Racial and Ethnic Disparities in Adverse Drug Events: A Systematic Review of the Literature

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Abstract The *2014 National Action Plan for Adverse Drug Event Prevention* has recognized adverse drug events (ADEs) as a national priority in order to facilitate a nationwide reduction in patient harms from these events. Throughout this effort, it will be integral to identify populations that may be at particular risk in order to improve care for these patients. We have undertaken a systematic review to evaluate the evidence regarding racial or ethnic disparities in ADEs with particular emphasis on anticoagulants, diabetes agents, and opioids due to the clinical significance and preventability of ADEs associated with these medication classes. From an initial search yielding 3302 studies, we identified 40 eligible studies. Twenty-seven of these included studies demonstrated the presence of a racial or ethnic disparity. There was no consistent evidence for racial or ethnic disparities in the eight studies of ADEs in general. Asians were most frequently determined to be at higher risk of anticoagulant-related ADEs, and black patients were most frequently determined to be at higher risk for diabetes agents-related ADEs. Whites were most frequently identified as at increased risk for opioid-related ADEs. However, few of these studies were specifically designed to evaluate racial or ethnic disparities, lacking a standardized approach to racial/ethnic categorization as well as control for potential confounders. We suggest the need for targeted interventions to reduce ADEs in populations that may be at increased risk, and we suggest strategies for future research.

Keywords Adverse drug events · Patient safety · Health care quality · Health care disparities

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Introduction

Racial and ethnic health disparities have been demonstrated in a number of health care quality and patient safety domains, including preventable hospitalizations [1] and health care-associated infections [2]. The need to reduce these differences and improve the quality of health care for vulnerable populations has been highlighted in the *2011 HHS Action Plan to Reduce Racial and Ethnic Health Disparities* [3]. One important area in health care quality and patient safety is adverse drug events (ADEs), which are defined as injuries "resulting from medical intervention related to a drug" and include medication errors, allergic reactions, and side effects [4]. These events were highlighted nearly 15 years ago in a landmark report by the Institute of Medicine (IOM) as a major contributor to avoidable health care-associated morbidity and mortality [4]. Although these events remain a significant barrier to patient safety, they are often preventable, especially among certain key drug classes [5]. Since the IOM report, a number of factors, such as an increasing proportion of older individuals as well as changing patterns in medication use, have contributed to an increase in exposure to prescription medications. From 2007 to 2010, nearly one half of all Americans reported taking at least one prescription drug in the past 30 days, and an increasing proportion of Americans reported using five or more drugs in the past month [6]. Not

surprisingly, the incidence of ADEs has also increased during this time, and in 2008, these events were implicated in nearly two million inpatient stays and were reported in over 800,000 emergency department treat-and-release visits [7].

Accordingly, the *2014 National Action Plan for Adverse Drug Event Prevention* was recently established to highlight ADEs as a national patient safety priority and to facilitate a nationwide reduction in patient harms from these events. The 2014 National Action Plan identifies three high-impact medication classes of narrow therapeutic index in which ADEs are common, clinically significant, preventable, and measurable: anticoagulants, diabetes agents, and opioids. The 2014 National Action Plan proposes a four-pronged approach in reducing these adverse events, involving surveillance, prevention, incentives and oversight, and research. Throughout this approach, one important goal is to identify patient populations that may be at relatively higher risk for ADEs in order to target efforts towards reducing these disparities [5]. Given the demonstrated impact of adverse drug events, we believe that this is a key patient safety area in which to evaluate the presence of any racial or ethnic disparities. The goals of this review were as follows: (1) to synthesize existing literature in order to understand the state of evidence for racial and ethnic disparities associated with ADEs in the USA and (2) to identify gaps in existing knowledge in order to target future research.

Methods

Inclusion Criteria and Literature Search

A literature search was conducted using PubMed and EMBASE with title and abstract search terms including the following: adverse drug event(s), adverse medication event(s), hypoglycem(ia/ic), opioid(s), anticoagula(tion/nt), race, racial, ethnic(ity), disparit(y/ies), inequalit(y/ies), and safety. Results were limited to original research published in the English language. Populations of interest included non-pregnant patients older than 1 year of age in the USA or its territories. Outcomes of interest included any adverse drug event. The review was targeted to examine ADEs in general as well as ADEs related to the three drug classes highlighted in the 2014 National Action Plan [5]. Specifically, outcomes of interest associated with target drug classes included bleeding events associated with anticoagulation, supratherapeutic anticoagulation, hypoglycemia associated with diabetes agents, respiratory depression and oversedation associated with opioids, and gastrointestinal distress and pruritus associated with opioids.

Studies were excluded from further review if they did not provide quantitative data on ADEs with a risk comparison between at least two racial or ethnic groups within the USA or if they did not analyze either ADEs in general or focus on any of the target drug classes. We limited our analysis to studies within the USA in order to best capture potential racial or ethnic disparies within the context of this country's particular racial/ethnic groups and historical factors. Because we defined ADEs as events related to drugs used in medical interventions, studies focusing on intentional abuse or misuse of medications were excluded.

PubMed and EMBASE databases were queried by one reviewer (AB), and unique results were compiled. Two independent reviewers (AB and JP) screened titles and abstracts for eligibility, and studies were eliminated from further review if both reviewers agreed on their exclusion. Remaining studies were reviewed in full text by two independent reviewers (AB and JP) on the basis of pre-determined eligibility criteria. Final eligibility determinations were compared between the two reviewers, and any disagreements were settled by consensus. Additional studies were identified by reviewing reference lists of eligible studies and from a Google search, and these were reviewed by both reviewers to determine eligibility (see Online Resource 1 for detailed search methodology).

Data Analysis and Reporting

Two reviewers (AB and JP) individually abstracted data from eligible studies, including data source, population studied, outcome(s) evaluated, sample size, racial/ethnic groups, disparity identified (yes/no), and at-risk racial/ethnic group with quantification.

Given the heterogeneity of the collection and reporting of race and ethnicity data, the racial/ethnic groups were simplified and consolidated as follows: white to include Caucasian and non-Hispanic white; black to include African American and non-Hispanic black; Hispanic to include Latino; Asian to include Asian/Pacific Islander; American Indian to include Native American; unspecified minority to include aggregated non-white; and other to include individuals with missing racial/ethnic data and/or persons of mixed racial/ethnic heritage or groups not otherwise included above. These simplified racial/ethnic groups were based on the most common categories used in the included studies.

A racial/ethnic disparity was identified to be present when a study reported that a specific racial/ethnic status was significantly associated with the risk of ADEs following statistical analysis. When available, the results of multivariate logistic regression were abstracted as the preferred method of disparity quantification. For each study that demonstrated a disparity, the at-risk racial/ethnic group was defined as the group that was associated with the highest incidence or risk of the ADE. Studies that demonstrated a risk difference only affecting the "other" group were not considered to have identified a disparity for the purposes of data abstraction. This requirement allowed us to isolate the studies that identified meaningful at-risk groups for ADEs.

Results

Initial queries of PubMed and EMBASE databases by one reviewer (AB) yielded 4062 studies, and nine additional studies were identified by reviewing relevant works cited in the eligible studies and from a targeted Google search. Forty studies were determined to be eligible for inclusion in the systematic literature review (Fig. 1), with 96 % agreement between two reviewers (Online Resource 1). Eight of the included studies analyzed ADEs in general, 8 studies analyzed anticoagulant-related ADEs, 16 analyzed ADEs related to diabetes agents, and 9 studies analyzed opioid-related ADEs. One study analyzed ADEs related to both anticoagulants and diabetes agents [8].

While the majority of the included studies were retrospective cohort studies, there was significant heterogeneity in methodologies. Primary ADE detection methods were categorized as follows: (1) administrative claims data including cause of death coding, (2) chart review including electronic health records and laboratory data, (3) patient or parent report or survey, and (4) prospective documentation by research staff. ADE verification methods included secondary confirmation of an ADE utilizing any of the above detection methods: for example, a study might have used laboratory data in order to confirm an ADE that was primarily identified by administrative claims coding.

Each of the first three ADE detection methods was utilized in approximately one third of included studies. Administrative claims data were the most common sources of primary ADE detection, used in 37.5 % (15/40) of studies [9–23]. Chart review was used as a primary ADE detection method in 35 % (14/40) of studies [8, 24–36], and survey or patient/parent report was used in 27.5 % (11/40) of the studies [27, 32, 33, 37–44]. Direct documentation by research staff was used by three studies (7.5 %) [45–47]. Three studies (7.5 %) used more than one method for ADE detection [27, 32, 33]; two of these studies that analyzed agreement between methods of ADE detection found that only 5–6 % of ADEs were detected by both chart review and patient report [27, 33]. In contrast to using more than one method for ADE detection, an additional three studies utilized chart review as a secondary method only for ADE verification [14, 20, 42].

All eligible studies included white patients in their analysis, although two studies aggregated data from other racial/ethnic groups within this group. White patients made up the majority of the sample size in 33 of the studies (Online Resource Tables S1, S2, S3, and S4). The majority of studies (90 %) included black patients as a separate group in their analysis, and half included Hispanics (Fig. 2). Two of these studies analyzed Hispanics as compared to non-Hispanics, including both blacks and whites in each group [17, 32].

Thirteen studies (32.5 %) analyzed national datasets [8–13, 17–19, 21, 36, 38, 40], of which seven analyzed nationally representative samples. Only two of these studies included patients of all ages. Twenty-seven studies (67.5 %) identified a racial or ethnic disparity (Online Resource Tables S1, S2,
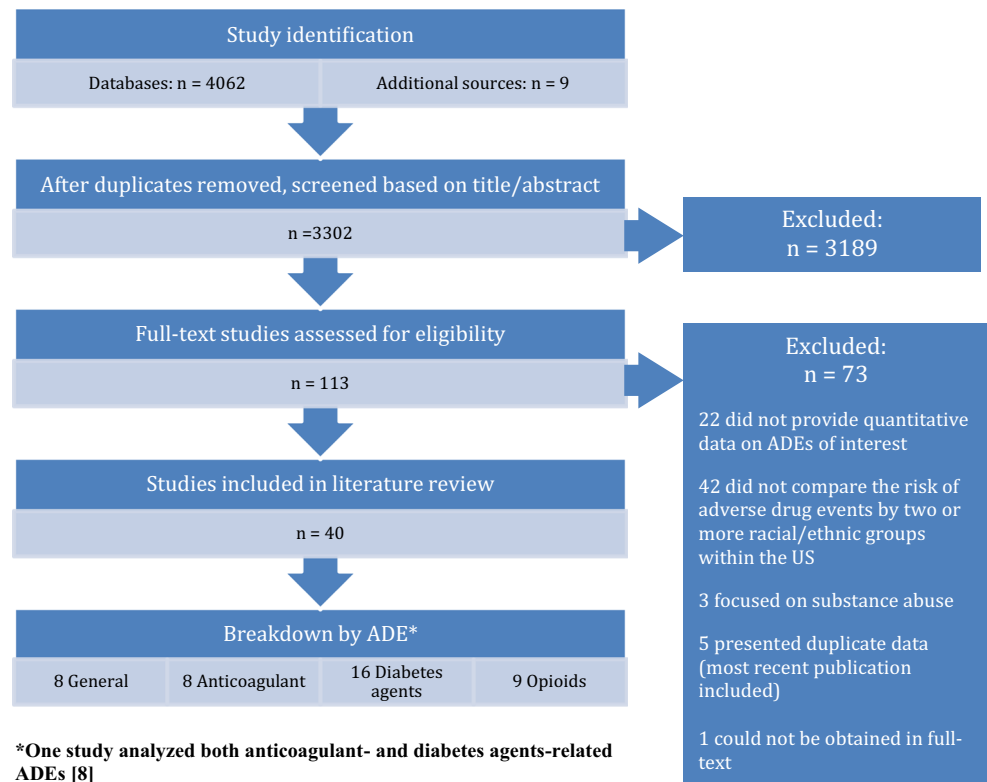
Fig. 1 Literature review process

*One study analyzed both anticoagulant- and diabetes agents-related ADEs [8]

Study identification
Databases: n = 4062   Additional sources: n = 9

After duplicates removed, screened based on title/abstract
n =3302

Excluded:
n = 3189

Full-text studies assessed for eligibility
n = 113

Excluded:
n = 73

22 did not provide quantitative data on ADEs of interest

42 did not compare the risk of adverse drug events by two or more racial/ethnic groups within the US

3 focused on substance abuse

5 presented duplicate data (most recent publication included)

1 could not be obtained in full-text

Studies included in literature review
n = 40

Breakdown by ADE*
8 General   8 Anticoagulant   16 Diabetes agents   9 Opioids

Fig. 2 Percent of studies that included specified racial/ethnic groups in the analysis of adverse drug events (*N*=40)
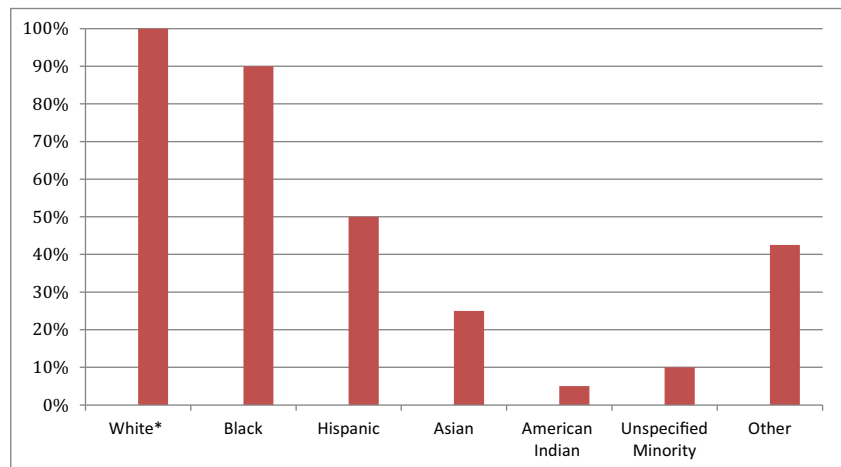
*Referent race; includes studies that aggregated Whites with other racial/ethnic groups, if Whites represented the majority of the group.

S3, and S4), of which 21 identified a minority group as the at-risk group. Racial or ethnic disparities were demonstrated in studies of inpatient, outpatient, and emergency department populations.

General Adverse Drug Events

Two of the eight studies examining ADEs in general (25 %) did identify a racial or ethnic disparity (Table 1). Both of these were studies of elderly inpatients in a national dataset; of interest, however, one of these studies identified blacks to be at risk (odds ratio [OR] 1.38, 95 % confidence interval [CI] 1.23–1.54) [12] and the other identified whites as at higher risk (OR 1.18, 95 % CI 1.18–1.18) compared to non-whites [11]. Although both studies analyzed ADEs using administrative claims data, these two studies were distinct in methodology and outcomes measured: the former analyzed the outcome of drug-related harms, including accidental overdose and adverse effects in therapeutic use, while the latter analyzed the outcome of deaths due to adverse effects of drugs in therapeutic use. Neither of those two studies adjusted for any socioeconomic factors. None of the five studies that analyzed

ADEs in the outpatient or emergency department setting demonstrated a disparity (Online Resource Table S1).

Anticoagulant-Related Adverse Drug Events

Of the eight studies analyzing anticoagulant-related ADEs, six studies assessed bleeding as an outcome and three assessed supratherapeutic anticoagulation. Five of these studies (62.5 %) found a racial or ethnic disparity to be present (Table 2). Asian patients were most frequently identified as at increased risk for anticoagulant-related ADEs, including both bleeding events and supratherapeutic anticoagulation: three of the four studies that included this group found that Asian race was associated with an approximately fourfold risk of anticoagulant-related ADEs. The other study including Asians found that this group might spend less time above therapeutic anticoagulation range (13.5 vs 16.1 % in whites), although this result was not statistically significant [25]. Two studies also found black patients to be at increased risk of anticoagulation-related ADEs compared to white patients, although the magnitude of the potential

Table 1 Summary of the evidence for racial or ethnic disparities in general ADEs

Racial/ethnic group	Studies that analyzed the group	Studies that identified the group as at risk[a]	Risk quantification (95 % CI)
White	8 [9–12, 27, 28, 31, 33]	1	OR 1.18 (1.18–1.18) compared to non-whites [11]
Black	6 [9, 10, 12, 27, 31, 33]	1	OR 1.38 (1.23–1.54) compared to whites [12]
Hispanic	5 [9, 10, 12, 27, 33]	0	OR 0.43 (0.37–0.52) compared to whites [12]
Asian	2 [12, 27]	0	OR 0.34 (0.25–0.47) compared to whites [12]
American Indian	1 [12]	0	OR 0.44 (0.24–0.79) compared to whites [12]
Unspecified minority	2 [11, 28]	0	–

CI confidence interval, *HR* hazard ratio, *OR* odds ratio

[a] At-risk racial/ethnic group was defined as the group that was associated with the highest incidence or point estimate of risk of the ADE

Table 2 Summary of the evidence for racial or ethnic disparities in drug class-specific ADEs

Racial/ethnic group	Studies that analyzed the group	Studies that identified the group as at risk[a]	Risk quantification (95 % CI)
Anticoagulant-related ADEs			
White	8 [8, 13–15, 24, 25, 29, 45]	1	Minor hemorrhage HR 1.0 compared to 0.76 (0.64–0.90) in blacks [45]
Black	8 [8, 13–15, 24, 25, 29, 45]	1	Major hemorrhage HR 1.67 (1.13–2.48) compared to whites [45]
Hispanic	5 [13–15, 25, 29]	0	—
Asian	4 [13, 14, 25, 29]	3	Elevated INR OR 3.8 (1.5–9.7), readmission for bleeding OR 4.0 (1.7–9.7), and intracranial hemorrhage HR 4.06 (2.48–6.66) compared to whites [13, 14, 29]
American Indian	0	—	—
Unspecified minority	1 [15]	1	Bleeding relative hazard 1.6 (1.2–2.1) for non-whites compared to whites [15]
Diabetes agents-related ADEs			
White	16 [8, 16–20, 32, 34–42]	1	Major hypoglycemia rate ratio 1.74–2.28 and minor hypoglycemia rate ratio 1.4–2.03 in whites compared to blacks or Hispanics [32]
Black	15 [8, 16–20, 32, 34–41]	9	Compared to whites, hypoglycemia OR 1.36–2.24 [19, 36, 38] and RR 2.0–2.13 [20, 35]; HR 2.5 for black men compared to whites [34]; rate 50/1000, versus 28/1000 in whites [17]; admission rate 4× that of whites [18]; 14.4 % of blacks versus 9.9 % of whites experienced hypoglycemia [8][b]
Hispanic[c]	8 [16, 17, 19, 32, 37–40]	3	OR 1.39 (1.36–1.42) for hypoglycemia admission [16] and 1.35 (1.16–1.58) for hypoglycemia report [37] compared to whites; hypoglycemia rates 21 (15–27)/1000 in Hispanics versus 12 (10–13)/1000 in non-Hispanics [17]
Asian	4 [16, 19, 37, 40]	0	Any hypoglycemia reported in 37.3 % of Asians and 50.1–68.4 % in other groups [40]
American Indian	1 [40]	1	Recent hypoglycemia reported in 45.6 % of American Indians and 21.7–27.6 % in other groups. Any hypoglycemia in 68.4 % of American Indians and 37.3–52.8 % in other groups [40]
Unspecified minority	1 [42]	0	—
Opioid-related ADEs			
White	9 [21–23, 26, 30, 43, 44, 46, 47]	4	Overdose death HR 1.0 in whites compared to 0.37 (0.24–0.59) in blacks [21]; nausea/vomiting OR 1.4 (1.1–1.7) and opioid side effect OR 2.8 (1.1–7.6) compared to blacks [26, 46]; nausea, vomiting, and pruritus in 34.4 % of whites versus 17.5 % of blacks [30]
Black	8 [21–23, 26, 30, 43, 44, 46]	2	Problems with side effects in 58 % of blacks compared to 32 % of whites [43]; ADE severity 8.4 points higher on Medication Side-Effect Checklist in Blacks compared to whites [44]
Hispanic	2 [23, 47]	1	At least one opioid-related ADE was experienced in 58 % of Hispanics, compared to 20 % of whites [47]
Asian	0	—	—
American Indian	0	—	—
Unspecified minority	0	—	—

CI confidence interval, *HR* hazard ratio, *INR* international normalized ratio, *OR* odds ratio, *RR* relative risk

[a] At-risk racial/ethnic group was defined as the group that was associated with the highest incidence or point estimate of risk of the ADE

[b] Due to the number of studies, confidence intervals were not included for this category. Confidence intervals can be found in Online Resource Table S3

[c] Hispanic tracked as an ethnicity, inclusive of whites/blacks in two studies [17, 32]

disparity was lower than that for Asians [14, 45]. Six studies analyzed ADEs in the inpatient setting and two studies analyzed outpatient settings, and results were variable across clinical settings (Online Resource Table S2).

Diabetes Agents-Related Adverse Drug Events

Hypoglycemia was the outcome of interest in all of the 16 included studies that examined diabetes agents-related ADEs, but definitions were highly variable. Of the studies that included a blood glucose measurement in the hypoglycemia definition, measurements ranged from 50 to 70 mg/dL. Clinical definitions included loss of consciousness, requiring assistance from another person, and hospital admission (Online Resource Table S3). Thirteen studies (81.2 %) demonstrated a racial or ethnic disparity. Blacks were the at-risk racial group in nine of these studies, and they were at increased risk compared to whites in 11 studies. The magnitude of increased risk ranged from approximately 1.25 to 2.5 (Online Resource Table S3). One study found that blacks had a fourfold higher admission rate for hypoglycemia, but this study did not control for the higher prevalence of diabetes in blacks [18]. American Indians were found to be at increased risk for hypoglycemia in the one study that analyzed this group separately. Two of the four studies that included Asians demonstrated them to be at increased risk compared to whites, with OR 1.28 (95 % CI 1.09–1.51) for report of hypoglycemia [37] and OR 1.15 (95 % CI 1.03–1.75) for acute hypoglycemia admissions [19]. One study found this group to be at decreased risk for diabetes agents-related ADEs, with 37.3 % of Asian participants reporting ever experiencing hypoglycemia, while over 50 % of the other racial or ethnic groups reported this outcome [40]. Eight studies analyzed ADEs in the inpatient setting, eight in the outpatient setting, and two in the emergency department. The three studies that did not demonstrate a racial or ethnic disparity all analyzed patients in the outpatient setting, detected ADEs via survey or report, and had relatively small sample sizes of less than 600 participants [39, 41, 42].

Opioid-Related Adverse Drug Events

Nine studies examined opioid-related ADEs. None of these studies examined a nationally representative database. Four of the studies assessed side effects in general; three studies assessed nausea, vomiting, or respiratory depression; one study assessed constipation; and one study assessed death. Seven studies (77.8 %) demonstrated a racial or ethnic disparity, with whites identified as at increased risk in four of these studies (Table 2). Of the eight studies that included blacks, the only two studies that identified ADEs by survey or patient report both found blacks to be at higher risk for opioid-related side effects [43, 44]. One of the three studies

(33.3 %) that analyzed Hispanics found this group to be at increased risk of side effects (Table 2). Four studies analyzed ADEs in the inpatient setting, three in the outpatient setting, and two in ambulatory surgery centers (Online Resource Table S4).

Discussion

Racial and ethnic disparities have been widely reported across the continuum of health, from disease prevention to health care access to patient safety and quality of care. While continued efforts towards correcting all of these health inequalities remain of utmost importance, the 2014 National Action Plan has highlighted ADEs as a national patient safety and health care quality priority [5]. The 2014 Nation Action Plan has recognized that certain populations might bear a disproportionate burden of ADEs, and it calls for a better understanding of these potential disparities.

While other literature reviews have examined racial or ethnic disparities in ADEs, these reviews have been limited by the inclusion of few studies [48] or the focus on a single medication class [49]. To our knowledge, this is the first systematic literature review to examine the state of evidence for racial or ethnic disparities in ADEs, both in general and with particular emphasis on the high-impact drug classes as outlined in the 2014 National Action Plan.

Twenty-seven of the 40 eligible studies demonstrated a racial or ethnic disparity, of which 21 identified a minority group as at risk. Sample sizes varied widely, however, and some of these studies might not have been adequately powered to detect any potential disparity. Although results were variable, Asians were most commonly identified as the at-risk group for anticoagulant-related ADEs and blacks were the most commonly identified group at risk for ADEs caused by diabetes agents. Whites were most frequently identified as at risk for opioid-related ADEs.

We identified limitations of research conducted to date regarding racial or ethnic disparities in ADEs. Most studies did not evaluate a nationally representative sample, and there was not a standardized approach to categorizing race or ethnicity. Many studies aggregated data from multiple racial or ethnic groups (e.g., non-white [11, 28, 42]), and the vast majority of studies did not include more detailed breakdowns of ethnicity by ancestry.

Furthermore, few of the included studies were specifically designed to evaluate the underlying factors that may have contributed to an identified racial or ethnic disparity: income, education, and geographical location were only analyzed in a minority of studies. Many of the studies excluded patients who did not speak English as their primary language, which may have led to underestimation of ADE rates among groups that have lower rates of English proficiency.

There were also significant limitations in the detection of ADEs. Administrative claims data has been demonstrated to grossly underestimate the incidence of ADEs [50–52]. Retrospectively detecting ADEs by chart review relies on provider recognition and documentation of the event, which also likely underestimates the true incidence and prevalence of ADEs. It has been proposed that the available methods for detecting ADEs might capture different categories of events, thus suggesting a complementary role for multiple ADE detection strategies [53]. However, only 7.5 % of the included studies used more than one method to detect ADEs. While this points to a much larger issue in ADE detection, it is not likely that this study limitation disproportionately affected a particular racial or ethnic group. We suggest the need for improved ADE detection methods, such as computer-based monitoring systems and increased electronic health record integration [5].

Limitations of our study itself include the exclusion of studies unavailable via PubMed or EMBASE and potential reviewer bias in identifying studies for consideration. Although we believe that we developed a sound and detailed methodology, it is still possible that we omitted some studies relevant to our analysis. The rationale for using electronic and common databases was that these sources were easily accessible and allowed for more efficient search filtering. The use of pre-determined inclusion and exclusion criteria, along with the high degree of agreement between two independent reviewers, makes it less likely that reviewer bias significantly impacted the results of our study.

Our study was also limited by the heterogeneity of results. Included studies differed in their approaches to categorizing patient race/ethnicity, ADE definitions and detection methods, and statistical analyses. Furthermore, studies spanned care settings and frequently did not differentiate between events occurring in the hospital or emergency department and those that first manifested in the outpatient setting. This heterogeneity, along with the relatively small number of eligible studies, limited our ability to further stratify the studies and analyze potential patterns in or contributing factors to the variable results. However, we recognize that the contributing factors for ADEs, and therefore for any potential racial/ethnic disparities, vary by care settings. In the future, a more standardized approach should be taken to study ADEs in different settings and populations, and stratification by site of ADE occurrence would be useful to inform prevention strategies.

Our study has identified critical gaps in the literature regarding racial or ethnic disparities in ADEs. Sensitive identification of ADEs remains a challenge, and 92.5 % of the studies that we included for analysis did not utilize a multimodal approach to ADE detection. Racial and ethnic data collection and reporting were neither comprehensive nor standardized, which makes it difficult to compare results across studies. Inadequate data on race/ethnicity and language can also obscure existing disparities and decreases the likelihood of effective actions to address health disparities, as emphasized by a 2009 IOM report [54]. There was no standardized approach to determining the contribution of potential confounders. Accordingly, we are unable to conclude what, if any, factors contributed to or accounted for the observed disparities. Genetics, food insecurity, and health literacy, for example, have been linked to increased risk of ADEs in certain populations [55–57].

Given the heterogeneity of the included studies, it is not surprising that the study results were highly variable. As a result, the generalizability and validity of currently available data are limited. Despite these limitations, our findings have implications for health policy and clinical practice. While we have demonstrated the need for further studies specifically designed to evaluate racial and ethnic disparities in ADEs, we have also demonstrated several potential disparities:

1. Asians may be at particular risk for anticoagulant-related ADEs. Pharmacogenomic studies have suggested that certain polymorphisms may contribute to increased warfarin sensitivity in Asians [55]. However, there is insufficient evidence to support the clinical utility of genetic testing prior to warfarin initiation [58]. Non-vitamin K antagonists have been proposed as a potentially safer option for anticoagulation in Asians [59], but more research is needed to determine the risks and benefits of these newer medications.

2. Blacks may be at increased risk for diabetes agents-related ADEs. The potential influence of patient race on diabetes management has been previously demonstrated. Black patients have been demonstrated to have lower rates of health literacy [57], which is a demonstrated risk factor for hypoglycemia [60]. In addition, race may impact a clinician's choice of diabetes agents and changes in regimens [61]. In the pediatric population, minority children were shown to be less likely than white children to receive diabetes management support in school [62].

3. In contrast to the more frequently reported instances where white patients may be at lower risk of certain adverse events, whites may be at increased risk for opioid-related ADEs. This effect may be due to a number of factors, including previously demonstrated disparities in pain management between whites and blacks [63]. While the potential undertreatment of pain in blacks remains a critical health care quality issue, it is also important to consider the impact of ADEs related to overtreatment, particularly in whites. In addition to the difference in pain management, less frequent monitoring of white patients [63] may also account for different rates of opioid-related ADEs.

Recommendations

In conclusion, we have demonstrated significant gaps in the literature regarding racial or ethnic disparities in ADEs. We have also demonstrated significant limitations in race/ethnicity reporting and ADE identification. We have highlighted several potential drug class-specific disparities, and we have suggested the need for targeted interventions. More research is needed in order to specifically tailor prevention strategies towards the most vulnerable groups for different ADEs, and we make the following recommendations in conducting further research: (1) use consistent and meaningful racial and ethnic definitions and (2) promote the evaluation of underlying factors that may be responsible for ADE disparities.

Compliance with Ethical Standards

Conflict of Interest Authors Baehr, Peña, and Hu declare that they have no conflicts of interest. The views expressed herein are those of the authors and do not necessarily reflect the views of the US Department of Health and Human Services.

Ethical Standards For this type of study, formal consent is not required. This article does not contain any studies with human participants or animals performed by any of the authors.

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