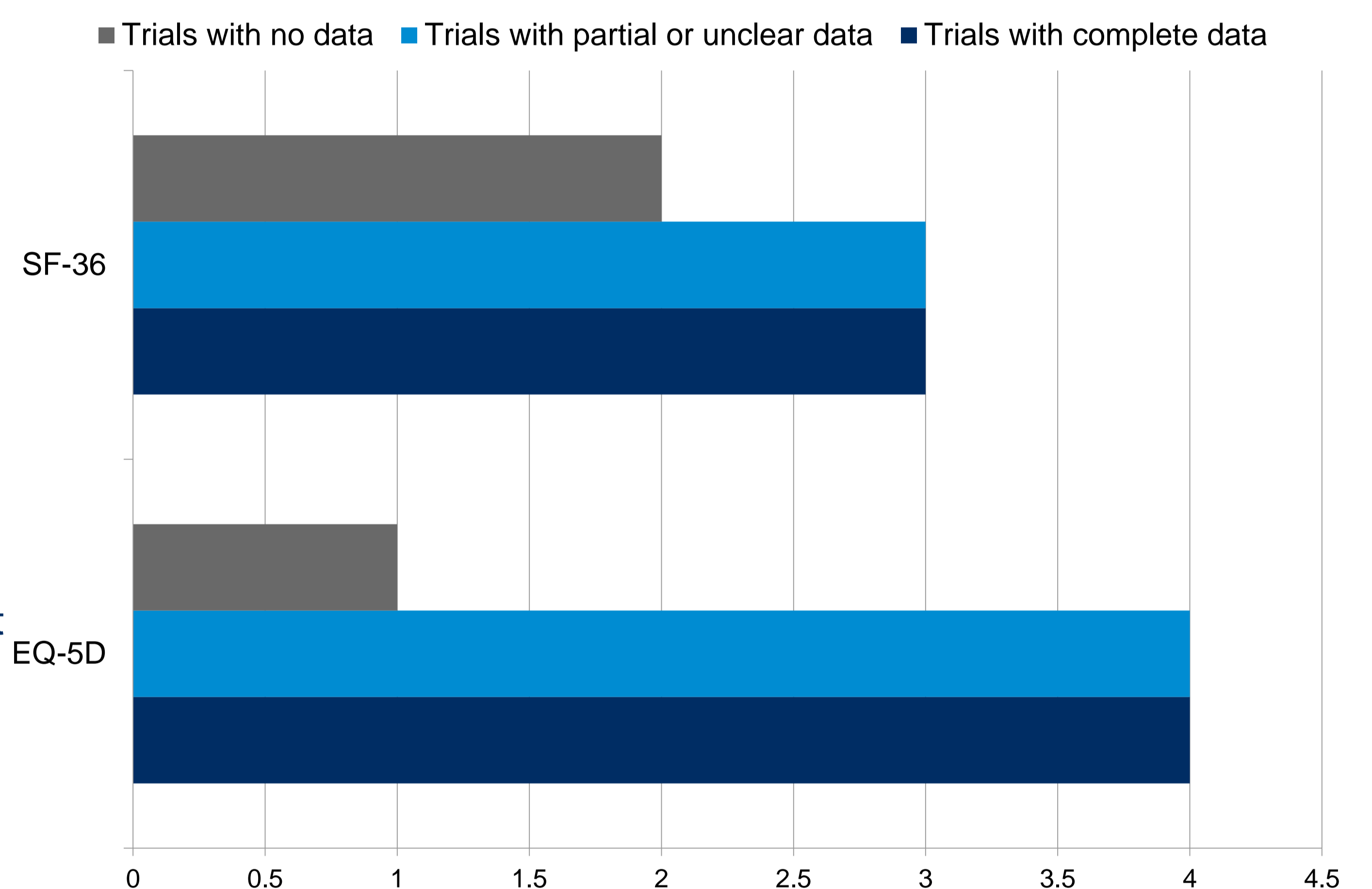


FIGURE 2 DATA AVAILABILITY FOR THE OUTCOMES IN THE CSRs

Discussion

We did not expect to find so much selective reporting and missing data within the CSRs that a proper evidence review and meta-analyses did not seem appropriate to conduct. The data from the CSRs did however seem to indicate no significant improvement on drugs using the EQ-5D scale compared to placebo and for SF-36 improvement on the mental health component score but a decline on the physical health component score. However, as we had very limited data, which was selectively reported on, drawing any conclusions would not be correct. The comparison with the published articles is currently ongoing.

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