

A Systematic Literature Review of the Humanistic Burden of Anaemia Associated With Chronic Kidney Disease

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No: MP198

Background

Anaemia is well recognised as a common comorbidity among patients with chronic kidney disease (CKD),¹ with the prevalence increasing with greater disease severity, as measured by CKD stages.²⁻⁴

The condition reduces the patients' physical capacity and energy levels, leading to a greater health-related quality of life (HRQoL) burden.^{4,5}

The humanistic burden associated with anaemia in patients with CKD and the instruments used to measure HRQoL in this setting have not recently been explored using systematic literature review methods. Therefore, these important topics were investigated using such an approach.

Methods

Search and Screening Strategy

- MEDLINE and Embase were systematically searched for English-language literature on anaemia in CKD from 2007 to 2012 and for HRQoL publications from any country.
- The Renal Association, the European Renal Association, the American Society of Nephrology and the International Society for Pharmacoeconomics and Outcomes Research were also searched from 2011 to 2012.
- The search identified publications with key terms related to the population of interest, such as chronic kidney failure and CKD, as well as keywords for a HRQoL burden in their title and abstracts.
- Articles were included in the review if they had abstracts and met the criteria in Table 1. Abstracts were reviewed for inclusion by a single researcher, while full-text articles were assessed by two independent researchers, with any discrepancies resolved by a third researcher.

Table 1: Selection Criteria

Requirements	
Population	Adults with anaemia in chronic kidney disease
Country	Any
Outcomes	<ul style="list-style-type: none">Health-related quality of life and utilitiesFunctional ability/statusTreatment satisfactionOther patient-reported outcomes
Study Design	<ul style="list-style-type: none">Any editorials, case studies and narrative non-systematic reviews were excludedSystematic literature reviews (including meta-analyses and indirect and mixed treatment comparisons) were excluded from the review; however, the bibliography lists of these studies were reviewed to ensure all relevant primary publications were included
Language	English
Date	Within the previous 5 years (November 2007–November 2012)

Data Abstraction, Quality Assessment and Synthesis of Results

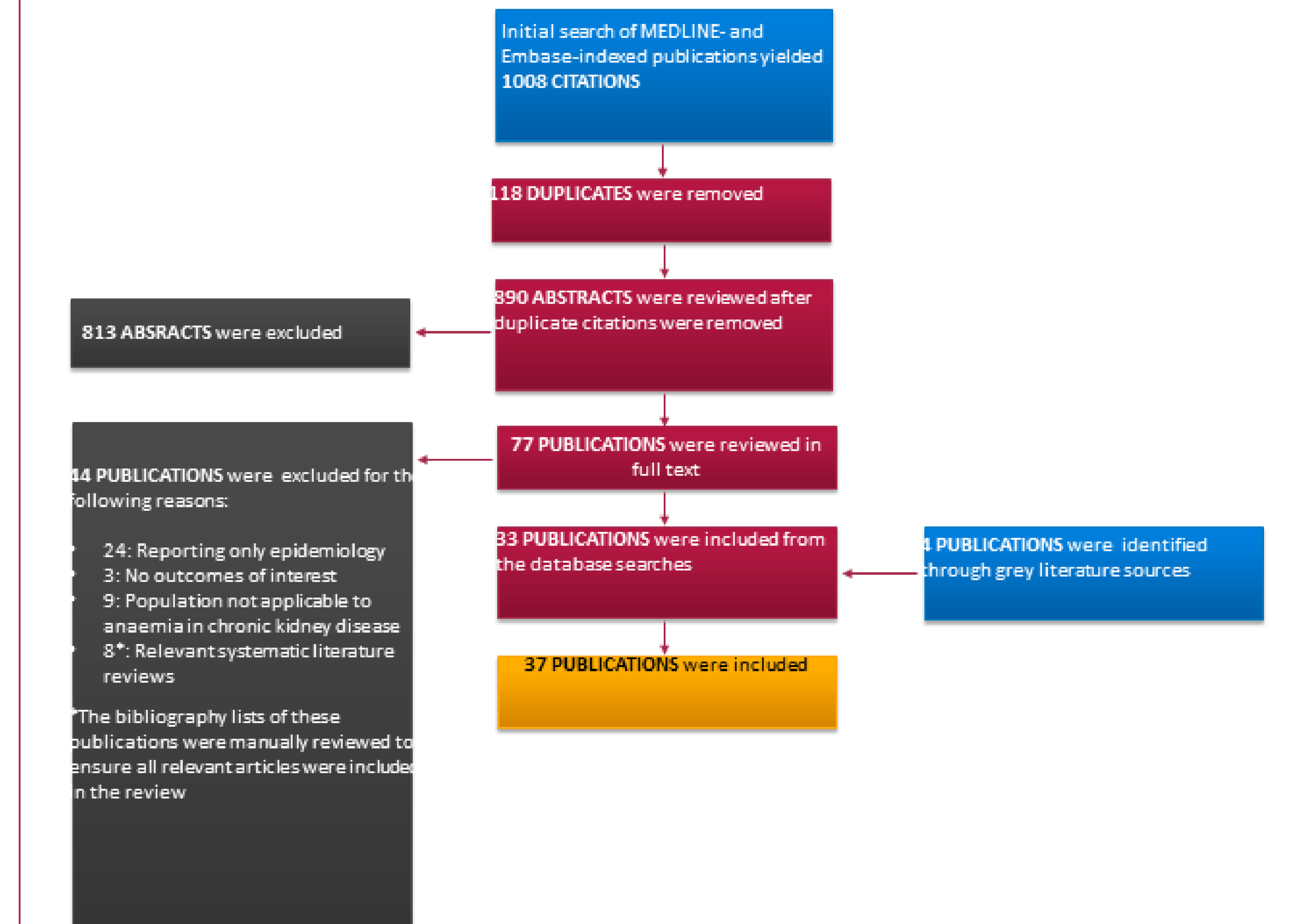
- Data were abstracted by a single researcher into a standardised data abstraction form and then validated by a second independent researcher.
- The results of the review were synthesised using qualitative methods.

Results

Search Results

- Figure 1 outlines the selection of studies from the initial search hits to the final number of studies synthesised in the review, using the preferred reporting items for systematic reviews and meta-analyses (PRISMA)[†] guidelines.

Figure 1: PRISMA Flow Diagram for the Systematic Literature Review



[†]The PRISMA Statement

Results (Cont'd)

Study Characteristics

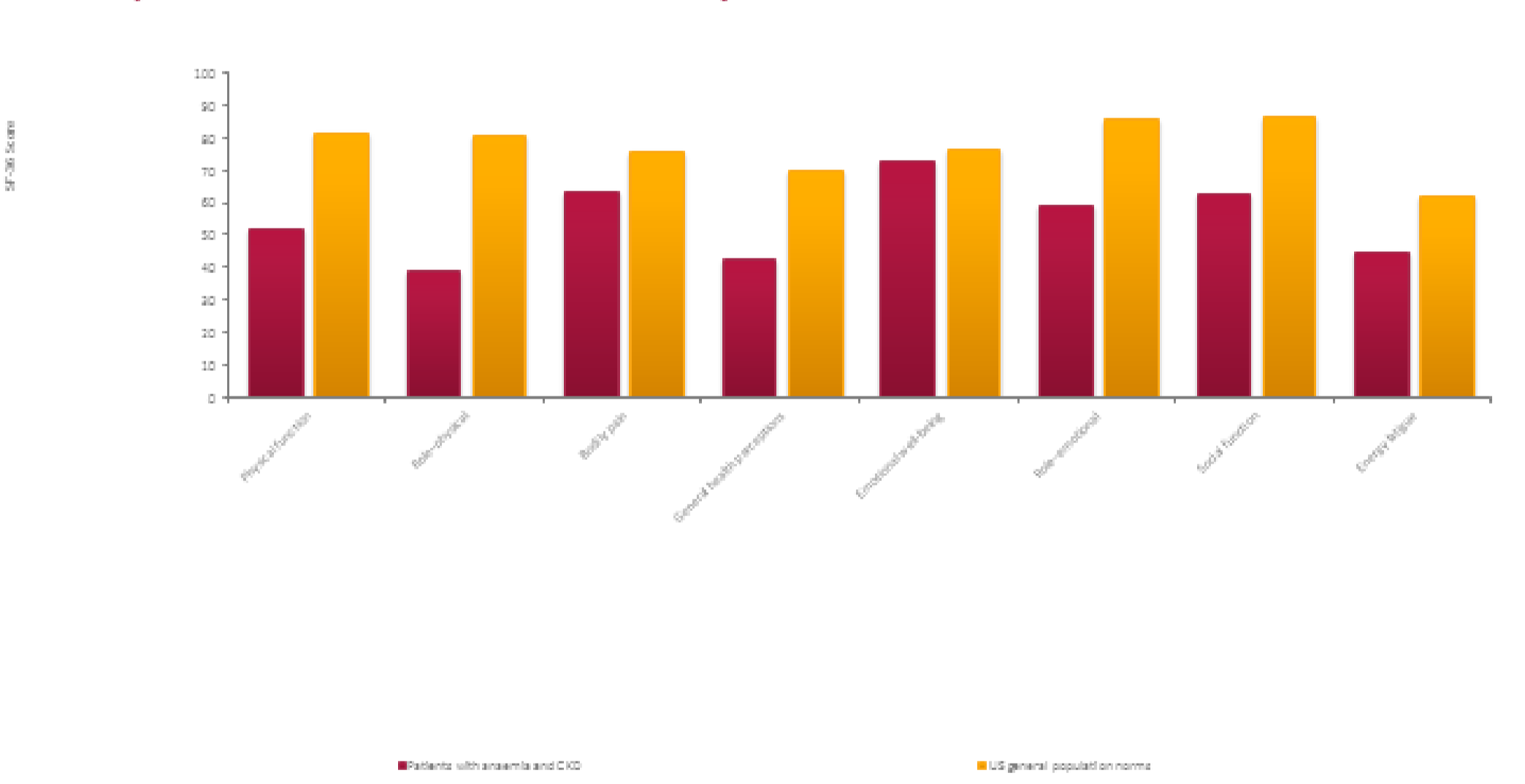
- The review identified 37 studies that reported on HRQoL.
- Most studies were of a cross-sectional design (n = 31), while a handful of publications were on prospective cohort studies (n = 6).
 - Among the cross-sectional studies, sample size ranged from 26–1,395. Among the prospective cohort studies sample size ranged from 30–1,186.
- CKD stage was reported in 16 studies, as below:
 - CKD all stages: 2 studies
 - CKD stages 2–5: 2 studies
 - CKD stages 3–5: 2 studies
 - CKD stages 4–5: 1 study
 - End-stage renal disease (ESRD): 9 studies
- In these, the Short Form (36) Health Survey (SF-36) was the most frequently employed measure of humanistic burden, having been used in 19 of the studies and is, therefore, the focus of the results presented below.
- Other measures of HRQoL were not often reported by more than one study.⁶⁻¹⁹

Study Results

HRQoL in Patients with Anaemia in CKD Compared with the General Population

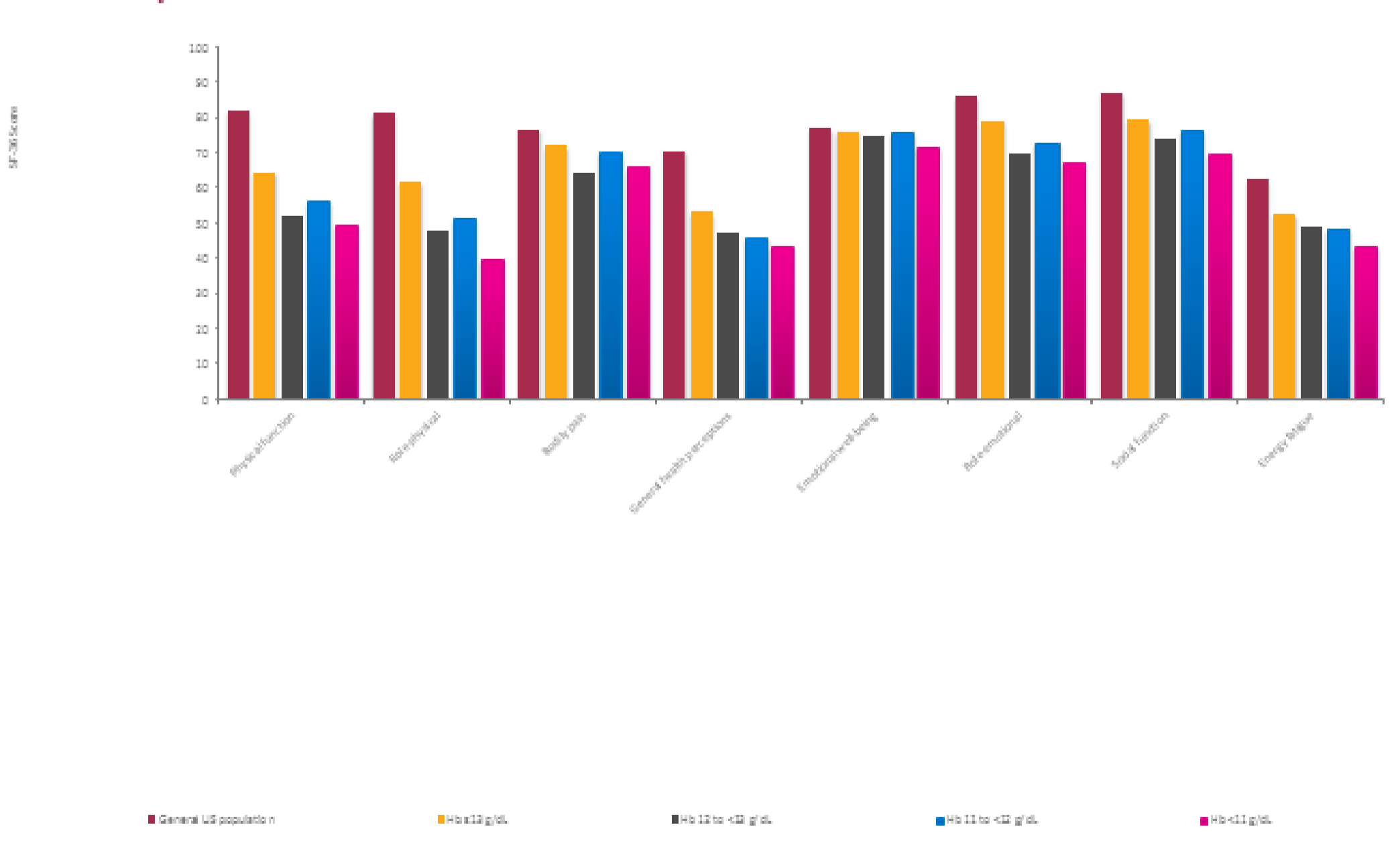
- Two studies of anaemia in non-dialysis patients with CKD (CKD-ND) found the SF-36 scores to be lower among this group, compared with the general United States (US) population, with the difference being generally more marked the lower the haemoglobin (Hb) threshold used to define anaemia is (Figures 2 and 3). For example:
 - One study in the US reported that the SF-36 scores of anaemia in CKD-ND were below the US population norms; where energy/fatigue and role-physical functioning were the lowest of these subscores.²⁰ Anaemia was measured using Hb levels only (Figure 2).
 - Similar results were found in the prospective cohort study, which included anaemia in CKD-ND (stages 3–5) in the US and Canada.²¹ Of note, this study found that, compared with the general population, patients with anaemia in CKD had particularly reduced subscores for physical function and general health perception, in addition to energy/fatigue and role-physical functioning. The study also found that quality of life was further reduced in patients with a lower Hb cut-off (Figure 3).

Figure 2: Mean SF-36 Scores in Patients with Anaemia in CKD Compared with US General Population Norms



Based on data from Hansen et al. (2009).²⁰

Figure 3: Mean SF-36 Scores in Patients with Anaemia in CKD Defined by Different Hb Thresholds Compared with the General US Population



Based on data from Finkelstein et al. (2009).⁶

The Association between Hb or Haematocrit Levels and the Physical Component Summary and Mental Component Summary Scores

- In seven cross-sectional studies there was a correlation between the severity of anaemia and HRQoL, in that as Hb or haematocrit (Ht) levels decreased across a group of patients so did scores for both the mean physical component summary (PCS)^{8,9,22-25} and the mean mental component summary (MCS)^{8,9,10,22-25} of the SF-36.
- Such an association was also found in one study evaluating patients with CKD and hepatitis C virus (HCV) infection.²⁶

- However, two studies did not find a statistically significant correlation between Hb levels and PCS scores (n = 6927)²⁸, while another did not find a statistically significant correlation with MCS scores (n = 26).²⁴
- Similarly, an additional four studies (two on CKD-ND patients^{7,21} and two on dialysis patients^{29,30}) found that among patients with CKD, those with lower Hb or Ht levels generally had poorer HRQoL for both mean PCS and mean MCS scores of the SF-36, compared with those with higher Hb or Ht levels.^{6,7,29,30}

Association between Hb or Ht Levels and Vitality and Functional Ability

- There was limited evidence on the relationship between Hb or Ht levels and vitality among studies included in the review. Four cross-sectional studies^{10,11,26,31} reported on this correlation and found the following:
 - One study found that as Hb or Ht levels increased, there was also a statistically significant increase in vitality in non-dialysis patients (CKD stage not reported; p = 0.003).³¹
 - This was also found in a study of patients with CKD (on haemodialysis [HD]) who had a comorbid HCV infection and anaemia (p < 0.0001).²⁶
 - However, two studies did not find a statistically significant correlation in non-dialysis¹⁰ and HD patients¹¹ (CKD stages not reported).
- There was also limited evidence on the relationship between Hb or Ht levels and functional ability, as identified in the following three studies:
 - One study assessed whether there was a correlation between Hb levels and individual items on the SF-36 related to functional ability (physical functioning and role-physical) among patients with CKD, and found no significant correlation among non-dialysis patients.¹⁰
 - However, in another study, a significant correlation between these variables was found among ESRD patients on HD who had a comorbid HCV infection.²⁶
 - One study found that over a 48-week period, there was no correlation between change in functional ability and a 10% increment of Ht levels in non-dialysis patients.³¹ Although at baseline there was a correlation between increase in functional ability per 1% increment of Ht levels.

Optimal Hb Thresholds

- A prospective cohort study suggested that HRQoL values at baseline among patients on erythropoietin therapy may be higher in those who were treated to an Hb target level between 10 and 11 g/dl compared with higher or lower values (below 9 g/dl and above 11 g/dl).³²
- Another prospective observational study among those not receiving evidence supporting routine for pre-existing anaemia in CKD, found improvement in PCS scores was greatest (and statistically significant; p < 0.0001) among those with Hb levels below 12 g/dl, suggesting that this may be the optimal threshold to target treatment.⁶

Discussion

- CKD-ND with anaemia had poorer HRQoL compared with the general US population; in particular, energy/vitality and role-physical functioning were the lowest subscores.
- CKD-ND and dialysis patients with lower Hb or Ht levels had lower PCS and MCS scores compared with those with higher Hb or Ht levels.
- Hb or Ht levels were also significantly correlated with PCS and MCS scores, such that the higher the Hb or Ht levels, the better the HRQoL among both non-dialysis and dialysis patients.
- Patients on dialysis with low Hb levels had lower vitality and physical function, and role-physical subscores compared to those with higher Hb levels; this was not found in non-dialysis patients.

Limitations

- SF-36 (the most commonly used instrument identified in the review) is a generic, rather than a disease-specific, measure of HRQoL.
- Most of these studies were cross-sectional and there were relatively few prospective cohorts.

Conclusions

- Anaemia in CKD is associated with a considerable humanistic burden.
- This highlights the need for appropriate management of anaemia in patients with CKD to improve their HRQoL outcomes.

This study was funded by Astellas Pharma Europe BV, Leiden, The Netherlands. FN is currently an employee of Astellas and participated in this research during her employment at Astellas. MR & II are employees of Evidera, which was paid by, and collaborated with, Astellas to conduct the review and develop the abstract.

References are available on a separate handout and from the study authors.

