Addiction

REVIEW

doi:10.1111/j.1360-0443.2012.04027.x

Racial/ethnic disparities in HIV infection among people who inject drugs: an international systematic review and meta-analysis

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ABSTRACT

Aims The Ethnic Minority Meta-Analysis (EMMA) aims to assess racial/ethnic disparities in HIV infection among people who inject drugs (PWID) across various countries. This is the first report of the data. **Methods** Standard systematic review/meta-analysis methods were utilized, including searching for, screening and coding published and unpublished reports and meta-analytical statistics. We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for reporting methods. Disparities were measured with the odds ratio (OR) for HIV prevalence among ethnic minority PWID compared to ethnic majority PWID; an OR >1.0 indicated higher prevalence among ethnic minorities. **Results** Racial/ethnic disparities in HIV prevalence among PWID were examined in 131 prevalence reports, with 214 racial/ethnic minority to majority comparisons, comprising 106 715 PWID. Overall, the pooled OR indicates an increased likelihood of higher HIV prevalence among racial/ethnic minority compared to racial/ethnic majority PWID [OR = 2.09, 95% confidence interval (CI): 1.92–2.28]. Among 214 comparisons, 106 produced a statistically significant higher OR for minorities; in 102 comparisons the OR was not significantly different from 1.0; six comparisons produced a statistically significant higher OR for majority group members. Disparities were particularly large in the United States, pooled OR = 2.22 (95% CI: 2.03–2.44). There was substantial variation in ORs—I^2 = 75.3%: interquartile range = 1.38–3.56—and an approximate Gaussian distribution of the log ORs. **Conclusions** Among people who inject drugs, ethnic minorities are approximately twice as likely to be HIV seropositive than ethnic majorities. The great heterogeneity and Gaussian distribution suggest multiple causal factors and a need to tailor interventions to local conditions.

Keywords HIV/AIDS, injection drug use, injection drug users (IDU), international, meta-analysis, people who inject drugs (PWID), racial ethnic disparities, systematic review.

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Submitted 16 November 2011; initial review completed 11 January 2012; final version accepted 17 July 2012

INTRODUCTION

Racial/ethnic group health disparities, with racial/ethnic minority group members typically having higher rates of disease and less access to health-care, are a fundamental problem in public health and social justice in many countries [1–3]. Reducing racial/ethnic health disparities is a primary goal of the US National Institutes of Health (NIH), and since 10 January 2002 all NIH human subjects research studies have been required to collect racial/ethnic data [4]. In addition, racial/ethnic data have been collected from other funding sources, leading to a vast amount of data on health disparities in racial/ethnic minorities.

HIV/AIDS is a significant infectious disease for which there are reports of racial/ethnic group disparities in many countries [5–7]. Racial/ethnic group disparities in HIV infection among people who inject drugs (PWID) are particularly important, for several reasons:

1 HIV, injecting drug use and racial/ethnic minority group membership are all stigmatized in many different cultures [8–12]. Stigmatization may lead to higher

stress among PWID, followed by anxiety and depression [13], followed by higher rates of risk behavior [14,15].

2 The stigmatization of drug use may lead community leaders of both majority and minority communities to fail to acknowledge drug use in minority communities and thus not provide appropriate services [16,17].

3 Mistrust between racial/ethnic minority and majority communities may generate conflict that impedes implementation of HIV prevention programs for PWID, particularly for controversial issues such as needle exchange programs [18].

4 The higher rates of HIV infection among racial/ethnic minority PWID are generally not explained by high rates of risk behaviors. Minority PWID tend to report equal or lower rates of injecting risk behavior compared to racial/ethnic majority PWID [19–22]. Thus, programs that focus on reducing self-reported risk behaviors may or may not be effective in reducing disparities in HIV infection.

5 Most PWID are also sexually active, so that disparities among PWID may lead to parallel disparities in the sexual transmission of HIV [23–26].

As noted above, there is a great volume of data on racial/ethnic disparities in HIV and other diseases. The problem is not in the absence of studies, but in the task of organizing and interpreting existing data. Systematic reviews, quantitative research synthesis and meta-analyses are particularly suitable techniques for organizing and interpreting the data from large numbers of studies [27]. In this report, we present a first analysis of the international data from a systematic review and meta-analysis of racial/ethnic group disparities in HIV prevalence among PWID. The inclusion of data from many different countries permits us to assess the extent to which such disparities are found in different national and cultural settings.

METHODS

This section is presented as a summary. For additional details please see Appendix S3, presented as online supplementary material only. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [28] and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed when devising and reporting our methods [29]. Inclusion criteria, abstract and paper selection and coding procedures were adapted from the methodology used in the HCV Synthesis Project [30,31].

To be included in the review and meta-analysis, an individual report had to: (i) contain HIV data obtained from PWID and presented separately for the PWID sample; (ii) report HIV prevalence or incidence measured via laboratory testing (self-reported serostatus data was not eligible); (iii) contain racial/ethnic data for the PWID subjects; and (iv) present the PWID HIV data separately by racial/ethnic categories. Reports that did not meet all these criteria were ineligible.

Data collection commenced in December 2008 and concluded in March 2012. Abstracts for published research reports were found primarily by searching PubMed, Embase, PsycInfo and Sociological Abstracts. We also searched conference abstracts and scanned the references in other literature reviews, as well in the reference lists of eligible papers for reports not found elsewhere (i.e. footnote-chasing). Foreign language papers were explored for data; however, we reviewed only those with abstracts in English. Grey (unpublished) literature made available during the years 2005–10 was also reviewed.

Abstracts were assessed independently by one of two research associates (RAs) to identify eligible research reports. If an abstract was not disqualified on the basis of the study methods or data presented in the abstract, a full copy of the report was obtained. All papers published through December 2010 were included. Longitudinal, retrospective and cross-sectional studies, as well as randomized clinical trials, were considered. However, the data included in this meta-analysis are only cross-sectional prevalence data. Data from longitudinal studies were included, with the use of baseline data only.

Once RAs determined reports were eligible, reports were coded using a paper code form. Extracted data were entered into a FileMaker Pro 10 database. The primary summary measures extracted from reports are summarized in Appendix S2. Bibliographic information for all coded reports used in this analysis can be found in Appendix S1. Both Appendices S1 and S2 can be found as online supporting information only; details are given at the end.

All eligible papers were assessed with a quality rating form based on select measures recommended by the MOOSE group [29] and adapted from those used in the HCV Synthesis Project [30,31]. The quality form we used was termed a Transparent Reporting and Risk of Bias (TAROB) scale, because it measured indicators on both the quality of the data as well as the transparency and completeness of data reporting.

For this systematic review and meta-analysis, individual racial/ethnic group comparisons of HIV prevalence within research reports were the primary unit of analysis. The primary measures of effect size were odds ratios (ORs) for HIV prevalence among racial/ethnic minority PWID compared to racial/ethnic majority PWID. When describing different racial/ethnic groups, we used the terminology given by the authors of each report. We assessed 'majority' groups in terms of the

most populous group in the country in which the study was conducted.

ORs were calculated and transformed to the natural logarithmic scale (log ORs). Summary effect sizes were exponentiated for ease of interpretation. Forest plots were used to present the distribution of log ORs and 95% confidence intervals (CIs) for individual minority/majority group comparisons. The log ORs provided visual symmetry in the forest plots for the confidence intervals around the specific effect size for each minority/majority comparison. We used a random-effects model to calculate the pooled log ORs weighted by the DerSimonian & Laird method. Funnel plots and Egger's tests were used to assess potential publication bias. The Q-test and I^2 were used to assess heterogeneity in the log ORs. All meta-analyses were conducted in Stata version 11 [32].

RESULTS

PRISMA flow diagram

The meta-analysis consisted of 131 reports, with 214 racial/ethnic comparisons, among a total of 106 715 PWID. Figure 1 is a PRISMA [28] diagram showing the number of abstracts screened, duplicate records removed, reports read for full-text review and report eligibility outcomes. As with most meta-analyses, there is a large reduction in the number of potentially usable reports with each subsequent stage in the screening process. A total of 42 040 abstracts were returned from our search via scientific databases. In addition, another 1927 abstracts were reviewed, retrieved from sources that included grey literature, reviews, footnote-chasing, literature from our office library and our scientific networks. It is important to note that during the abstract review phase duplicates existed, and not all abstracts were read in depth if they could be eliminated unequivocally by title alone. There were 37 458 records excluded from full-text review; we were unable to locate another 320 because either we could not retrieve a copy of them via our library access, or we no longer had the financial, time or personnel resources to continue searching for them. Of the 5616 papers read for full-text review, 215 were eligible (4%); 5401 were ineligible (96%).

Diversity of racial/ethnic groups

Racial/ethnic categories of study participants were determined by using the labels given by authors of the coded reports. Table 1 shows the considerable variety of racial/ethnic groups found in the reports, as well as the variability in the way groups are labeled. Clearly, racial/ethnic disparities in HIV infection among PWID include a great number of different racial/ethnic groups throughout the world.

Funnel plots

Funnel plots are used to inspect visually for potential publication bias in meta-analyses. Asymmetry and/or gaps in the plot (particularly a lack of reports with small precision and null effects) would suggest publication bias against small studies. The funnel plot distribution of the log ORs (Fig. 2) does not suggest publication bias. We also

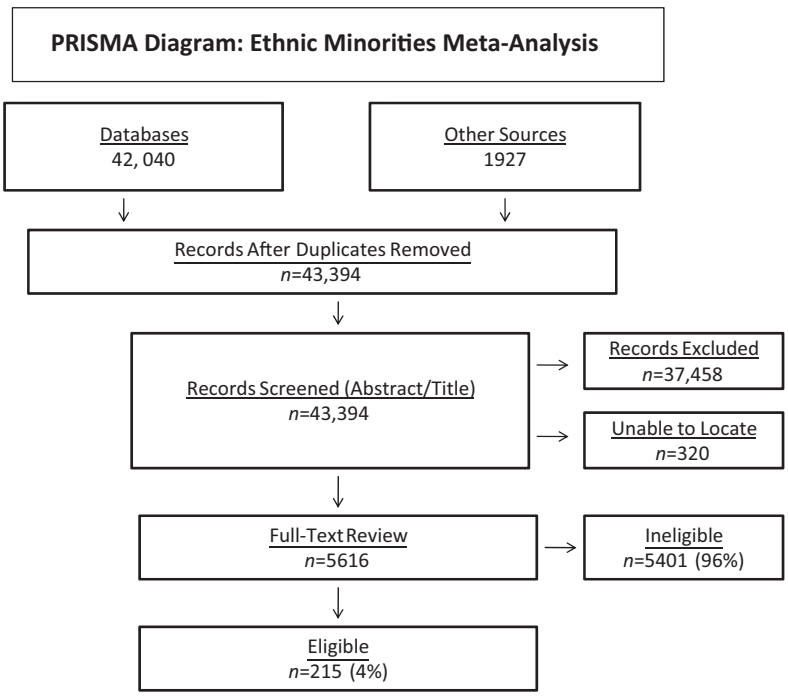

Figure 1 Flowchart showing number of abstracts reviewed, reports read, report eligibility rate and racial/ethnic comparisons in the analysis

Table 1 Diversity of racial/ethnic groups among people who inject drugs.

US studies	*Non-US studies*	
African American	Aboriginal	Native
American Indian/Alaskan Native	Anglo-Indian	Roma
Asian	Azerbaijani	Russian
Asian/Pacific Islander	Black	Tajik
Black	Caucasian	Tamil
Black/non-Hispanic	Dai	Telugu
Caucasian	Dutch	Uighur
Hispanic	English	Uzbek
Hispanic/black	Estonian	White
Hispanic/non-black	French	Yi
Latino	Fars	
Native American/Inuit	Gypsy	
Puerto Rican	Han	
White	Kazakh	
White/non-Hispanic	Malayalee	

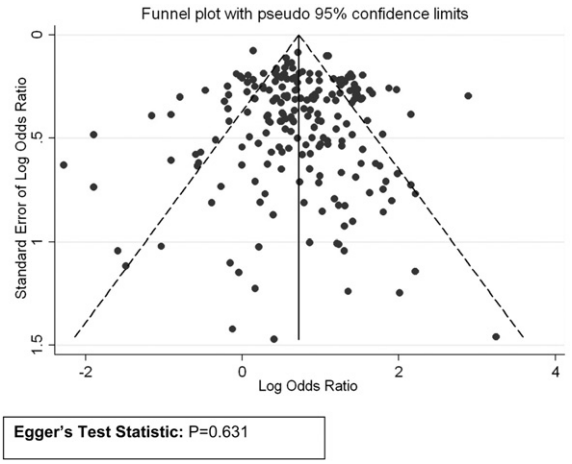

Figure 2 Funnel plot showing relation between the association of HIV infection with racial/ethnic minority status (log odds ratio) and the standard error of the log odds ratio

conducted an Egger's test to check for possible publication bias by study size. The test was not significant ($P = 0.631$).

Heterogeneity

There was substantial variation in ORs—I squared = 75.3%: IQR = 1.38–3.56. There was statistically significant heterogeneity among the log ORs in the reports assessed ($Q = 862$, $P < 0.001$, $I^2 = 75.3\%$). There was also relatively great heterogeneity of racial/ethnic comparisons within the US reports ($I^2 = 74.8\%$) and within the reports from non-US locations ($I^2 = 75.3\%$).

Forest plots

Figure 3 presents a forest plot along with the pooled log OR for all reports organized by country of report. The

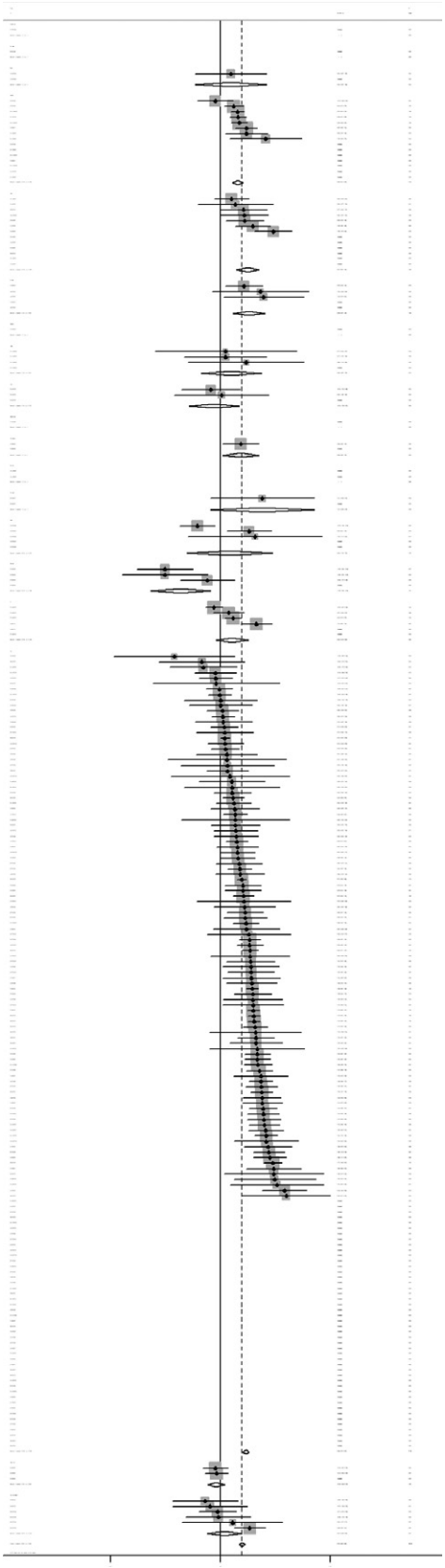

Figure 3 Forest plot with pooled log odds ratios (ORs) for all reports organized by country of report; overall log OR 0.74 (95% confidence interval 0.65–0.82)

pooled log OR comparing HIV prevalence among racial/ethnic minority PWID to racial/ethnic majority PWID was 0.74 (95% CI: 0.65–0.82). This corresponds to an OR of 2.09 (95% CI: 1.92–2.28) and indicates a very substantial difference in HIV prevalence by minority versus majority racial/ethnic group. Among the 214 comparisons, 106 produced a statistically significant higher OR for racial/ethnic minority group members compared to the majority group. In 102 the OR was not significantly different from 1.0, and in only six was there a significant OR with the majority group members having higher HIV prevalence than the minority group members. The pooled OR restricted to US comparisons was 2.22 (95% CI: 2.03–2.44) which was significantly higher than the pooled OR of 1.43 (95% CI: 1.15–1.80) for all non-US comparisons. There were eight comparisons from reports in Canada. The pooled OR for the Canadian comparisons was 1.85 (95% CI: 1.64–2.09).

Distribution of ORs

Figure 4 presents a histogram showing the log OR distribution of the racial/ethnic minority/majority comparisons with a Gaussian distribution imposed on the histogram. The histogram approximates a Gaussian distribution, with a mean of 0.72 and a standard deviation of 0.79.

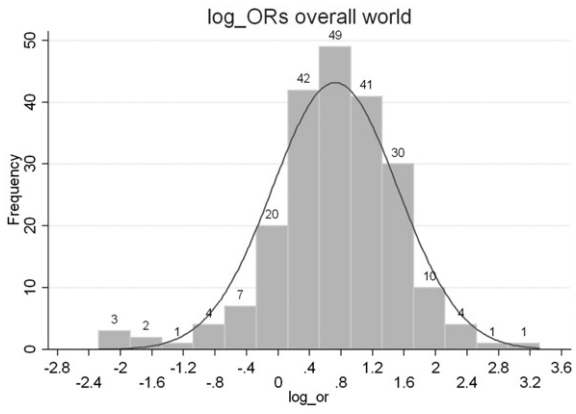

Figure 4 Histogram showing the distribution of the log odds ratios (ORs) of the racial/ethnic minority/majority comparisons with a Gaussian distribution imposed on diagram (mean = 0.72; standard deviation = 0.79)

Mean ORs by HIV prevalence

We stratified into quartiles the overall range of HIV prevalence found among the eligible reports. Table 2 presents the mean OR and its 95% CI for each of four quartiles (1–25th percentile, 26–50th percentile, 51–75th percentile and >75th percentile). Although the lowest pooled OR was for the lowest quartile (1–25th percentile), the mean ORs were quite similar across the quartiles and there was a great overlap in the 95% CIs. There were no significant differences in any pair of mean ORs for the different HIV percentile levels.

Quality assessment

We used linear regression to test the association between a report's quality score and the OR. There is no association present (R-squared = 0.003, $P = 0.39$).

DISCUSSION

To our knowledge, this is the first international systematic review/meta-analysis to examine racial/ethnic disparities in HIV prevalence among PWID. The data from this systematic review/meta-analysis show several clear patterns. First, we found great heterogeneity among all reports combined and among the US and non-US reports separately. There are undoubtedly many sources for this considerable heterogeneity, including sampling error and differences in research methods. However, this heterogeneity indicates that there are probably very important local determinants of differences in HIV prevalence among racial/ethnic minority versus racial/ethnic majority PWID.

Secondly, the log ORs approximated a Gaussian (or 'normal') distribution. Gaussian distributions are very common in natural and social sciences, and are usually taken as an indication that the phenomenon under examination is complex, with a large number of causal factors, none of which is predominant [33]. As noted by Goertzel, 'The assumption that social phenomena should be normally distributed is consistent with pluralist or other multicausal theoretical models, since a large number of unrelated and equipotent causes lead to a normal distribution' [34,35]. The likelihood that there

Table 2 A comparison of pooled racial/ethnic odds ratios of HIV infection stratified by quartile of background prevalence found among the individual study sample.

Percentile of study sample	0–25%	>25–50%	>50–75%	>75%
Background prevalence range	0–0.121	0.122–0.232	0.241–0.394	0.396–0.797
Comparisons (*n*)	53	54	48	53
Odds ratio	1.65	2.46	2.57	1.77
Confidence interval	1.30–2.08	2.07–2.92	2.24–2.94	1.50–2.09

are multiple causal factors that determine the log ORs for racial/ethnic minority versus racial/ethnic majority HIV prevalence among PWID is consistent not only with the observed Gaussian distribution, but also with the relatively great heterogeneity among the log ORs, and with conceptualizations of minority/majority health disparities as multi-faceted phenomena [23,36–38].

It is also clear that racial/ethnic minority PWID are likely to have higher HIV prevalence than racial/ethnic majority PWID in many settings. The pooled OR was 2.09 (95% CI: 1.92–2.28), indicating that across all of the reports the racial/ethnic minority PWID had a twofold-increased likelihood of higher HIV prevalence than the racial/ethnic majority PWID. This is clearly a very substantial effect size, and public health actions are needed to ameliorate existing disparities and prevent the emergence of future disparities.

Potential causal mechanisms for disparities

The purpose of this first EMMA paper is simply to present the data on ethnic disparities in HIV infection among PWID, and not to 'theoretically explain' these disparities. Nevertheless, the data presented here have important implications for developing adequate explanations of the disparities.

First, given the Gaussian distribution and great heterogeneity observed in the ORs, it is very likely that the disparities result from multiple causal factors operating at multiple levels of analysis. Simple, single-factor explanations of the disparities are likely to be incomplete, at best.

Secondly, any adequate explanation needs to address the great variation observed in the disparities, explaining not only the existence of many large disparities (ORs > 2.0) but also the existence of many small disparities (ORs < 1.2).

Thirdly, we observed significant disparities at low HIV prevalence levels (Table 2). It is likely that disparities emerge early in HIV epidemics among PWID and persist over time. As both minority and majority PWID may change risk behavior during the course of an HIV epidemic, one should not expect that current risk behaviors reflect the conditions that generated the disparities.

Fourthly, an adequate explanation of the disparities has to include a mechanism that leads ethnic-minority PWID to be more likely to inject with needles/syringes contaminated with HIV than do ethnic-majority PWID. Large historical and socio-economic factors, e.g. stigmatization and poverty, may indeed be critical for generating disparities, but the causal chains from such factors to actual disparities must include differences in the likelihood of injecting with a needle/syringe that is contaminated with HIV.

With these considerations in mind, we present one proximal causal mechanism for generating large ethnic disparities. Based on the very large minority/majority ORs in the northeastern United States and China, we propose that: *very large disparities can develop when distribution of drugs for injecting use is concentrated in racial/ethnic minority areas.* The injecting drug distribution in the United States has been concentrated traditionally in inner-city racial/ethnic minority neighborhoods [39,40]. Distribution routes for injecting drugs in southern China (and Southeast Asia as a whole) go through many racial/ethnic minority areas [41]. HIV tends to spread along injecting drug distribution routes [42,43], and thus would probably be introduced first into racial/ethnic minority areas. The social networks among drug injectors living in drug distribution areas may also be large and have many interconnections [44], creating the potential for the rapid spread of HIV.

Many factors could lead to the concentration of the distribution of drugs for injecting use in racial/ethnic minority areas, including governmental disinvestment in public services and lack of legitimate employment opportunities. Many factors may also lead to racial/ethnic segregation within cities, including discriminatory housing practices and housing-group preferences for living near members of one's own group.

This hypothesis thus provides a proximate causal mechanism to generate ethnic disparities in HIV infection among PWID and can incorporate multiple potential factors that might serve as causes at a second level of analysis (concentration of injecting drug distribution in ethnic minority areas) and multiple causes at a third level of analysis (ethnic geographic segregation). Thus, it is one example of a hypothesis that could explain very high disparities, and incorporate multiple distal causes. We are not, however, proposing this proximate cause as a universal explanation of the disparities in HIV infection among PWID.

Limitations

Several limitations for this systematic review/meta-analysis should be noted. As in all systematic reviews, it is not possible during the review process to correct for limitations found in the original studies. There are the obvious difficulties in obtaining 'representative' samples of PWID, particularly within racial/ethnic minority groups. The reports also provided little information on the characteristics of the 'majority' groups and 'minority' groups. We used the racial/ethnic group's population proportion within the country as a means to categorize racial/ethnic groups as a majority or minority. While this provides a replicable classification system, it provides little information about differences between minority and majority groups. Report authors rarely provided information on the extent of stigmatization or economic

disadvantages among minority group injectors. Additionally, in a subsequent paper we will analyze the limited information presented in the reports regarding how authors both classified racial/ethnic groups and identified which groups hold minority/majority status, including the basis for minority/majority designation.

Thirdly, our search retrieved multiple reports generated from the same research project. There are a number of long-running studies of HIV among PWID that used serial cross-sectional or replenished cohort designs that produced multiple publications. We excluded reports that clearly had the same subjects (those with the same population *n*, *n*+ and dates of data collection). Including different reports that incorporated some of the same subjects would create a design effect/interclass correlation effect and reduce the effective sample size. However, we had a total of 106 715 subjects in the studies used in our analyses, so that even a very substantial reduction in the effective total sample size would not have affected power for our statistical tests.

Implications for public health practice

While this report contains the first results of our systematic review/meta-analysis, the findings have several clear implications for public health. First, we found minority/majority group disparities in 14 countries. Countries with substantial injecting drug use among racial/ethnic minority group members should not assume that minority/majority disparities in HIV infection will not develop.

Secondly, the relatively great amount of heterogeneity observed among the reports suggests that local factors may be of great importance in determining the extent of such disparities. Public health responses may need to be tailored to local conditions. In particular, public health authorities should investigate the extent to which disparities exist in the local area, and whether ethnic majority and minority injecting networks overlap. (Overlap would create the conditions for HIV to spread across groups, but also for information and safer behavior supplies—sterile needles and syringes, condoms—to spread across groups.) Part of understanding the local HIV epidemic includes investigating the location of services that reach minority group members, as well as whether service providers need cultural competence training.

Thirdly, the relatively great heterogeneity and the Gaussian distribution suggest that these disparities are complex phenomena, with multiple causal factors. Interventions that address only a single potential casual factor of these disparities are not likely to be particularly effective.

Finally, given the high likelihood of racial/ethnic disparities in HIV among PWID, and our current lack of interventions with demonstrated effectiveness to reduce disparities, the best strategy may be to implement public health-scale interventions (needle/syringe programs, drug dependence treatment, HIV testing and antiretroviral treatment) to reduce HIV transmission among entire populations of PWID [45]. Public health-scale implementation of such interventions involves having PWID as partners, especially racial/ethnic minority group members, and respecting the human rights of PWID, with particular emphasis on those rights of racial/ethnic minorities.

Declarations of interest

The funding for this research study was provided by the National Institutes of Health through grant 5R01DA024612. The work is the sole responsibility of the authors. The researcher(s) declare they have no competing interests. The researchers declare that they do not have any connection with the tobacco, alcohol, pharmaceutical or gaming industries or anybody substantially funded by one of these organizations. There are no contractual constraints on publishing imposed by the funder.

Acknowledgements

The authors gratefully acknowledge our funding from the National Institutes of Health, through grant 5R01DA024612. The authors would also like to thank and acknowledge Jessica Speer, Krissa Corbett Cavouras and Hannah Barber for their contributions to EMMA.

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Supporting information

Additional Supporting Information may be found in the online version of this article

Appendix S1 Bibliographic characteristics of studies presented in this analysis (total publications included $n = 131$, total injection drug user (IDU) population in analysis $n = 106\ 715$)

Appendix S2 Data items extracted and coded from eligible reports

Appendix S3 Description of methods for the Ethnic Minority Meta-Analysis (EMMA)