**OBJECTIVES:** Administrative databases are increasingly used in research studies to capture clinical outcomes such as sepsis. This systematic review and meta-analysis examines the accuracy of *International Classification of Diseases*, 10th revision (ICD-10), codes for identifying sepsis in adult and pediatric patients.

**DATA SOURCES:** We searched MEDLINE, EMBASE, Web of Science, CENTRAL, Epistemonikos, and McMaster Superfilters from inception to September 7, 2021.

**STUDY SELECTION:** We included studies that validated the accuracy of sepsis ICD-10 codes against any reference standard.

**DATA EXTRACTION:** Three authors, working in duplicate, independently extracted data. We conducted meta-analysis using a random effects model to pool sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). We evaluated individual study risk of bias using the Quality Assessment of Diagnostic Accuracy Studies tool and assessed certainty in pooled diagnostic effect measures using the Grading of Recommendations Assessment, Development, and Evaluation framework.

**DATA SYNTHESIS:** Thirteen eligible studies were included in the qualitative synthesis and the meta-analysis. Eleven studies used manual chart review as the reference standard, and four studies used registry databases. Only one study evaluated pediatric patients exclusively. Compared with the reference standard of detailed chart review and/or registry databases, the pooled sensitivity for sepsis ICD-10 codes was 35% (95% CI: 22–48, low certainty), whereas the pooled specificity was 98% (95% CI: 98–99, low certainty). The PPV for ICD-10 codes ranged from 9.8% to 100% (median, 72.0%; interquartile range [IQR], 50.0–84.7%). NPV ranged from 54.7% to 99.1% (median, 95.9%; interquartile range, 85.5–98.3%).

**CONCLUSIONS:** Sepsis is undercoded in administrative databases. Future research is needed to explore if greater consistency in ICD-10 code definitions and enhanced quality measures for ICD-10 coders can improve the coding accuracy of sepsis in large databases.

**KEY WORDS:** administrative; *International Classification of Diseases*, 10th revision codes, medical records; sepsis; systematic review; validation

Sepsis is characterized by life-threatening organ dysfunction caused by dysregulated host responses to infection (1, 2). In 2017, sepsis was estimated to affect 48.9 million people globally and caused 11.0 million deaths, representing 19.7% of all global deaths (3).
The World Health Assembly has called for improved research, monitoring, prevention, diagnosis, and management of sepsis globally (4). The International Classification of Diseases (ICD), a standardized set of codes created by the World Health Organization, are relied upon to inform accurate epidemiologic monitoring, global mortality estimates, insurance reimbursement, resource allocation, and database-driven research of sepsis (5, 6). At most institutions, ICD codes are manually applied by trained health record coders to capture diseases and injuries over the course of a patient’s hospital stay (7). After undergoing many revisions for improvements in its use and structure, the 10th revision of ICD (ICD-10) was endorsed by the World Health Organization in 1990 and is used in over 100 countries (8). The quality of ICD-10 coding is influenced by not only the clarity, precision, and completeness of patient charts but also the accuracy and consistency of health record coders (9).

Epidemiologic trends suggest that although the incidence of sepsis is increasing, sepsis-associated mortality is decreasing (10–15). However, other studies have found that the age-standardized incidence of sepsis is decreasing (3) and that the combined rate of death or discharge to hospice in sepsis patients has remained stable (15). Although temporal trends and variations in care may explain these discrepancies, it is also possible that coding disparities, claims-based coding bias, and other factors may influence these conflicting trends (16).

ICD-10 codes are increasingly used to identify sepsis in administrative databases to capture this important outcome, but their accuracy for the identification of sepsis remains unclear. During the transition of 9th revision of ICD (ICD-9) to ICD-10, several studies that broadly compared the accuracy of ICD-9 to ICD-10 codes reported comparable sensitivity values for selected conditions (17, 18). For sepsis, a 2007 study that directly compared ICD-9 and ICD-10 reported higher sensitivity for sepsis and lower sensitivity for community-acquired sepsis for ICD-10 codes; ICD-9 had higher specificity for sepsis but lower specificity for community-acquired sepsis when compared with ICD-10 codes (19). Additionally, the authors reported that ICD-10 code sensitivity for sepsis and community-acquired sepsis differed significantly, whereas ICD-9 code sensitivity for the two diagnoses was similar. To date, systematic reviews and meta-analyses of ICD validation for sepsis have focused on ICD-9 or have pooled ICD-9 with ICD-10 rather than reporting ICD-10 alone (20, 21). Since many international health systems have replaced ICD-9 use with ICD-10, ICD-10-specific sepsis validation is necessary for understanding the current quality of sepsis code reporting (22).

This has implications for academic research on sepsis and health insurance reimbursement (23). The aim of this systematic review and meta-analysis is to examine the accuracy of ICD-10 codes when used to identify sepsis among pediatric and adult patients.

**MATERIALS AND METHODS**

**Data Sources and Searches**

We developed this systematic review and meta-analysis to conform to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) standards, subset Diagnostic Test Accuracy (DTA) (24). The PRISMA-DTA checklist is provided in Supplementary Table 1 (http://links.lww.com/CCX/B81). The protocol was not registered.

We searched the following electronic databases from inception until September 7, 2021: Medical Literature Analysis and Retrieval System Online (MEDLINE) (1946–), Excerpta Medica Database (EMBASE) (1974–), Institute for Scientific Information (ISI) Web of Science (1970–), Cochrane Central Register of Controlled Trials (CENTRAL), Epistemonikos, and McMaster SuperFilters. The search strategy consisted of: 1) terms
to identify ICD-10 codes; 2) keywords and Medical Subject Heading terms relating to sources of codes, validation study types, and measures of statistical accuracy; and 3) terms to identify sepsis or septic shock. The full search strategies are provided in the Supplementary Appendix 1 (http://links.lww.com/CCX/B81).

We did not apply any restrictions for date, publication status, study design (e.g., retrospective, prospective, randomized, case cohort, systematic review), or case definition, although only English language studies were included. If the search strategy identified a systematic review, references were screened for additional eligible studies.

**Study Selection**

Potential citations were screened in two stages. First, three investigators (B.L., A.G., S.L.) independently and in duplicate screened the titles and abstracts against the inclusion criteria and selected studies for full-text review. In the second stage, the same reviewers screened the full-texts in duplicate for final study inclusion. Disagreements were resolved through discussion and third-party adjudication (K.J.L., S.N.).

We included studies that met the following criteria: 1) evaluated the accuracy of ICD-10 codes for sepsis; 2) applied any reference standard such as chart review, blood cultures, or other patient registries; and 3) reported at least one measure of accuracy: sensitivity, specificity, positive predictive value (PPV), or negative predictive value (NPV) or provided the information necessary to craft 2 × 2 tables for calculation. We are choosing to use the term reference standard instead of gold standard because all reference standards used by studies may not have been the best standard available to investigators.

We excluded studies if they: 1) combined both ICD-9 and ICD-10 in their analysis, 2) lacked a clear reference standard, or 3) used ICD-9 as reference standard. There were no restrictions for age, sex, region, or clinical setting. We did not require studies to provide the full list of ICD-10 codes used.

**Data Extraction and Quality Assessment**

We developed a data abstraction form and collected the following information from the final included studies: article title, first author name, year of publication, country of origin, study duration, method of identifying sepsis, patient population (inpatient or outpatient), patient age (adult or pediatric), and any patients grouped by their diagnoses. Additionally, we collected the study’s definition of sepsis, validation procedure and reference standard, sample size, outcomes (e.g., sensitivity, specificity, PPV, NPV), and any subgroup analyses. ICD-10 codes used and their positions (e.g., primary, secondary, or any position) were documented if provided. Data were abstracted independently and in duplicate (B.L., A.G., S.L.) and compared for consistency. Disagreements were resolved through discussion or third-party adjudication if necessary (K.J.L., S.N.).

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool was used to assess the risk-of-bias of included studies (25). All studies were reviewed independently by at least two investigators (B.L., A.G., S.L.) trained in applying the QUADAS tool, and any discordance was resolved through discussion and consensus. To evaluate the certainty of evidence in the pooled diagnostic characteristics, two investigators (B.L., A.G.) independently assessed the pooled evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (26).

**Data Analysis**

We evaluated the PPV, NPV, sensitivity, and specificity for sepsis ICD-10 codes compared with the reference standard. We performed meta-analysis for sensitivity and specificity using a DerSimonian-Laird (27) and Jackson (28) method random effect model and inverse variance method for study weights. If se was not reported, we used the 95% CIs to calculate se to allow for meta-analysis using the formula: $\theta \pm 1.96 \times s.e(\theta)$. We assumed a Wald’s CI method, unless otherwise stated.

Three secondary analyses were performed. First, we compared the diagnostic accuracy of ICD-10 codes with manual chart review as reference standard compared with other reference standards. Second, we compared the accuracy of codes when studies provided a full list of codes compared with studies that did not. Finally, to determine whether certain ICD-10 codes had lower levels of accuracy at capturing sepsis diagnosis, we evaluated studies that provided individual codes across all PPV, NPV, sensitivity, and specificity and categorized them into quartiles of accuracy. We chose the 25% quartile as a cut-off point for lower accuracy values and the 75% quartile as a cut-off point for higher accuracy values.
Two analyses were performed to verify the accuracy of our sensitivity and specificity meta-analyzed estimates given the possible intercorrelation and interdependence between values from the same patient cohort/studies. In the first analyses, we selected only one subgroup from each study for inclusion in the random effects meta-analysis. Details on the subgroup selection process can be found in Supplementary Appendix 2 (http://links.lww.com/CCX/B81). In the second analyses, we first pooled the subgroups of each study to generate study-specific sensitivity and specificity values; we then pooled these study-specific values for a final sensitivity and specificity value.

All analyses were performed using R Version 4.0.2 (29) with meta package Version 4.16-2 (R Foundation for Statistical Computing, Vienna, Austria). We assessed statistical heterogeneity using the $I^2$ statistic, the chi-square test (30), and visual inspection of the forest plots.

RESULTS

Study Characteristics

After removing duplicates, we identified a total of 878 citations from our search, of which 42 underwent full text review, and ultimately 13 eligible studies were included in the systematic review and meta-analysis (Fig. 1). The results of individual sepsis studies are summarized in Supplementary Table 2 (http://links.lww.com/CCX/B81). Supplementary Table 3 (http://links.lww.com/CCX/B81) summarizes each study’s methodology.

The 13 included studies were published from 1998 to 2020, with data collection between 1994 and 2018. Sample size ranged from 78 to 1,645 participants. Four studies were conducted in Denmark (31–34), three in Australia (35–37), one in Germany (38), two in Canada (39, 40), one in England (41), one in Switzerland (42), and one in the United States (43).

Eleven studies were retrospective observational studies, and two were prospective observational studies (42, 43). ICD–10 codes were evaluated in insurance claims data (38), national patient registries (31, 32, 34), hospital discharge registries/data (33, 36, 39, 40, 42), emergency department information systems and hospital morbidity data system (35), perioperative registries (37), and National Health Service hospital episode statistics (41).

Septic shock was included by three studies (37, 38, 41). Severe sepsis was included by three studies and was defined as the ICD-10 code R65.1! (38), an Acute Physiology and Chronic Health Evaluation II diagnosis with or without additional disease ICD-9 codes (35), and a combination of sepsis codes and at least one organ dysfunction code (40). Two studies, which used bacteremia database and blood cultures, included septicemia (31, 33). The remaining studies included sepsis, with severity not explicitly outlined.

In terms of patient population, one study evaluated pediatric patients exclusively (42); one evaluated both pediatric and adult in-patients (37); seven exclusively evaluated adult in-patients (31, 32, 34, 35, 38, 40, 43); one evaluated adult outpatients in combination with inpatients, accident, emergency, and surgery patients (41); one evaluated postoperative patients (age unspecified) (39); and two evaluated hospital patients (age and patient type unspecified) (33, 36).

Of the 13 studies reviewed, seven used manual chart review exclusively as the reference standard for sepsis diagnosis (32, 34, 37–40, 43). One study used manual chart review paired with a bacteremia database as the reference standard (33), whereas three studies used laboratory information systems/blood cultures (31, 36, 42). Additionally, one study used an ICU clinical database (35), where sepsis was confirmed by an Acute Physiology Chronic Health Evaluation score and up to four corresponding ICD-9-CM codes, and one used a National Surgical Quality Improvement database (41), where sepsis was confirmed by matching text strings.

Eleven studies reported their ICD-10 sepsis codes (31–41), whereas two studies did not report their codes (42, 43). Full list of ICD-10 codes used by studies is provided in Supplementary Table 3 (http://links.lww.com/CCX/B81). Sepsis diagnosis was in the primary position for two studies (34, 35), in the “any” position for three studies (16, 32, 40), in the secondary position for one study (31), and in an unknown position for the remaining studies. Overall, codes in the primary position had comparable PPVs (68.9–93.9%) to codes in “any” position (50–100%) (16, 32, 34, 35, 40). However, one study (Søgaard et al [31]) found that sepsis codes in the secondary position had a higher PPV than codes in the primary or “any” position.

Risk of Bias Assessment

Supplementary Figure 1 (http://links.lww.com/CCX/B81) summarizes risk of bias assessments using
QUADAS. Most articles had a low risk of bias, resulting from incomplete reporting of missing data, vague index test and reference standard descriptions, and the investigator's awareness of a chart's ICD-10 codes when completing the sepsis assessment as a reference standard.
Synthesis of Results

Supplementary Table 4 (http://links.lww.com/CCX/B81) shows the nonpooled and unweighted mean, median, sample sd, and range of sepsis ICD-10 code PPV, NPV, sensitivity, and specificity.

Sensitivity was provided by nine studies (33, 35–38, 40–43) and ranged from 2.2% to 71.9% (median, 41.9%; interquartile range [IQR], 19.3–57.5%). Six studies (35, 37, 38, 40, 41, 43) provided specificity, which ranged from 85.4% to 100% (median, 99.5%; IQR, 96.2–99.6%). Twelve studies (31–41, 43) reported PPV, which ranged from 9.8% to 100% (median, 72%; IQR, 50–84.7%). Six studies (35, 37, 38, 40, 41, 43) reported NPV, which ranged from 54.7% to 99.1% (median, 95.9%; IQR, 85.5–98.3%).

Compared with a reference standard, pooled sensitivity was 35% (95% CI, 22–48%; 5 studies; low certainty) (Fig. 2A), whereas the pooled specificity was 98% (95% CI, 98–99%; 3 studies; low certainty) (Fig. 2B). Given that studies reported different sensitivity and specificity estimates based on population type (e.g., ICU, non-ICU), abstraction method (e.g., implicit coding which abstracts sepsis cases based on infectious disease and organ dysfunction codes so as to mirror the clinical sepsis criteria, explicit coding which abstracts sepsis cases based on all sepsis codes, or R codes which are clinical sepsis codes related to general signs and symptoms) (38), administrative database source (e.g., emergency department information system, hospital mortality data system), and sepsis type (e.g. sepsis, severe sepsis, septicemia), we isolated all subgroups for the sensitivity and specificity analysis.

Supplementary Appendix 2 (http://links.lww.com/CCX/B81) details our two analyses, which reassessed and confirmed the accuracy of our pooled sensitivity and specificity estimates. The first analysis, which used one isolated subgroup from each study, produced a pooled sensitivity of 33% (95% CI, 5–61%) and pooled specificity of 97% (95% CI, 95–99%). The second analysis, which pooled subgroups and then pooled conglomeration study values, produced a sensitivity of 32% (95% CI, 6–58%) and pooled specificity of 98% (95% CI, 97–99%).

Supplementary Table 5 (http://links.lww.com/CCX/B81) summarizes the GRADE evaluation for the accuracy of sepsis ICD-10 codes. Certainty of evidence was rated down by two levels for inconsistency for both sensitivity and specificity. There was significant clinical and methodological heterogeneity (e.g., use of different ICD-10 codes, outcome definitions, reference standards), which also translated into significant statistical heterogeneity ($I^2$ of pooled sensitivity = 99%; $I^2$ of pooled specificity = 94%). The five studies included in the sensitivity analysis and the three studies included in the specificity analysis did not demonstrate significant risk of bias because only one study in both analyses failed to blind investigators to patient’s ICD-10 codes. It is important to note that the low risk of bias for the sensitivity and specificity analyses is separate from the QUADAS evaluation, which evaluated all 13 studies cumulatively. We have incorporated and contextualized these concerns around inconsistency into the low certainty of evidence for sensitivity and specificity using GRADE evaluation.

Our secondary analyses showed that studies exclusively using manual chart review as reference standard yielded a lower median PPV but higher median sensitivity compared with studies that did not use manual chart review exclusively (Supplementary Table 6, http://links.lww.com/CCX/B81). Secondary analyses demonstrated that studies that explicitly reported their specific ICD-10 codes had a lower mean PPV, NPV, and sensitivity compared with studies that did not report their codes (Supplementary Table 7, http://links.lww.com/CCX/B81); however, this finding may be confounded by the greater number of studies, and thus heterogeneity, reporting explicit codes. Of the 303 different codes captured in this systematic review, the use of code A41.9A (sepsis with unspecified organism) corresponded to the highest quartile of diagnostic accuracy as it exceeded the 75% quartile of PPV, NPV, sensitivity, and specificity. However, codes O85.9, P36.0, P36.1, P36.2, P36.3, P36.4, P36.5, P36.8, P36.9, and P36 corresponded to the lowest quartile of diagnostic accuracy (Supplementary Table 8, http://links.lww.com/CCX/B81).

DISCUSSION

This systematic review and meta-analysis evaluated the accuracy of ICD-10 codes for identifying sepsis in pediatric and adult patients. We found that sepsis ICD-10 codes have consistently high NPV (median, 95.9%; IQR, 85.5–98.3%) and specificity (median, 99.5%; IQR,
but low sensitivity (median, 41.9%, IQR, 19.3–57.5%) and low PPV (median, 72.0%; IQR, 50.0–84.7%) compared with chart review and registries. The low sensitivity indicates that patients with sepsis are often not coded with sepsis ICD-10 codes, whereas the high specificity indicates the accuracy of such ICD-10 codes.

**Figure 2.** Sensitivity and specificity forest plots of sepsis *International Classification of Diseases*, 10th revision (ICD-10) codes. Forest plots of the sensitivity (5 studies; A) and specificity (3 studies; B) of sepsis ICD-10 codes compared with the reference standard of detailed chart review and/or registry databases. a = A41.0, b = implicit abstraction for severe sepsis, c = explicit abstraction with organ dysfunction codes for severe sepsis, d = R code (R65.0, R65.1, R572) abstraction for sepsis, e = R code (R65.1, R572) abstraction for severe sepsis, f = explicit abstraction for sepsis, g = diagnosis-based code categories in emergency department information system, h = diagnosis-based code categories in hospital mortality data system, i = optimized coding algorithm for ICU sepsis, j = optimized coding algorithm for ICU severe sepsis, k = optimized coding algorithm for non-ICU sepsis, l = CIHI coding algorithm for ICU severe sepsis, m = CIHI coding algorithm for ICU sepsis, n = Canadian Institute for Health Information (CIHI) coding algorithm for non-ICU Sepsis, o = septicemia, p = sepsis and septicemia.
codes when present. Thus, our findings highlight an
issue of undercoding. We also found that there is sig-
nificant heterogeneity in the sensitivity ($I^2 = 99\%$) and
specificity ($I^2 = 94\%$) of sepsis ICD-10 codes in clin-
cical, claims, and administrative or registry databases.
Overall, the certainty of evidence is rated as low.

These findings are consistent with published liter-
ature on the coding accuracy of ICD-9 and ICD-10
sepsis codes. Previous systematic reviews from 2013
and 2015 reported that ICD-9 and ICD-10 coding
failed to comprehensively capture sepsis (sensitivity
median, 42.4%) and that both coding systems demon-
strated high heterogeneity across studies (sensitivity
range, 5.9–82.3%) (20, 21). It should be noted however
that ICD-10 codes in previous studies were not inde-
pendently assessed from ICD-9 codes. In our system-
atic review, the sensitivity of ICD-10 codes for severe
sepsis and septic shock ranged 7.1–65.1% and 2.22–
59.0%, respectively; this range is comparable with the
range of sensitivity of ICD-9 codes for severe sepsis
(20.5–50.3%) and septic shock (42.4–75.1%) (20).
Previous studies have highlighted the underreport-
ing of sepsis (19). One population-based survey found
that the incidence of severe sepsis was 7.1 times lower
when ICD-10 codes were used compared with when
symptom and clinical findings were used to identify
sepsis (44). Our systematic review and meta-analysis
provide a timely confirmatory update to the literature,
as ICD-9 codes become progressively outdated.

A number of factors have been identified which may
play a role in sepsis undercoding. A 2015 study showed
that sepsis codes in non-ICU patients had a lower sen-
sitivity compared with ICU patients, even when coding
strategies were optimized (40); the authors hypothe-
sized that sepsis prevalence in non-ICU settings may be
playing a role because non-ICU physicians, who may
encounter sepsis less frequently due to lower disease
prevalence, may identify, and document sepsis differ-
ently than ICU physicians. Although depending on the
institution and clinical practice variations, prevalence
of sepsis may vary and may be significantly higher in
non-ICU settings at select centers (e.g., emergency
departments) (45, 46). Other factors such as surgical
status and timing of disease onset may also be impor-
tant for sepsis identification; one study reported that
patients presenting with postoperative sepsis at admis-
sion had ICD-10 codes with lower PPV compared with
patients who developed postoperative sepsis during
hospital stay (39). The sensitivity of ICD-10 coding is
also affected by the type of sepsis evaluated (general vs
community-acquired) (19), the site of infection (47),
and the severity of sepsis (48). In our study, we identi-
fied that the use of code A41.9A (sepsis with unspecified
organism) corresponded to the highest quartile of diag-
nostic accuracy, although sensitivity was still limited at
57.5%. The importance of coding abstraction strategies
(35, 38) and the human challenges that come with cod-
ing (clerical errors, experience and training differences,
challenges with the interpretation of healthcare docu-
mentation) cannot be understated. The qualifications,
training, and years of experience of medical coders may
influence the validity of ICD-10 coding, leading to vari-
ability between included studies (49).

Considerations to reduce undercoding may include
having specialized coding procedures for ICU patients
(where sepsis is most common) (50), including sepsis
codes found in primary and secondary diagnostic fields
when capturing outcomes (51) and pairing sepsis ICD-
10 codes and electronic medical record data to other
data sources (e.g., laboratory, pharmacy, microbiology
data) or with other clinical factors (e.g., heart rate,
respiratory rate, body temperature, WBC count, and
markers for organ dysfunction) (19, 20). Combination
coding algorithms are another consideration, although
our review found mixed results on their efficacy. One
study (Fleischmann-Struzek et al [38]) reported that
adding organ dysfunction codes increased the ability
of explicit sepsis codes to rule out disease (sensitivity)
but decreased the probability that patients with those
codes truly had sepsis (PPV); another study (Jolley et al
[40]) found that appending an optimized set of sepsis
codes to existing CIHI code definitions increased sen-
sitivity and NPV but decreased specificity and PPV.
Finally, one study (Lauridsen et al [32]) confirmed
that adding therapy codes, specifically inotropic and
vasopressor codes, substantially increased the proba-
bility that those with septic shock codes had experi-
enced septic shock (PPV). The use of an implicit sepsis
coding strategy, which abstracts sepsis cases based on
the combination of infection codes and organ dysfunc-
tion codes rather than sepsis documentation, has been
investigated by two studies in our systematic review
(35, 38). An implicit coding strategy increased the sen-
sitivity of severe sepsis ICD-10 codes (R65.1!, R57.2)
by 33.9% and sepsis ICD-10 codes by 72.9% at a cost
of PPV decrease in 34% and 44.8%, respectively (38).
There is a need for new studies which test novel ways of applying sepsis diagnostic codes, methods of data linkage, and combination coding algorithms to improve the diagnostic accuracy of ICD-10 codes for sepsis. Since coding can be confounded by changing policies, other efforts such as clinical documentation improvement programs, continuous coder training and audits, and diagnosis cover sheets or financial incentives may also be considered (52–55).

Ultimately, the undercoding of sepsis ICD-10 codes in clinical, claims, and administrative/registry databases adversely impacts epidemiologic monitoring, global mortality estimates, insurance reimbursement, resource allocation, and database-driven research of sepsis (40).

Since ICD codes are commonly used as outcome definitions, the inaccuracy of sepsis ICD-10 codes may also have implications on the development of machine-learning algorithms and electronic predictive tools for early identification of sepsis (56), as well as the implementation of big data analytics in healthcare (57). Underdiagnosis of sepsis by physicians may exacerbate the undercoding of sepsis ICD-10 codes since coders rely on physician documentation for coding. In one study (Rezende et al [58]), only 31% of septic patients seen in the emergency department were diagnosed by emergency physicians. Given the high prevalence of sepsis in ICU settings (59), and in certain hospital institutions, an even higher prevalence of sepsis in emergency departments (45, 46), targeting ICU and emergency clinicians to improve documentation may lead to improvements in coding. Methods to improve the clinician documentation and the accuracy of sepsis diagnosis include the use of combination biomarkers (60), hospital performance improvement programs (58, 61), awareness campaigns (62), checklist-based bundles, and advanced electronic screening algorithms (63). Altogether, inadequate sepsis surveillance can impact the improvement and development of sepsis management programs, which would affect the outcomes of future patients (64).

Given the inaccuracy and significant variability of ICD-10 code sensitivity between different databases and centers, we recommend that internal validation of ICD-10 code characteristics (sensitivity, specificity) should be performed prior to using such codes for research, epidemiologic studies, and/or decision making. For example, data from chart reviews and/or registry databases can be obtained and compared with a standardized sepsis definition (such as Sepsis-3 definitions [65]) to help assess the validity of ICD-10 codes the team wishes to use. Chart reviewers should be blinded to the corresponding chart’s ICD-10 codes to decrease risk of bias. Although most studies in this systematic review employed retrospective methods to assess ICD-10 code validity, prospective collection and review of clinical and laboratory data prove an option as well. Researchers may consider accessing data from ongoing or pre-existing randomized control trials to identify patients with validated diagnoses/outcomes of interest. We also encourage investigators to delineate the type of sepsis evaluated (e.g., sepsis, severe sepsis, septic shock), and we highlight the need for assessment of ICD-10 coding among pediatric populations for which there is a paucity of data.

The strengths of this systematic review include the focus only on ICD-10 codes for identifying sepsis and a comprehensive search strategy that was not restricted to time, place, age, or inpatient/outpatient status. A careful evaluation of risk of bias using QUADAS and an overall certainty of evidence using GRADE were undertaken. Additionally, we conducted a meta-analysis to ascertain the pooled sensitivity and specificity of sepsis ICD-10 codes and secondary analyses to evaluate how study designs affect sepsis ICD-10 code accuracy.

There are several limitations to our review. First, we only included English language studies and did not perform a search on unpublished literature, although missing data are small and unlikely to change conclusions. Second, despite our broad search strategy, only two studies evaluated pediatric populations (37, 42) limiting generalizability to this population (41). Third, there was significant clinical and methodological heterogeneity since studies used different reference standard definitions, outcome definitions, study designs, clinical settings, coder quality (qualification, training, and years of experience), and ICD-10 codes studied. Fourth, given that the use of the terms sepsis, severe sepsis, and septicemia were not consistent across studies, we could not differentiate these terms in our analyses. Fifth, studies included in the meta-analysis were limited in methodology as they did not test ICD-10 accuracy against the 2017 Sepsis-3 definition (65) and did not include multicenter cohorts. Sixth, although one American abstract (Dunatchik et al [43]) was included in our systematic
review, no studies in the meta-analysis were conducted in the United States. Thus, our meta-analysis’ sensitivity and specificity values do not fully reflect the potential bias from healthcare system payment incentives on ICD-10 sepsis codes (66).

The successor to ICD-10, 11th revision of ICD (ICD-11), is scheduled for release in January 2022 (67). The leap between coding versions will be significant, as ICD-11 will include more than triple the number of codes as ICD-10. Thus, future research should evaluate the accuracy of ICD-11 in identifying sepsis and whether there is a loss of coding quality during the transition (68).

CONCLUSIONS

Sepsis is underreported by ICD-10 coding, which may affect the perceived incidence of sepsis in clinical, claims, and administrative databases. Future research is needed to explore if greater consistency in ICD-10 code definitions and enhanced quality measures for ICD-10 coders can improve the diagnostic accuracy of sepsis from these large databases.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s website (http://journals.lww.com/ccejournal).

Bonnie Liu wrote the article. Bonnie Liu, Kayla J. Lucier, and Nancy M. Heddle coordinated the systematic review. Bonnie Liu and Anchit Garg developed the search strategy, and created the Grading of Recommendations, Assessment, Development, and Evaluation evidence profiles. Bonnie Liu, Anchit Garg, and Sophie Li screened and extracted the data, and evaluated studies for Quality Assessment of Diagnostic Accuracy Studies. Kayla J. Lucier and Dr. Ning acted as third-party adjudication during the screening and data extraction process. Melina Hadzi-Posev and Yang Liu provided statistical data analysis. Melina Hadzi-Posev, Kayla J. Lucier, Dr. Rochwerger, and Dr. Ning revised the article. Dr. Ning came up with the study idea. All authors approve of article submission and agree to be responsible for all aspects of work.

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