The Prevalence and Severity of Chronic Pain in Patients With Chronic Kidney Disease: A Systematic Review and Meta-Analysis

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Abstract

Background: Chronic pain is a common and distressing symptom reported by patients with chronic kidney disease (CKD). Clinical practice and research in this area do not appear to be advancing sufficiently to address the issue of chronic pain management in patients with CKD.

Objectives: To determine the prevalence and severity of chronic pain in patients with CKD.

Design: Systematic review and meta-analysis.

Setting: Interventional and observational studies presenting data from 2000 or later. Exclusion criteria included acute kidney injury or studies that limited the study population to a specific cause, symptom, and/or comorbidity.

Patients: Adults with glomerular filtration rate (GFR) category 3 to 5 CKD including dialysis patients and those managed conservatively without dialysis.

Measurements: Data extracted included title, first author, design, country, year of data collection, publication year, mean age, stage of CKD, prevalence of pain, and severity of pain.

Methods: Databases searched included MEDLINE, CINAHL, EMBASE, and Cochrane Library, last searched on February 3, 2020. Two reviewers independently screened all titles and abstracts, assessed potentially relevant articles, and extracted data. We estimated pooled prevalence of overall chronic pain, musculoskeletal pain, bone/joint pain, muscle pain/soreness, and neuropathic pain and the I² statistic was computed to measure heterogeneity. Random effects models were used to account for variations in study design and sample populations and a double arcsine transformation was used in the model calculations to account for potential overweighting of studies reporting either very high or very low prevalence measurements. Pain severity scores were calibrated to a score out of 10, to compare across studies. Weighted mean severity scores and 95% confidence intervals were reported.

Results: Sixty-eight studies representing 16,558 patients from 26 countries were included. The mean prevalence of chronic pain in hemodialysis patients was 60.5%, and the mean prevalence of moderate or severe pain was 43.6%. Although limited, pain prevalence data for peritoneal dialysis patients (35.9%), those managed conservatively without dialysis (59.8%), those following withdrawal of dialysis (39.2%), and patients with earlier GFR category of CKD (61.2%) suggest similarly high prevalence rates.

Limitations: Studies lacked a consistent approach to defining the chronicity and nature of pain. There was also variability in the measures used to determine pain severity, limiting the ability to compare findings across populations. Furthermore, most studies reported mean severity scores for the entire cohort, rather than reporting the prevalence (numerator and denominator) for each of the pain severity categories (mild, moderate, and severe). Mean severity scores for a population do not allow for “responder analyses” nor allow for an understanding of clinically relevant pain.

Conclusions: Chronic pain is common and often severe across diverse CKD populations providing a strong imperative to establish chronic pain management as a clinical and research priority. Future research needs to move toward a better understanding of the determinants of chronic pain and to evaluating the effectiveness of pain management strategies with particular attention to the patient outcomes such as overall symptom burden, physical function, and quality of life. The current variability in the outcome measures used to assess pain limits the ability to pool data or make comparisons among studies, which will hinder future evaluations of the efficacy and effectiveness of treatments. Recommendations for measuring and reporting pain in future CKD studies are provided.

Trial registration: PROSPERO Registration number CRD42020166965
Abrégé

**Contexte:** La douleur chronique est un symptôme affligeant fréquemment rapporté par les patients atteints d’insuffisance rénale chronique (IRC). Cependant, la recherche et la pratique clinique dans ce domaine ne semblent pas progresser suffisamment pour aborder sa gestion dans cette population.

**Objectif:** Déterminer la prévalence et l’intensité de la douleur chronique chez les patients atteints d’IRC.

**Type d’étude:** Revue systématique et méta-analyse.

**Sources:** Les études observationnelles et interventionnelles présentant des données depuis l’an 2000. Ont été exclus les cas d’insuffisance rénale aiguë et les études portant sur une population ayant une cause, un symptôme ou une maladie concomitante en particulier.

**Sujets:** Des adultes atteints d’IRC de stade 3 à 5, y compris des patients dialysés et des patients non dialysés pris en charge de façon conservatrice.

**Mesures:** Les données extraites comprenaient le titre de l’article, le nom de l’auteur principal, le type d’étude, le pays où s’est tenue l’étude, l’année de collection des données, l’année de publication, l’âge médian des sujets, le stade de l’IRC, la prévalence de la douleur et son intensité.

**Méthodologie:** Les données ont été colligées dans MEDLINE, CINAHL, EMBASE et la bibliothèque Cochrane. La dernière consultation date du 3 février 2020. Deux examinateurs ont, de façon indépendante, trié les titres et les abrégés, évalué les articles potentiellement pertinents et extrait les données. La prévalence combinée de la douleur chronique globale, de la douleur musculo-squelettique, de la douleur osseuse/articulaire, de la douleur musculaire et de la douleur neuropathique a été évaluée, et le calcul de la statistique I² a servi à mesurer l’hétérogénéité. Des modèles à effets aléatoires ont été employés pour tenir compte des variations selon le type d’étude et les populations échantillonnées. Les calculs de ces modèles ont subi une double transformation arc-sinus pour tenir compte d’une potentielle surpondération des études comportant des mesures de prévalence très importantes ou très faibles. Pour fins de comparaison, les scores d’intensité de la douleur ont été étalonnés à un score sur 10. Des scores d’intensité moyenne pondérée et des intervalles de confiance à 95 % ont été mentionnés.

**Résultats:** Soixante-huit études ont été incluses, lesquelles portaient sur un total de 16 558 patients dans 26 pays. La prévalence moyenne de la douleur chronique chez les patients hémodialysés était de 60,5 %; la prévalence moyenne de la douleur modérée ou sévère était de 43,6 %. Quoique limitées, les données portant sur des patients sous dialyse péritonéale (35,9 %), des patients suivant des traitements conservateurs sans dialyse (59,8 %), des patients ayant arrêté la dialyse (39,2 %) ou des patients atteints d’un stade inférieur d’IRC (61,2 %) suggèrent une prévalence tout aussi élevée.

**Limites:** Les études incluses manquaient de cohérence dans leur approche pour définir la chronicité et la nature de la douleur. Les mesures utilisées pour déterminer l’intensité de la douleur étaient variables, ce qui a limité la comparaison des résultats entre les populations. La plupart des études indiquaient des scores moyens d’intensité pour l’ensemble de la cohorte plutôt que la prévalence (numérateur et dénominateur) de chacune des catégories d’intensité (légère, modérée et sévère). Les scores moyens d’intensité pour une population ne permettent pas « les analyses de répondants » et la compréhension de la douleur cliniquement pertinente.

**Conclusion:** La douleur chronique est fréquente et souvent intense dans les diverses populations de patients atteints d’IRC, ce qui confirme la gestion de la douleur chronique comme priorité clinique et de recherche. Les recherches futures devraient permettre une meilleure compréhension des déterminants de la douleur chronique et évaluer l’efficacité des stratégies de gestion de la douleur en accordant une attention particulière aux résultats des patients, notamment au fardeau global des symptômes, à la fonction physique et à la qualité de vie. La capacité de regrouper des données ou de faire des comparaisons entre les études est limitée par la variabilité actuelle des mesures utilisées pour évaluer la douleur, ce qui entravera les futures évaluations de l’efficacité des traitements. Des recommandations pour mesurer et signaler la douleur dans les futures études sur l’IRC sont fournies.

**Keywords**

systematic review, meta-analysis, chronic pain, prevalence, chronic kidney disease

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**Introduction**

Patients with chronic kidney disease (CKD) experience multiple and burdensome symptoms, the number and severity of which have been described as being similar to those of cancer patients hospitalized in palliative care settings. The high symptom burden in patients with CKD negatively affects patients’ health-related quality of life (HRQL) and functional capacity. Hence, symptom management has been identified as a top priority for patients with CKD. A recent scoping review conducted as part of Kidney Disease: Improving Global Outcomes’ (KDIGO) effort to develop formal international recommendations for kidney supportive care reinforced that chronic pain is a common and distressing symptom reported by patients with CKD. It is often not possible to completely alleviate chronic pain. The clinical aim is to reduce pain to levels where function is not adversely affected, which is typically perceived as “mild” pain or pain rated as 0 to 3 on a 0 to 10 numerical rating scale (NRS). However, clinical practice and research in this area do not appear to be advancing sufficiently to address the issue of chronic pain management in patients with CKD. If quality person-centered care is to be delivered, assessment and treatment strategies must be developed and integrated to align care with patient preferences and treatment goals.

Our main objective was to determine the prevalence and severity of chronic pain across broad populations of patients with CKD glomerular filtration rate (GFR) categories (G) 3 to 5. We hypothesized that extensive data exists illustrating a high pain burden across CKD G3-5.

**Methods**

**Eligibility Criteria and Search Strategy**

The literature search was developed and conducted by an experienced librarian; PROSPERO Registration number CRD42020166965. Inclusion and exclusion criteria are listed in Table 1. We included all interventional and observational studies that presented original data of the prevalence and severity of chronic pain in patients with CKD G3-5. We included studies presenting data from 2000 or later, given that the CKD population, especially those starting dialysis, have become increasingly older with greater comorbidity, which may add to the burden of chronic pain. Single case studies or case series were excluded, as were studies that were presented only as abstracts, posters, or letters to the Editor. Articles published in a language other than English were translated and included. Eligible patient populations included CKD G3-5 and ≥18 years of age. Studies that only enrolled patients with a primary diagnosis of acute kidney injury or kidney transplant patients were excluded as were studies that limited the study population to a specific cause, symptom, and/or comorbidity (with the exception of chronic pain) of CKD as these studies were outside the scope of our study objectives. Dialysis patients also experience acute pain syndromes, but these are distinct entities from chronic pain with different trajectories and impact on HRQL and function. Hence, studies that were limited to acute pain or pain related to dialysis treatment were also excluded.

**Data Items**

Outcomes of interest were prevalence and severity of chronic or persistent pain, as defined by the individual studies, recognizing that definitions of chronic pain were likely to vary. To determine prevalence, both the number of cases of pain and the total number within the cohort had to be reported. In addition, eligible studies needed to report pain as either general overall pain or pain broken down into categories of musculoskeletal pain, bone/joint pain, muscle pain/soreness, and/or neuropathic pain. This was considered important as the commonly used symptom screening tools in CKD use a combination of these categories to classify pain. In cases when more than one study appeared to report on the same cohort of patients, the study with the most complete data or highest methodological quality was included.

**Information Sources**

Information sources included electronic databases, reference lists of relevant literature, and Web sites of relevant networks, organizations, and societies. Relevant information sources that were obtained from colleagues and stakeholders and unpublished studies were also considered for inclusion. The electronic databases searched included MEDLINE, CINAHL, EMBASE, and Cochrane Library databases. These were last searched on February 3, 2020.

**Study Selection, Data Collection, and Quality Assessment**

Two reviewers independently screened all titles and abstracts to identify potentially relevant articles. Full texts of potentially relevant articles were retrieved and independently assessed by 2 reviewers for possible inclusion based on the predetermined selection criteria. The reference lists of reviews, systematic reviews, and guidelines were also reviewed to ensure all relevant studies were identified. The 2 reviewers compared individually recorded decisions for inclusion and exclusion and disagreements were resolved based on discussion and consensus with a third reviewer. The research team developed a standardized data extraction table using Microsoft Excel. The 2 reviewers independently populated the table from the selected full-text articles. The data extracted from each study included year and country of study, number of study participants, patient population, age, definition of pain, pain assessment tools used, and the
Table 1. Inclusion and Exclusion Criteria.

| Description |
|-------------|
| **Population** |
| CKD GFR categories 3,4,5 (pre-dialysis, dialysis, or CKM) |
| ≥18 years of age |
| Any treatment type (peritoneal dialysis, hemodialysis, or CKM) |
| Must be identified as having CKD prior to enrollment in study |
| **Outcome** |
| Prevalence of pain (%) |
| Prevalence of pain in categories of severity (%) (eg, mild/mod/severe; or 0-3/10, 4-6/10, 7-10/10, respectively) |
| Studies must have identified cases (pain) and total cohort number to calculate prevalence |
| **Study design** |
| Cross-sectional studies |
| Observational studies |
| Case-control studies |
| Cross-over trials |
| Clinical trials |
| Chart reviews |
| **Exclusion criteria** |
| <18 years of age |
| Case series, abstracts, posters, reviews, opinions |
| Acute kidney injury |
| Kidney transplant, unless clearly identified as having CKD (stage 3-5 or eGFR lower than 60) |
| Data (initial assessment) prior to 2000 |
| Population limited to a specific cause of ESKD or selected based on specific symptom/comorbidity (except for chronic pain) |
| Acute pain or pain related to dialysis treatment |
| Missing raw data, numerator, or denominator |

Note. CKD = chronic kidney disease; GFR = glomerular filtration rate; CKM = conservative kidney management; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease.

prevalence and severity of pain. The 2 data extraction tables were subsequently compared and cross-checked for accuracy and then merged into a single unified table for data analysis and presentation in the article. Study quality was also reviewed independently by 2 reviewers using the McMaster University Critical Review for Quantitative Studies.14 This included assessing the study design, study sample, outcomes of interest, statistical analysis, and final conclusions.

**Data Analysis**

Meta-analyses of prevalence data were conducted in Microsoft R Open version 3.4.1, using package meta to estimate the pooled prevalence and 95% confidence intervals.15,16 Random effects models were used to account for variations in study design and sample populations with results plotted using forest plots. A double arcsine transformation was used in the model calculations to account for the possible overweighting of studies reporting either very high or very low prevalence measurements.17 Heterogeneity between the estimates was assessed using I² statistics.18 The I² value is the percentage of total observed variation across studies due to real heterogeneity rather than chance; a value of greater than 75% is indicative of high heterogeneity. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist was used in the reporting of this work.

The prevalence of overall chronic pain, musculoskeletal pain, bone/joint pain, muscle pain/soreness, and neuropathic pain were estimated. Some studies presented the prevalence of pain based on severity characterized as mild, moderate, or severe, with others reporting the prevalence of moderate to severe chronic pain. For those studies that reported prevalence by pain intensity, information on clinically relevant moderate to severe and severe pain was included.

Pain severity scores were calibrated to a score out of 10, to compare across studies. We ensured all scales were oriented such that a severity score of 0 represented no pain and 10 represented the worst pain. One of the studies had its score presented in the opposite orientation, which was reversed for the sake of this analysis.19 Pain scores of zero were assumed for patients not reporting pain. Mean pain severity scores were recalculated to reflect the severity of pain for patients reporting pain in the cases where reported severity scores included those not experiencing pain (ie, removal of scores equaling 0). Weighted mean severity scores and 95% confidence intervals were reported.20 Meta-regressions were conducted where the number of studies was sufficiently large enough to yield robust results (ie, 10 or more).21,22 Funnel-plot asymmetry was tested using a Peters’ regression to assess the possibility of publication bias.16,23 Meta-regressions on various categorical and continuous variables were conducted, both to estimate
the effect of these variables on estimated prevalence and to investigate possible sources of heterogeneity. Covariates included publication year, sample size, age, country, definition of pain, and type of measurement scale used. Bubble plots were used to illustrate the effect of continuous covariates and stratified forest plots to illustrate the effects of categorical covariates.

**Results**

The literature review yielded 3336 citations of which 220 were deemed eligible for full-text review. Of these, 152 studies were excluded leaving 68 studies for inclusion in the analysis.2,3,7,8,14,19,24-84 The flow chart in Figure 1 outlines this process, including reasons for exclusion. Supplemental Table S1 provides a list of excluded studies with reasons for exclusion.

**Details of Included Studies**

Details of the 68 included studies are reported in Table 2 and include data from 16,558 patients from 26 countries. Forty-eight of the studies examined 8464 hemodialysis (HD) patients from 23 countries,5,7,8,14,24,28,29,32,34-41,43-46,49,51-56,58,59,61-63,65-68,70,72,73,75,76,78-84 3 studies from 3 countries included data from 679 peritoneal dialysis (PD) patients,24,49,81 and 8 studies from 6 countries reported data from 3701 patients on either HD or PD (without separating treatment groups).2,3,25,26,60,69,71,77 Two
Table 2. Characteristics and Results of Included Studies.

| Study                  | Country          | Patient population | Number of patients | Mean age (years) | Type of pain | Pain definition/tool | Prevalence of pain | Type of severity scale | Description of severity scale | Pain prevalence |
|------------------------|------------------|--------------------|--------------------|------------------|--------------|----------------------|-------------------|------------------------|-----------------------------|-----------------|
| Abdel-Kader et al.     | United States    | CKD G3-5ND (Pre-dialysis) | 177               | CKD: 51 HD/PD: 54 | Bone/Joint   | Pain in the last 7 days as measured by the Dialysis Symptom Index | Prevalence of bone/joint pain was 33.3% and 39.1% in the CKD group. Prevalence of muscle soreness pain in the dialysis group was 33.3% and 24.1% in the CKD group. | 1-5 VRS          | 1 = Not at all bothersome; 3 = Bother very much | Median Bone/Joint Pain Score: CKD: 3/5; Dialysis: 3/5 | Prevalence of muscle soreness in total cohort was 60%.
|                        |                  | Prevalent HD or PD |                   |                  | Joint        |                     |                   |                        |                            |                 |
| Almutairy et al.       | Saudi Arabia     | CKD G4-SND (Pre-dialysis) | 48               | CKD: 287 HD/PD: 42 | Muscle Soreness | Pain as measured by the Chronic Kidney Disease Symptom Burden Index, duration not specified | Prevalence of muscle soreness in total cohort was 46.1%. Prevalence of muscle soreness in the individual groups was 55.4% for HD, 30.0% for PD, 40.4% for CKD G4, and 41.7% for CKD G5ND. | 0-10 NRS     | 0 = None; 10 = Very much | Median Muscle Soreness Score: CKD: 2/5; Dialysis: 2/5 | Prevalence of muscle soreness in total cohort was 46.1%.
|                        |                  | Prevalent HD or PD |                   |                  | Soreness    |                     |                   |                        |                            |                 |
| Amro et al.            | Norway           | Prevalent HD or PD | 60                | HD: 243 PD: 58   | Muscle Soreness | Pain in last 4 weeks as measured by the Kidney Disease and Quality of Life Short Form | Prevalence of muscle soreness in total cohort was 77% and 27% reported severe pain (4/5). | 1-5 VRS          | 1 = Not bothered at all; 5 = Extremely bothered | Muscle Soreness: 63/100 (scores recalculated to 0-100, 0 not bothered at all) | Prevalence of muscle soreness in total cohort was 78%.
|                        |                  |                    |                   |                  |            |                     |                   |                        |                            |                 |
| Amro et al.            | Norway           | Prevalent HD or PD | 110               | HD: 42 PD: 68    | Muscle Soreness | Pain in last 4 weeks as measured by the Kidney Disease and Quality of Life Short Form | Prevalence of muscle soreness in total cohort was 78%.
|                        |                  |                    |                   |                  |            |                     |                   |                        |                            |                 |
| Bah et al.             | Republic of Cuba | CKD GSN (CKD)     | 49                | Cases: 54 Control: 55 | Muscle Soreness | Pain in last 4 weeks as measured by the Chronic Kidney Disease Symptom Burden Index (does not specify version) | Of the group that missed at least one dialysis session prior to a visit to the emergency department 12% reported very mild/mild pain, 12% reported moderate pain, and 64% reported severe/very severe pain. | 1-6 VRS          | 1 = None; 6 = Very severe | N/A | Prevalence of severe muscle soreness was 27.
|                        |                  |                    |                   |                  |            |                     |                   |                        |                            |                 |
| Bashara et al.         | India            | Prevalent HD       | 49                | Cases: 25 Control: 25 | Muscle Soreness | Pain measured by the Short-Form McGill Pain Questionnaire, duration not specified | Of the group that missed no dialysis sessions 45.8% reported very mild/mild pain, 42% reported moderate pain, and 8.3% reported severe/very severe pain. | 1-6 VRS          | 1 = None; 6 = Very severe | N/A | Prevalence of severe muscle soreness (4-5) was 27.
|                        |                  |                    |                   |                  |            |                     |                   |                        |                            |                 |
| Bankston and Mossi     | United States    | Prevalent HD       | 62                | HD: 65           | Pain          | Pain in the last 7 days as measured by the Dialysis Symptom Index | Prevalence of bone/joint pain = 40% and the prevalence of muscle soreness was 31. |
|                        |                  |                    |                   |                  |              |                     |                   |                        |                            |                 |
| Berman et al.          | United States    | Prevalent HD       | 57                | Transplant Ineligible: 32; Transplant Eligible: 25 | Muscles | Pain in the last 7 days as measured by the Dialysis Symptom Index | Total prevalence of bone or joint pain was 58.4%. The fatigued group reported a higher prevalence of bone and joint pain than the non-fatigued group (64.4% vs 34.6%, respectively). The total prevalence of muscle soreness was 46.7%. The fatigued group reported a higher prevalence of muscle soreness than the non-fatigued group (58.3% vs 44.2%, respectively). Prevalence of pain was 50.7%. The intensity of pain was low in 3%, moderate in 44%, severe in 44%, and very severe in 12% of patients reporting pain. | 1-5 VRS          | 1 = Not bothered at all; 5 = Extremely bothered | Bone/Joint Pain (estimated from figure): Transplant Ineligible = 4/5; Transplant Eligible = 2/5 | Prevalence of bone/joint pain = 40% and the prevalence of muscle soreness was 31. |
|                        |                  |                    |                   |                  |              |                     |                   |                        |                            |                 |
| Bossola et al.         | Italy            | Prevalent HD       | 37                | Fatigued: 107 Not Fatigued: 57 | Muscles | Pain in the last 7 days as measured by the Dialysis Symptom Index | Total prevalence of bone or joint pain was 58.4%. The fatigued group reported a higher prevalence of bone and joint pain than the non-fatigued group (44.6% vs 34.6%, respectively). The total prevalence of muscle soreness was 46.7%. The fatigued group reported a higher prevalence of muscle soreness than the non-fatigued group (58.4% vs 44.2%, respectively). Prevalence of pain was 50.7%. The intensity of pain was low in 3%, moderate in 44%, severe in 44%, and very severe in 12% of patients reporting pain. | 1-5 VRS          | 1 = Not bothered at all; 5 = Extremely bothered | Bone/Joint Pain (estimated from figure): Transplant Ineligible = 4/5; Transplant Eligible = 2/5 | Prevalence of bone/joint pain = 40% and the prevalence of muscle soreness was 31. |
|                        |                  |                    |                   |                  |              |                     |                   |                        |                            |                 |
| Bouattar et al.        | Morocco          | Prevalent HD       | 67                | Pain lasting more than 3 months | Muscles | Pain          | Prevalence of bone/joint pain = 40% and the prevalence of muscle soreness was 31. |
|                        |                  |                    |                   |                  |              |                     |                   |                        |                            |                 |

(continued)
Table 2. (continued)

| Study                          | Country       | Patient population | Number of patients | Mean age (years) | Pain definition/tool | Type of severity scale | Description of severity scale | Mean pain severity | Pain prevalence |
|-------------------------------|---------------|--------------------|--------------------|------------------|----------------------|------------------------|--------------------------|------------------|-----------------|
| Brennan et al.                | Australia     | CKD G5SND (CKM)   | 42                 | 83               | Pain in the last 7 days as measured by the Patient Outcome Scale symptom module (renal version) | 1-5 VRS             | 1 = None; 5 = Overwhelming | N/A              | Pain was reported by 45% of patients at their first visit to the renal supportive care clinic. Prevalence of moderate pain was 17% and prevalence of severe and overwhelming pain was 16%. |
| Caraveo et al.                | Spain         | CKD G4-SND         | 1169              | 65               | Pain for more than 3 months, not attributed to trauma and requiring analgesic therapy at least 3 times/week | Yes/No              | N/A; N/A                  | N/A              | Prevalence of chronic musculoskeletal pain was 38%. |
| Carreon et al.                | United States | Prevalent HD       | 75                | 59               | Pain in the last 7 days as measured by the Dialysis Symptom Index | 1-5 VRS             | 1 = None; 5 = Overwhelming | N/A              | Bone and joint pain was reported by 37% of patients; 7% of patients described it as moderate to severe. Of those reporting bone and joint pain, ~29% were somewhat bothered, ~36% were bothered quite a bit, and ~14% were bothered very much (estimated from graph). |
| Chan et al.                   | Hong Kong     | CKD G5SND (CKM)   | Total: 253 Patients with Pain: 107 Patients without pain: 146 | Patients with Pain: 79 Patients without pain: 80 | Chronic Pain lasting more than 3 months | 10 cm VAS           | 0-3 = Mild; 4-6 = Moderate; 7-10 = Intense | N/A              | Of those with pain at the first consultative visit, 49% had chronic pain. |
| Chaste et al.                 | Canada        | Dialysis Withdrawal | 33 over study period 32 for last 24 hours | 70               | Pain during the entire dialysis discontinuation period and in the last 24 hours | Yes/No              | N/A; N/A                  | N/A              | Pain prevalence was 53% at the time of withdrawal of dialysis and decreased to 20% in the last 24 hours with provision of palliative care. |
| Cho et al.                    | South Korea   | Prevalent HD       | 230               | 61               | Pain in the last 7 days as measured by the Dialysis Symptom Index—Korean Version | 0-4 VRS             | 0 = Not at all bothersome; 4 = Very bothersome | 2.8/4             | The prevalence of bone/joint pain was 42.2% and the prevalence of muscle soreness was 38.3%. |
| Gaxton et al.                 | United States | Prevalent HD       | 62                | 59               | Pain in the last 7 days as measured by the Dialysis Symptom Index | 0-4 VRS             | 0 = Not bothersome; 4 = Bother me a little; 7 = Bother me much | N/A              | Prevalence of bone and joint pain was 53%. |
| Cohen et al.                  | United States | Dialysis Withdrawal | 79                | 70               | Pain in the last 24 hours of life as measured by the Dialysis Symptom Assessment. Quality of Dying questionnaire | 1-5 VRS             | 1 = Severe; 5 = Absent | N/A              | Pain was the most common symptom in the last 24 hours; prevalence was 42% and prevalence of severe pain was 5% |
| Danquah et al.                | United States | Prevalent HD       | 100               | 56               | Pain since last dialysis session as measured 1-10 NRS by the Dialysis Symptom Frequency, Severity, and Symptom Burden Index | 1-10 NRS            | 1 = Least severe; 5 = Most severe | N/A              | Prevalence of bone/joint pain was 39%. |
| da Costa et al.               | Brazil        | Prevalent HD       | 49                | Ranged from 20 to 88 (46.9% were older than 50) | Pain in the last 4 weeks as measured by the Kidney Disease and Quality of Life Short Form | 1-5 VRS             | 1 = Not bothered at all; 5 = Extremely bothered | N/A              | Prevalence of muscle pain was 69.4%. 34.7% of patients were bothered a little by pain, 14.3% were moderately bothered, 14.3% were very much bothered, and 6.1% were extremely bothered by muscle soreness. |
| Davison et al.                | Canada        | Prevalent HD       | 205               | 60               | Pain lasting more than 3 months measured by the Brief Pain Inventory | 0-10 NRS            | 0 = No pain; 10 = Severe pain | 5.6/10             | Prevalence of pain was 50%. Moderate/severe pain was reported in 82.5% of the patients with pain (41.3% of total study cohort). |
| Davison et al.                | Canada        | Prevalent HD or PD | 507               | 64               | Pain lasting more than 3 months measured by the modified Edmonton Symptom Assessment System | 0-10 NRS            | 0 = No pain; 10 = Severe pain | 3.6/10             | The prevalence of moderate or severe pain was 47.7% of total study cohort. |
| Davison and Jhangri           | Canada        | Prevalent HD or PD | 591               | 61               | Pain measured by the modified Edmonton Symptom Assessment System, duration not stated | 0-10 NRS            | 0 = No pain; 10 = Severe pain | 3.5/10             | Prevalence of pain in total cohort was 72.4%. Prevalence of moderate or severe pain was 46.5% of those with pain (33.7% of the total study cohort). |
| de Freitas et al.             | Brazil        | Prevalent HD       | 35                | N/A              | Pain in the last 4 weeks as measured by the Kidney Disease and Quality of Life Short Form | 1-5 VRS             | 1 = Do not bother me at all; 5 = Extremely bothered | N/A              | The total prevalence of muscle aches was 34.2%. Of the total study sample, 31.4% reported muscle pain that bothered them a little bit, 11.4% reported moderately bothered by pain, 2.9% reported being very bothered by pain, and 8.6% reported being extremely bothered. |
| Demiro et al.                 | Turkey        | Prevalent HD       | 140               | FMS: 20 Non-FMS: 120 | Chronic widespread pain for at least 3 months | N/A                 | N/A; N/A                  | N/A              | Prevalence of chronic widespread pain in the total study cohort was 44.9%. |

(continued)
| Study                        | Country            | Patient population | Number of patients | Mean age (years) | Pain definition/tool                                                                 | Type of severity scale | Description of severity scale | Mean pain severity | Pain prevalence |
|-----------------------------|--------------------|--------------------|--------------------|------------------|--------------------------------------------------------------------------------------|------------------------|------------------------------|-------------------|-----------------|
| El Harraki et al.           | Morocco            | Prevalent HD       | 93                 | 55               | Pain lasting more than 3 months                                                      | 10 cm VAS              | 0 = None 1-4 = Mild 5-6 = Moderate 7-8 = Severe 9-10 = Unbearable | N/A               | 70.9%           |
| Er et al.                   | Turkey             | Prevalent HD       | 95                 | 52               | Pain lasting more than 3 months measured by the McGill-Melzack pain questionnaire   | 0-5 VRS                 | 0 = No pain 1 = Mild 2 = Disturbing 3 = Severe 4 = Very Severe 5 = Unbearable | N/A               | 32.6%           |
| Fidan et al.                | Turkey             | Prevalent HD       | 50                 | 56               | Presence of musculoskeletal problems recorded patient's medical history via yeshno.        | N/A                    | N/A                          | N/A               | 60.9%           |
| Reishman et al.             | Israel             | Prevalent HD       | 336                | 64               | Pain over the past 24 hours as measured by the Brief Pain Inventory                  | 10 cm VAS              | 0 = None 10 = Worst possible                                      | 7.2/10            | 32.6%           |
| Flythe et al.               | United States      | Prevalent HD       | 87                 | N/A              | Pain in the past 4 weeks as measured by a 28-question online survey created by investigators | N/A                   | N/A                          | N/A               | 58.7%           |
| Galain et al.               | Uruguay            | Prevalent HD or PD | 493                | 61               | Pain in the last 4 weeks as measured by the Kidney Disease and Quality of Life 36 items | 100 mm VAS             | 0 = Extremely bothered 100 = Not bothered at all                      | Muscle Soreness: 70 |
| Gamondi et al.              | Southern Switzerland | Prevalent HD or HDF | 123               | 71               | Pain in the last 4 weeks                                                             | 10 cm VAS              | 0 = No pain 10 = Unbearable pain                                     | ~5.8/10 (estimated from figure) |
| Golan et al.                | Israel             | Prevalent HD       | 100                | 65               | Pain lasting more than 3 months measured by the Brief Pain Inventory                  | 0-10 NRS               | 0 = No pain 10 = Pain as bad as you can imagine                      | N/A               | 51.9%           |
| Gómez Pozo et al.           | Spain              | Prevalent HD       | 134                | 68               | Pain in the last 7 days as measured by Brief Pain Inventory and McGill Pain Questionnaire (Spanish Versions) | 10 cm VAS              | 0-4 = Mild 5-7 = Moderate 8-10 = Severe                              | N/A               | 64%             |
| Gutiérrez Sánchez et al.    | Spain              | OKD G4-SND (Pre-dialysis) | 180              | 66               | Pain in the last 7 days as measured by the Palliative Outcome Symptom Scale Renal | 0-4 VRS                 | 0 = None 4 = Overwhelming                                           | N/A               | 51.9%           |
| Hage et al.                 | Lebanon            | Prevalent HD       | 89                 | 68               | Clinical diagnosis of musculoskeletal symptoms                                       | N/A                    | N/A                          | N/A               | 76.4%           |
| Harris et al.               | United States      | Prevalent HD       | 128                | 57               | Pain at times between dialysis sessions as measured by the Modified McGill Pain Questionnaire | 10 cm VAS              | 0 = No pain 10 = Pain as bad as you can imagine                      | Non-dialysis Days: 3/1/10 |

(continued)
| Study                        | Country       | Patient population | Number of patients | Mean age (years) | Pain definition/tool | Mean pain severity | Description of severity scale | Type of severity scale | Pain prevalence |
|-----------------------------|---------------|--------------------|--------------------|------------------|---------------------|--------------------|-----------------------------|------------------------|-------------------|
| Hsu et al42                 | Taiwan        | CKD G1-5ND (GFR < 90, Pre-dialysis) | 456                | 63               | Non-traumatic musculoskeletal pain with a VAS score of >1 for more than 3 months | 0 = No pain | 100 = Very painful | 100 mm VAS | Prevalence of chronic musculoskeletal pain in the total study cohort was 53.3%. Of those with pain, 15.6% reported mild pain, 28.4% moderate pain, and 58% severe pain. |
| Jablonski43                 | United States | Prevalent HD       | 130                | 60               | Pain not defined. Investigators created an 11-item symptom measure. | 1 = Not at all severe | 0 = None | 1-5 VRS | Prevalence of chronic pain was 63.4%. Of those with chronic pain, 84% had bone-joint-muscle pain. Also, of those with pain 43% reported mild pain (1-3/10) and 57% reported moderate pain (4-6/10). |
| Jamb et al44                | United States | Prevalent HD       | 893                | 65               | Pain measured by a Short-form McGill Pain Questionnaire score > 0; duration not specified | 0-3 VRS | 0 = None | 3 = Severe | Prevalence of pain was 81.8%. Prevalence of pain for patients less than 60 years was 85% and for patients more than 60 years was 76%. |
| Kuzeta et al45              | Poland        | Prevalent HD       | 205                | 60               | Chronic pain lasting more than 3 months | 0-10 VRS | 100 mm VAS | 0-5 VRS | Prevalence of pain was 81.8%. Prevalence of pain for patients less than 60 years was 85% and for patients more than 60 years was 76%. |
| Lamau et al46               | United States | Prevalent HD       | 109                | 61               | Pain lasting for at least 3 months as measured by the 11-item symptom module (renal version) | 0-5 VRS | 0 = None | 3 = Severe | Prevalence of pain was 81.8%. Prevalence of pain for patients less than 60 years was 85% and for patients more than 60 years was 76%. |
| Lowney et al47              | United Kingdom/ Ireland | Prevalent HD | 278                  | 61              | Pain lasting for at least 3 months as measured by the 11-item symptom module (renal version) | 0-5 VRS | 0 = None | 3 = Severe | Prevalence of pain was 81.8%. Prevalence of pain for patients less than 60 years was 85% and for patients more than 60 years was 76%. |
| Masajtis-Zagajewska et al48 | Poland        | Transplant        | 278                | 61               | Pain lasting for at least 3 months as measured by the Short-form McGill Pain Questionnaire | 0-5 VRS | 0 = None | 3 = Severe | Prevalence of pain was 81.8%. Prevalence of pain for patients less than 60 years was 85% and for patients more than 60 years was 76%. |
| Mathews49                   | India         | Prevalent HD       | 110                | Majority (63.64% were 50-60) | Pain not defined. | Yes/No | None | 0-5 VRS | Prevalence of pain was 81.8%. |
| Murphy et al50              | United Kingdom | CKD G4-5ND (CKM) | 55                 | 82               | Pain in the last 3 days as measured by a modified Patient Outcome Scale symptom module | 0-4 VRS | 0 = Absent | 4 = Overwhelming | Physical symptoms identified using Memorial Symptom Assessment Scale Short Form. The overall prevalence of pain was 56.4%. Of those reporting pain, mild pain prevalence was 51.6%, moderate pain was 25.8%, severe pain was 12.7%, and overwhealing pain prevalence was 9.7%. |
| Murtough et al51            | United Kingdom | CKD G5ND (CKM) | 66                 | 82               | Pain in the last 7 days as measured by the 11-item symptom module | 0-5 VRS | 0 = Not at all | 5 = Very much | Prevalence of Added Renal Symptoms: Prevalence of Bone/Joint Pain was 58%; 20% experienced moderate/severe pain. Prevalence of muscle soreness was 30%; 5% experienced moderate/severe pain. |

(continued)
| Study                  | Country          | Patient population | Number of patients | Mean age (years) | Pain definition/tool | Type of severity scale | Description of severity scale | Mean pain severity | Pain prevalence                        |
|-----------------------|------------------|--------------------|--------------------|------------------|---------------------|------------------------|-----------------------------|-------------------|----------------------------------------|
| Murtagh et al.        | United Kingdom   | CKD GSND (CKM)     | 49                 | 81               | Pain in the last 7 days as measured by the Memorial Symptom Assessment Scale Short Form | 0-5 VRS               | 0 = Not at all 5 = Very much        | N/A               | Physical symptoms identified using Memorial Symptom Assessment Scale Short Form  |
|                       |                  |                    |                    |                  |                     |                       |                             |                   | Prevalence was 73% 41% had “very” distressing pain in the last month of life  |
|                       |                  |                    |                    |                  |                     |                       |                             |                   | Prevalence of Added Renal Symptoms: pain 57% 24% had very distressing bone joint pain. |
|                       |                  |                    |                    |                  |                     |                       |                             |                   | Prevalence of muscle soreness was 49% 12% had very distressing muscle soreness. |
| Noordzij et al.       | Netherlands      | Prevalent HD or PD | 1469               | 59               | Pain in last 4 weeks as measured by the Kidney Disease and Quality of Life Short Form | 1-5 VRS               | 1 = Not bothered at all 5 = Extremely bothered | N/A               | Prevalence of muscle pain in total cohort was 68% Prevalence of muscle pain was significantly higher in patients treated with HD (71%) compared to patients treated with PD (64);  
P = .02. The prevalence of muscle pain in total cohort at baseline was 68% and increased to 81% by year 4 In the total cohort the prevalence of muscle pain at baseline was significantly higher in patients who died (73% vs 67;  
P = .03). |
|                       |                  |                    |                    |                  |                     |                       |                             |                   | Prevalence of overall chronic pain lasting at least 2 weeks for the entire cohort was 72.9%. Prevalence of pain in CKD G1 was 64%, 70% in G2, 71% in G3, and 75% for G4-SND (estimated from figure). |
| Pham et al.           | United States    | CKD G1-SND         | 130                | 52               | Pain lasting at least 2 weeks | 10-point Rating Scale, does not specify typical rating | 0-4 VRS | 0 = None 4 = Overwheming | N/A               | Prevalence of patients reporting pain as major (severe) was 35% |
|                       |                  | (Pre-dialysis)     |                    |                  |                     |                       |                             |                   | The prevalence of pain felt outside of dialysis was 82.1% 53.1% had pain severity scores between 0-2.3/10, 43.5% had scores 2.4/10, 9.3% had scores 3.1-7.9/10, and 0% had scores 7.6-10/10. |
|                       |                  | (Compared to 100 non-CKD controls) |                    |                  |                     |                       |                             |                   | Prevalence of pain/discomfort was 47.8% |
| Raj et al.            | Australia        | Prevalent HD       | 43                 | 64               | Pain as measured by the Patient Outcome Scale symptom module (renal version), duration not specified | 0-4 VRS               | 0 = None 4 = Overwheming | N/A               | Prevalence of moderate pain/discomfort was 62% Prevalence of severe pain/discomfort was 5% |
| Rodriguez Cabero et al | Spain            | Prevalent HD       | 32                 | 67               | Pain in the past 24 hours (outside the dialysis session) as measured by the Brief Pain Inventory | 0-10 NRS | 0 = No pain 10 = Worst pain you can imagine | 2.4/10 | The overall prevalence of bone joint pain was 28.7% 48.8% had moderate pain 35.1% had severe pain. Prevalence of bone joint pain in CKD G1-4 was 88.7% 87.7% in G4, 19.8% for GSND CKM, and 97.4% for HD. |
| Saffari et al.        | Iran             | Prevalent HD       | 362                | 58               | Pain as measured by the EQ-SD-3L, duration not specified | 1-3 VRS               | 1 = No pain/discomfort 3 = Severe pain/discomfort | N/A               | Prevalence of bone joint pain was 23% The prevalence of bone joint pain was 21% and the prevalence of bone joint pain was 44% |
| Sanchez et al.        | Spain            | Prevalent HD       | 47                 | 62               | Pain as measured by the EQ-SD-3L, duration not specified | 1-3 VRS               | 1 = No pain/discomfort 3 = Severe pain/discomfort | N/A               | Prevalence of muscle pain was approximately 71% 35% of patients were somewhat bothered (2/5); 19% were moderately bothered (3/5), 12% were very much bothered (4/5), and 5% were extremely bothered (5/5) by muscle soreness (estimated from figure). |
| Senanayake et al.     | Sri Lanka        | CKD G1-4 (GFR>15) | 1174               | 58               | Pain in the last 7 days as measured by the CKD Symptom Index—Sri Lanka | 1-5 VRS               | 1 = Not at all 5 = Very severe | N/A               | The prevalence of muscle pain was 73% 41% had “very” distressing pain in the last month of life. |
|                       |                  | (Pre-dialysis)     |                    |                  |                     |                       |                             |                   | Prevalence of Added Renal Symptoms: pain 57% 24% had very distressing bone joint pain. |
|                       |                  | CKD GSND (CKM)     |                    |                  |                     |                       |                             |                   | Prevalence of muscle soreness was 49% 12% had very distressing muscle soreness. |
| Sheshadri et al.      | United States    | Prevalent HD       | 48                 | 57               | Median Age (32,65) | 1-5 VRS               | 1 = Not at all 5 = Very severe | N/A               | Prevalence of bone joint pain was 23% The prevalence of bone joint pain was 21% and the prevalence of bone joint pain was 44% |
| Surendra et al.       | Malaysia         | Prevalent HD or PD | 141                | 54               | Current pain measured by the EQ-SD-3L | 1-3 VRS               | 1 = Not at all 3 = Severe pain/discomfort | N/A               | Prevalence of bone joint pain was 23% The prevalence of bone joint pain was 21% and the prevalence of bone joint pain was 44% |
| Thong et al.          | Netherlands      | Prevalent HD or PD | 1553               | 63               | Pain in last 4 weeks as measured by the Kidney Disease and Quality of Life Short Form | 1-5 VRS               | 1 = Not bothered at all 5 = Extremely bothered | N/A               | Prevalence of bone joint pain was 23% The prevalence of bone joint pain was 21% and the prevalence of bone joint pain was 44% |
| Study | Country | Patient population | Number of patients | Mean age (years) | Pain definition/tool | Description of severity scale | Mean pain severity | Pain prevalence |
|-------|---------|---------------------|--------------------|------------------|---------------------|------------------------------|--------------------|----------------|
| Wan Zukiman et al | Malaysia | CKD GSND (CKM) Prevalent Dialysis (Does not specify) | 187 | Not Dialyzed: 61 | Pain in the last 7 days as measured by the 0-5 VRS | Bone/Joint Pain: 3.6/5 | N/A | The total prevalence of bone/joint pain was 36.4%. The prevalence of bone and joint pain was 38% for the not dialyzed group and 34.5% for the dialyzed group. The prevalence of mild-moderate bone/joint pain was 35% and 3% for severe bone/joint pain in the non-dialyzed group. The prevalence of mild-moderate bone/joint pain was 29.9% and 4.6% for severe bone/joint pain in the dialyzed group. The total prevalence of muscle soreness was 32.1%. The prevalence of muscle soreness was 37% for the not dialyzed group and 26.4% for the dialyzed group. The prevalence of mild-moderate muscle soreness was 37.0% and 0% for severe muscle soreness in the non-dialyzed group. The prevalence of mild-moderate muscle soreness was 23.3% and 1.1% for severe muscle soreness in the dialyzed group. |
| Wesbord et al | United States | Prevalent HD | 162 | 62 | Pain in the last 7 days as measured by the 1-5 VRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Wesbord et al | United States | Prevalent HD | 75 | 59 | Pain in the last 7 days as measured by the 1-5 VRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Wesbord et al | United States and Italy | Prevalent HD | Italian Patients: 63 | 63 | Pain in the last 7 days as measured by the 1-5 VRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Wesbord et al | United States | Prevalent HD | 286 | Median Age = 64 [56-73] | Pain measured by the Short-form McGill Pain Questionnaire, duration not specified | Bone/Joint Pain: 3.1/5 | Muscle Soreness: 3.1/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Weiss et al | Germany | Prevalent HD | 860 | 68 | Pain in the past 6 weeks 1-5 VRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Wu et al | United States | CKD G3-SND (GFR < 60, Pre-dialysis) | 308 | No Pain: 66 Mild Pain: 67 Severe Pain: 65 | Pain lasting weeks, months, or even years 0-10 VRS measured by Wong-Baker Faces Pain Rating Scale | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Yong et al | China | CKD GSND (CKM) Prevalent HD or PD HD: 107 PD: 77 GSNOM/CKM: 45 | 179 | 62 | Pain as measured by the Brief Pain Inventory, duration not specified 0-10 NRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Yu et al | Taiwan | Prevalent HD | 117 | 52 | Pain in the past 7 days as measured by the 0-3 VRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |
| Zuo et al | Malaysia | CKD GSND (CKM) Prevalent Dialysis (Does not specify) | 187 | Not Dialyzed: 61 | Pain in the last 7 days as measured by the 0-5 VRS | Bone/Joint Pain: 3.2/5 | Muscle Soreness: 2.6/5 | Prevalence of bone/joint pain was 50% and the prevalence of muscle soreness was 28%. |

Note. CKD = chronic kidney disease; HD = hemodialysis; PD = peritoneal dialysis; VRS = verbal rating scale; G4 = glomerular filtration rate category G4; GSND = glomerular filtration rate category G5 not treated with maintenance dialysis; NRS = numerical rating scale; N/A = not available; CKM = conservative kidney management; VAS = visual analogue scale; VDS = verbal descriptive scale; FMS = fibromyalgia syndrome; HDF = hemodiafiltration; GFR = glomerular filtration rate; G1 = glomerular filtration rate category G1; G2 = glomerular filtration rate category G2; G3 = glomerular filtration rate category G3; NECOSAD = Netherlands Cooperative Study on the Adequacy if Dialysis.
studies assessed 112 patients from Canada and the United States following the withdrawal of dialysis. Eight studies explored pain in 1361 conservative kidney management (CKM), ie, GFR category 4 (G4) and/or 5 (G5), patients from 5 countries who had chosen conservative (non-dialytic) kidney management (CKM). Nine studies from 5 countries who had chosen conservative (non-dialytic) kidney management (CKM), ie, GFR category 4 (G4) and/or 5 (G5), patients explored pain in 1361 conservative kidney management patients.

Pain ranged from pain in the past 24 hours in 1 study, 67 a duration of pain of 3 days in 1 study, 74 a duration of pain of 3 days in 1 study, 67 a duration of pain of 24 hours in 1 study, 74 and “lasting weeks, months, or even years” in 1 study. Fifteen studies did not specify a duration, despite the intent to understand chronic pain burden. Further details of the quality assessment for each included study are presented in Supplemental Table S2.

### Prevalence and Severity of Pain

Tables 4 and 5 outline the estimated pooled prevalence of pain, and weighted mean severity of pain, for various CKD cohorts. Across the studies reporting overall pain in patients on HD, the estimated pooled prevalence was 60.5% (52.3%-68.3%) (Figure 2A). The estimated pooled prevalence of moderate or severe overall chronic pain was 43.6% (34.8%-52.7%), and the estimated pooled prevalence of severe overall chronic pain was 21.1% (12.2%-31.6%). Chronic bone/joint pain and muscle pain in patients on HD were also common with estimated pooled prevalence rates of 45.8% (35.2%-54.5%) and 44.6% (33.7%-55.7%), respectively (Figure 2B and 2C). In all cases heterogeneity was extremely high (ie, $I^2 > 95$%). For those reporting pain, the mean severity score was 6.4 (3.7-9.0) out of 10 for overall pain, 5.9 (3.4-8.3) for bone/joint pain, and 5.3 (3.3-7.4) for muscle pain. For studies reporting median pain scores, severity of overall, bone/joint, and muscle pain were reported as 5.8, 6.0, and 2.0 out of 10, respectively. Median scores could not be adjusted for the removal of patients not experiencing pain, as such these should be interpreted with caution.

Pain prevalence rates and severity scores were similar across the other CKD cohorts. For patients on either HD or PD, the estimated pooled prevalence of overall pain was 68.3% (56.6%-78.9%), moderate to severe overall pain 40.5% (27.4%-54.3%), bone/joint pain 38.9% (29.0%-49.2%), and muscle pain 65.7% (53.9%-74.8%). Severe overall pain was not reported for this group. Heterogeneity in all groups was extremely high except for the overall pain measurement, where heterogeneity was moderate ($I^2 = 69.5$%). Patients on PD had prevalence estimates for overall pain, bone/joint pain, and muscle pain of 35.9% (52.3%-68.3%), 50.0% (34.9%-65.2%), and 42.9% (7.4%-83.3%), respectively, although only 3 studies provided measures. Weighted mean severity scores for those reporting pain on either HD or PD were 4.4 (2.8-6.0) out of 10 for overall pain, and 5.0 (4.6-5.5) for muscle pain. Reported median severity scores for bone/joint pain and muscle pain were 5.0 and 4.0 out of 10, respectively. Peritoneal dialysis severity scores for bone/joint pain and muscle pain were reported as 3.2 (2.2-4.1) and 2.7 (2.2-3.1) out of 10, respectively.

Overall pain prevalence remained high in patients following withdrawal from dialysis (54.6%; 37.3%-71.3%), even in the last 24 hours of life (32.6%; 15.1%-52.8%). For patients with G4-5 CKD not on dialysis, the estimated pooled prevalence of overall pain and moderate to severe pain was 56.4% (43.0%-69.3%) and 27.3% (16.2%-39.9%).
Table 3. Summary of Pain Assessment Tools Used for the Reporting of Pain Prevalence and Severity.

| Tool                                                                 | Severity scale | Study |
|----------------------------------------------------------------------|----------------|-------|
| **Multidimensional or Multi-Symptom Assessment Tools**               |                |       |
| 36-Item Short Form Health Survey                                    | 1-6 VRS        | 27    |
| Brief Pain Inventory                                                | 0-10 NRS       | 36,40,52,58 |
| 10 cm VAS                                                           | 67             |       |
| Chronic Kidney Disease Dialysis Symptom Burden Index (adapted from the Dialysis Symptom Index) | 0-10 NRS       | 24    |
| Chronic Kidney Disease Symptom Index                                | 1-5 VRS        | 75    |
| Dialysis Discontinuation Quality of Death                           | 1-5 VRS (this scale was reversed) | 19    |
| Dialysis Frequency, Severity, and Symptom Burden Index (adapted from the Dialysis Symptom Index) | 1-10 NRS       | 35    |
| Dialysis Symptom Index                                              | 1-5 VRS        | 7,14,28,32,60,62,76,78,79 |
| 0-4 VRS                                                            | 34             |       |
| Dialysis Symptom Index—Korean Version                               | 0-4 VRS        | 63    |
| Edmonton Symptom Assessment Scale: renal                            | 0-10 NRS       | 2,3   |
| EQ-5D-3L                                                            | 53,54,81       |       |
| Kidney Disease and Quality of Life                                   | 1-6 VRS        | 84    |
| Kidney Disease and Quality of Life Short Form                       | 1-5 VRS        | 25,26,37,49,65,69,77 |
| Memorial Symptom Assessment Scale Short Form (with additional 7 renal symptom appended to end of survey) | 0-5 VRS        | 47,48 |
| Palliative Outcome Symptom Scale—Renal                              | 0-4 VRS        | 71    |
| Patient Outcome Scale Symptom Module (renal version)               | 1-5 VRS        | 30    |
| 0-4 VRS                                                            | 44,51,74       |       |
| Short Form 36                                                       | 0-100 NRS (this scale was reversed) | 72    |
| Short Form McGill Pain Questionnaire                                | 0-3 VRS        | 5,55,61 |
| 10 cm VAS                                                           | 41             |       |
| 0-5 VRS                                                            | 39,45          |       |
| Somatic Symptom Distress Scale (adapted from the Dialysis Symptom Index) | 0-3 VRS        | 59    |
| Spanish Pain Questionnaire                                          | 10 cm VAS      | 70    |
| Unnamed 11-Item Symptom Measure (created for the study but used a validated severity scale) | 1-5 VRS        | 43    |
| Unnamed 28-Item Symptom Measure                                     | 1-5 VRS        | 68    |
| Unnamed Y/N Demographic Questionnaire                              | Binary         | 80    |
| Unnamed Data Collection Sheet                                       | Unknown        | 82    |
| **Unidimensional, Single Item Pain Scales**                        |                |       |
| 0-10 VDS                                                           | 29             |       |
| 1-5 VRS                                                            | 56             |       |
| 10 cm VAS                                                           | 8,38,64,66     |       |
| 10 Point Rating Scale                                               | 50             |       |
| 100 mm VAS                                                          | 42,73          |       |
| Wong-Baker FACES Pain Rating Scale, 0-10 Likert Scale               | 57             |       |
| Binary Yes/No                                                       | 31,33,46,83    |       |

Note. VRS = verbal rating scale; NRS = numerical rating scale; VAS = visual analogue scale; VDS = verbal descriptive scale.

aThe VDS is a combination of a NRS and a VRS in that each numbers has a verbal descriptor (eg, no pain, slight pain, mild pain, moderate pain, severe pain, very severe pain, the most intense pain imaginable).

respectively. Cohorts specifying only G5 CKD patients managed conservatively had higher estimated pooled prevalence of overall pain and moderate to severe pain at 60.4% (27.7%-88.8%) and 35.0% (27.6%-42.7%), respectively. Heterogeneity was extremely high for overall pain reporting, but negligible in the studies reporting moderate to severe pain ($I^2 = 0\%$). The reported mean severity for these patients was 4.2 (3.5-4.9) out of 10.

Data were limited for the prevalence of pain in patients with earlier stages of CKD. While there was some variability in the reported prevalences, the combining of CKD G category in some studies and separation in others made the data difficult to interpret. In one small study, there were no statistically or clinically significant differences in mean overall pain severity scores between CKD G3 and G4-5, which ranged from 5.4 to 5.7 out of 10.50
## Table 4. Pain Prevalence by CKD Cohort.

| CKD cohort | Measure | Studies | Pooled prevalence (95% CI) |  
|------------|---------|---------|----------------------------|  
| **Dialysis** |  |  |  |  
| **HD Pain** |  | 23 | 60.5% (52.3%-68.3%) |  
| Moderate to Severe |  | 16 | 43.6% (34.8%-52.7%) | 96.2%  
| Severe |  | 14 | 21.1% (12.2%-31.6%) | 96.9%  
| Musculoskeletal Pain |  | 6 | 30.6% (17.1%-46.0%) | 95.2%  
| Bone or Joint Pain |  | 18 | 45.8% (35.2%-54.5%) | 95.7%  
| Moderate to Severe |  | 1 | 26.7% (17.2%-37.3%) | N/A  
| Severe |  | 2 | 8.4% (1.8%-18.8%) | 73.6%  
| Muscle Soreness |  | 13 | 44.6% (33.7%-55.7%) | 95.6%  
| Bone or Joint Pain |  | 18 | 45.8% (35.2%-54.5%) | N/A  
| Muscle Soreness |  | 3 | 9.0% (0.2%-26.0%) | 87.9%  
| Neuropathic Pain |  | 3 | 9.6% (1.1%-24.2%) | N/A  
| **HD or PD Pain** |  | 2 | 68.3% (56.6%-78.9%) | 69.5%  
| Moderate to Severe |  | 2 | 40.5% (27.4%-54.3%) | 95.4%  
| Bone or Joint Pain |  | 1 | 38.9% (29.0%-49.2%) | N/A  
| Muscle Soreness |  | 5 | 65.7% (53.9%-74.8%) | 95.5%  
| Moderate to Severe |  | 2 | 25.0% (17.5%-33.3%) | 92.3%  
| Severe |  | 3 | 23.1% (15.4%-31.8%) | 89.8%  
| **PD Pain** |  | 1 | 35.9% (52.3%-68.3%) | N/A  
| Bone or Joint Pain |  | 1 | 50.0% (34.9%-65.2%) | N/A  
| Muscle Soreness |  | 2 | 42.9% (7.4%-83.3%) | 96.7%  
| **Pre-Dialysis** |  |  |  |  
| **G3 Pain** |  | 1 | 70.8% (50.8%-87.6%) | N/A  
| **G3-4 Pain** |  | 1 | 58.3% (51.2%-64.1%) | N/A  
| Moderate to Severe |  | 1 | 50.5% (43.5%-57.6%) | N/A  
| Severe |  | 1 | 32.0% (25.6%-38.7%) | N/A  
| **G3-5ND Pain** |  | 1 | 60.7% (55.2%-66.1%) | N/A  
| Moderate to Severe |  | 1 | 29.2% (24.3%-34.4%) | N/A  
| Severe |  | 1 | 33.3% (23.9%-43.5%) | N/A  
| Bone or Joint Pain |  | 1 | 24.4% (16.1%-33.9%) | N/A  
| **G4 Pain** |  | 1 | 30.4% (20.1%-41.9%) | N/A  
| Bone or Joint Pain |  | 1 | 36.2% (25.2%-48.0%) | N/A  
| Muscle Soreness |  | 2 | 61.8% (36.8%-84.1%) | 78.9%  
| Moderate to Severe |  | 1 | 28.4% (19.0%-38.8%) | N/A  
| **G5ND Pain** |  | 1 | 37.7% (35.0%-40.5%) | N/A  
| Moderate to Severe |  | 1 | 52.2% (31.5%-72.5%) | N/A  
| Severe |  | 1 | 43.5% (26.7%-64.4%) | N/A  
| Bone or Joint Pain |  | 2 | 39.1% (31.0%-47.5%) | 0.0%  
| Severe |  | 1 | 3.0% (0.4%-7.5%) | N/A  
| Muscle Soreness |  | 2 | 29.9% (15.9%-46.1%) | 68.8%  
| **Bone or Joint Pain** |  | 1 | 0.0% (0.0%-1.7%) | N/A  
| **Post-Dialysis** |  |  |  |  
| At withdrawal |  | 1 | 54.6% (37.3%-71.3%) | N/A  
| 24 hours prior to death |  | 2 | 32.6% (15.1%-52.8%) | 74.7%  
| **CKM** |  |  |  |  
| **G4 Pain** |  | 1 | 87.4% (84.7%-90.0%) | N/A  
| Moderate to Severe |  | 1 | 56.4% (43.0%-69.3%) | N/A  
| Severe |  | 1 | 27.5% (16.2%-39.9%) | N/A  
| **G4-5ND Pain** |  | 6 | 60.4% (27.7%-88.8%) | 98.0%  
| Moderate to Severe |  | 3 | 35.0% (27.6%-42.7%) | 0.0%  
| Severe |  | 2 | 27.7% (9.0%-51.5%) | 84.4%  
| Bone or Joint Pain |  | 3 | 70.7% (41.4%-92.9%) | 95.3%  
| **G5ND Pain** |  | 2 | 13.0% (7.3%-19.9%) | 0.0%  
| Moderate to Severe |  | 2 | 39.1% (21.8%-57.8%) | 75.4%  
| Bone or Joint Pain |  | 2 | 3.3% (0.1%-9.1%) | 37.8%  

Note. CKD = chronic kidney disease; CI = confidence interval; HD = hemodialysis; PD = peritoneal dialysis; CKM = conservative kidney management; G3 = glomerular filtration rate category G3; G4 = glomerular filtration rate category G4; G5ND = glomerular filtration rate category G5 not treated with maintenance dialysis.
Table 5. Pain Severity Synthesis by CKD Cohort.

| CKD cohort | Measure | Studies | Weighted mean severity (95% CI) | Studies | Median severity^a |
|------------|---------|---------|--------------------------------|---------|-----------------|
| Dialysis   |         |         |                                |         |                 |
| HD         | Pain^8,36,41,52,58,67 | 5 | 6.38 (3.72-9.04) | 1 | 5.8 |
|            | Bone or Joint Pain^7,14,28,34,35,43,59,62,63,79 | 10 | 5.88 (3.42-8.34) | 1 | 6.0 |
|            | Muscle Soreness^7,14,28,34,62,63,79 | 6 | 5.34 (3.29-7.39) | 1 | 2.0 |
|            |         |         |                                |         |                 |
| HD and PD  | Pain^2,3 | 2 | 4.39 (2.75-6.03) |         |                 |
| PD         | Bone or Joint Pain^40 | 2 | 5.02 (4.59-5.45) | 1 | 4.0 |
|            | Muscle Soreness^26,60,69 | 2 | 3.15 (2.18-4.12) | 1 | 2.0 |
| PD         | Bone or Joint Pain^24 | 1 | 2.67 (2.24-3.10) |         |                 |
|            | Muscle Soreness^24 | 1 | 2.67 (2.24-3.10) |         |                 |
| Pre-Dialysis|         |         |                                |         |                 |
| G3         | Pain^50 | 1 | 5.40 (4.48-6.32) |         | 6.0 |
| G3-5ND     | Bone or Joint Pain^40 | 1 | 3.48 (3.06-3.90) | 1 | 4.0 |
|            | Muscle Soreness^60 | 1 | 3.48 (3.06-3.90) | 1 | 4.0 |
| G4         | Bone or Joint Pain^24 | 1 | 2.36 (2.07-2.66) | 1 | 2.36 |
|            | Muscle Soreness^24 | 1 | 2.36 (2.07-2.66) | 1 | 2.36 |
| G4-5ND     | Pain^50 | 1 | 5.70 (4.80-6.60) |         |                 |
| G5ND       | Bone or Joint Pain^24 | 1 | 2.69 (2.23-3.15) | 1 | 2.69 |
|            | Muscle Soreness^24 | 1 | 2.75 (2.31-3.19) | 1 | 2.75 |
| CKM        |         |         |                                |         |                 |
| G5ND       | Pain^58 | 1 | 4.20 (3.50-4.90) |         |                 |

Note. CKD = chronic kidney disease; CI = confidence interval; HD = hemodialysis; PD = peritoneal dialysis; G3 = glomerular filtration rate category G3; G4 = glomerular filtration rate category G4; G5ND = glomerular filtration rate category G5 not treated with maintenance dialysis; CKM = conservative kidney management.

^aMedian severity may include patients who reported no pain.

Meta-regressions were completed for pain prevalence in HD patients reporting overall pain, moderate to severe and severe overall pain, bone/joint pain, and muscle pain. No evidence was found for a publication bias in any of the above measures (P = .61, .89, .64, .62, and .10, respectively).

None of the meta-regressions returned evidence suggesting a difference in prevalence by either publication year or scale type. While there was evidence that muscle pain prevalence increased with larger sample sizes (P = .03), this appears to be the result of one very large sample influencing results (Figure 3). There was also evidence that overall pain prevalence reports increase with cohort average age (P = .02, Figure 4). In both cases, heterogeneity was only marginally reduced (I^2 = 86.7% and 94.4%, respectively).

There was strong evidence to suggest an effect of both country and pain definition on bone/joint pain as well as muscle pain (P < .001 in all cases). Supplemental Figures S1-S4 illustrate the model results in stratified forest plots. Stratifying by country significantly reduced heterogeneity in both cases: residual I^2 was 15.3% in bone/joint pain prevalence and approximately 0% in muscle pain prevalence. In both groups, there was a small cluster of Italian studies with negligible heterogeneity (I^2 = 0% in both cases), at or above the ungrouped estimated pooled prevalence estimates (stratified estimates for bone/joint pain were 60.1% [53.2%-66.8%] and 47.0% [40.0%-54.0%] for muscle pain), and a larger cluster of studies out of the United States with negligible or low heterogeneity (I^2 = 0% and 21.6%, respectively), estimating stratified pooled prevalence at or below the ungrouped estimates (44.6% [40.4%-48.8%] for bone/joint pain and 27.9% [23.3%-32.9%] for muscle pain). One additional cluster of 2 studies out of Brazil was present in the muscle pain model, which had a high estimated pooled prevalence and moderate heterogeneity (62.7% [47.5%-76.7%], I^2 = 48.5%). The remaining countries (Malaysia, Netherlands, Saudi Arabia, South Korea, Turkey, Poland, Israel, Sri Lanka, and Taiwan) were present in one or both of the models, each with only one study and large variations of reported prevalence, with ranges of 6.0% to 97.4% for bone/joint pain and 26.4% to 71.0% for muscle pain.

When stratified by pain definition, bone/joint pain prevalence heterogeneity improved marginally, but remained high (residual I^2 = 87.8). Groups included pain lasting more than 3 months, pain lasting 7 days, pain between dialysis, and no definition. The 3-month group had significantly lower scores than the rest, with an estimated pooled prevalence of 8.2% (5.0%-12.0%) and had low heterogeneity (I^2 = 6.3%). Both the 7-day group and the no definition group had high pooled prevalence estimates and high heterogeneity (50.2% [41.5%-58.9%] with I^2 = 88.2%, and 60.4% [44.0%-75.7%] with I^2 = 90.2%, respectively). The between dialysis group only contained one study (with a reported prevalence of 39.0%).
Figure 2. Forest plot of pooled prevalence estimates for (A) overall chronic pain, (B) bone/joint pain, and (C) muscle pain for patients on hemodialysis.

Note. Random effects model with 95% CIs plotted, double arcsine transformation used. CI = confidence interval.
Stratification of muscle pain prevalence by pain definition only decreased heterogeneity to a moderate level (residual $I^2 = 66.8\%$). Three clusters of pain definitions in the model were pain lasting 4 weeks, pain lasting 7 days, and no definition. The stratified pooled prevalence estimates for each group were 67.6\% (58.8\%-75.8\%), 33.9\% (27.7\%-40.4\%), and 56.4\% (51.0\%-61.7\%), with subgroup heterogeneity scores of $I^2 = 52.4\%, 72.2\%, \text{and} 0\%$, respectively.

**Discussion**

This systematic review contributes to the overall aim to address gaps in current knowledge around effective approaches to the evaluation and management of chronic pain for patients with CKD. The findings illustrate that chronic pain is extremely common and often severe across diverse CKD populations. Most patients who report pain rate their pain as either moderate (typically defined as 4-6 out of 10) or severe (7-10 out of 10) in severity. Data on PD patients and those cared for conservatively without dialysis are more limited, as are studies involving patients with CKD G3-5 not yet requiring renal replacement therapy, although the pain prevalence rates appear similar. The lowest reported prevalence of severe pain was in patients managed conservatively; this finding may reflect active pain management in CKM. Prevalence rates in patients with earlier stages of CKD were also high and did not appear to change with the severity of their CKD. This may reflect the fact that much of the pain in CKD is associated with the burden of comorbidity.

A recent qualitative systematic review explored prevalence and severity of pain in HD patients. The 2 distinct syndromes of acute and chronic pain were synthesized together and no quantitative analyses or meta-analyses were conducted. However, the main message of the review that pain is common in patients with CKD and is typically perceived as moderate or severe in intensity is consistent with our results.

These findings have clinical implications, particularly given that symptom management is a top priority for patients with CKD. Routine screening for pain in all patients with CKD should be integrated into nephrology care. This is consistent with KDIGO recommendations that state “Symptom assessment and management is an integral component of quality care for patients with advanced CKD.” Regular global symptom screening using validated tools such as the Edmonton Symptom Assessment System-revised: Renal (ESAS-r: Renal) and Palliative Care Outcome Scale-Renal (POS-renal) should be incorporated into routine clinical practice. This systematic review suggests that routine symptom assessment should extend to patients with earlier GFR categories of CKD as well.

The ESAS-r:Renal and the POS-renal are simple assessment tools that screen for several common symptoms experienced by patients with CKD. Both tools have been translated into several languages, are appropriate for screening patients even when they are pre-terminal, and perhaps, most importantly, provide the opportunity to redirect care toward a more patient-centered model. More comprehensive pain assessment tools with evidence for validity in patients with CKD are also available. The VAS, VRS, and the NRS are all valid, reliable, and appropriate for use in clinical practice, although the VAS tends to be more difficult to use than the other two. The NRS is often recommended as it has good sensitivity and generates data that can be more easily analyzed for research and audit purposes.

Many health care providers have limited expertise and feel unprepared to pursue effective treatment options for chronic pain. Some feel that it is not their responsibility to treat symptoms that are not directly related to CKD or dialysis and are therefore reluctant to prescribe and monitor analgesics. Many of these barriers result from inadequate training in the basic principles of palliative care such as symptom and pain management. Several surveys of renal fellows reported that they receive little education in
Table 6. Recommendations for Assessing and Reporting the Presence and Severity of Chronic Pain.

| Task                                      | Recommendation                                                                 |
|-------------------------------------------|--------------------------------------------------------------------------------|
| Explicit and standardized definition of chronic pain | Any painful condition that persists for greater than 3 months.94 |
| Use of a standardized severity rating scale | Assess intensity of pain by either a 0 to 10 NRS or 0-100 mm VAS95             |
| Consistent characterization of severity of pain | Mild pain: 1-3/10; moderate pain 4-6/10; severe pain 7-10/1096 |
| Present data to allow for responder analyses | Report prevalence (numerator and denominator) for each of the pain severity (mild, moderate, and severe). Mean severity scores for a population do not allow for "responder analyses" nor allow for an understanding of clinically relevant pain.95 |

Note. NRS = numerical rating scale; VAS = visual analogue scale.

palliative and end-of-life care; only 44% of fellows in 2013 reported being explicitly taught how to treat dialysis patients’ pain91 (although this was an increase from 30% in 2003)92 and only 9.4% felt very comfortable treating pain in patients with advanced CKD.93 However, nearly all the fellows thought that it was important to receive education on appropriate palliative care. Enhanced education in pain management will be required to address the burden of pain experienced by patients with CKD.96 These findings also have research implications. Developing and evaluating the relative effectiveness of pain management strategies should be assessed with particular attention to the impact on patient outcomes such as overall symptom burden, physical function, and HRQL. Most treatment recommendations have been extrapolated from treatments used successfully in the general population, with special considerations made for the selection of various analgesics based on their different pharmacokinetic properties in renal failure. In addition, future studies should be more inclusive across CKD G3-5 populations and renal replacement modalities, including patients cared for with CKM, to ensure appropriate strategies are in place for the monitoring and management of pain for all patients in need.

Several limitations of the studies included in this review were identified. If these limitations are not addressed in future studies, this will introduce bias, limit our ability to interpret the data, and ultimately compromise our ability to improve pain management. First, studies lacked a consistent approach to determining or reporting the chronicity of pain. Dialysis patients also experience recurring episodes of acute pain such as intra-dialytic headaches and cramps. This acute pain is often associated with tissue damage but typically has no progressive pattern, lasts a predictable period, subsides as healing occurs, and is episodic with periods of no pain. In contrast, chronic pain is more likely to result in functional impairment and disability, psychological distress (eg, anxiety or depression), sleep deprivation, disruption of activities of daily living, and poor HRQL as it is present for long periods of time and is often out of proportion with the extent of pain from the originating injury. Chronic pain is most commonly defined as any painful condition that persists for greater than 3 months.94 Studies that report pain should make a clear and consistent distinction between these 2 different pain syndromes. Given the variability in the reporting and defining of chronic pain in these studies, patients with acute pain may also have been included, falsely elevating the prevalence rates of true chronic pain.

There was also variability in the measures used to determine pain severity that differed in range and format (including numerical, visual, or verbal scales). Hence, a recalibration of different scales was required to compare different studies which may have introduced bias in the results of the meta-analysis. While each of these approaches has evidence for validity, they may be interpreted differently by patients, limiting the ability to compare findings across populations. There are data around what constitutes clinically significant pain and what constitutes clinically important differences in pain relief based on 0 to 10 scales and the consensus recommendation from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) to use a 0 to 10 NRS in pain studies.95

Substantial variability in the reported prevalence of pain was present in nearly all of the pooled groups, yielding very high heterogeneity measurements. As such the estimates should be interpreted with caution and may not reflect the true prevalence of pain. However, stratification by country and pain definition in some cases decreased the $I^2$ substantially, which suggests that at least some of this variability may be explained by regional practices and differences in what constitutes chronic pain.

Another limitation was that these studies reported mean severity scores for the entire cohort. The reporting of average severity scores is problematic as the distribution of pain tends to be “U-shaped” rather than bell shaped. This highly skewed distribution has the maximum frequencies at the 2 extremes of the range of variables, ie, patients with no pain and patients with severe pain, or patients having good pain relief or poor pain relief. If few patients are “average,” the use of average values is misleading. To better understand patterns of pain, it is important to determine the prevalence of clinically significant pain (such as moderate and severe pain) and for those with pain to report its severity. Finally, we did not reach out to primary authors for additional information. Recommendations for future studies that explore pain prevalence and severity are outlined in Table 6 and are in keeping with international recommendations for the reporting of pain in clinical studies.
Conclusions
This review illustrates that chronic pain is extremely common and often severe across diverse CKD populations. Routine symptom assessment, therefore, should extend to patients across GFR categories of CKD. Current data provide a strong imperative to establish pain management as educational, clinical, and research priorities in nephrology. Future research needs to move beyond describing the problem to evaluating the efficacy of pain management strategies. Establishing consistent standards for measuring presence, chronicity, type, and severity of pain is needed to appropriately conduct and interpret clinical evaluation and clinical trials and determine the impact of pain management strategies on patients’ lives.

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Not applicable

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Not applicable

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