#### **REVIEW**



# Inequities in Medically Assisted Reproduction: a Scoping Review

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#### **Abstract**

Infertility has a high prevalence in the USA and health inequities play a large role in access to medically assisted reproduction (MAR). The aim of this study was to identify gaps in research pertaining to inequities in MAR and propose suggestions for future research directions. Searches were performed using MEDLINE and Ovid Embase. Articles that reported on MAR inequities, published between 2016 and 2021 in the USA, and written in English were included. The inequities investigated were adapted from the NIH-designated health disparities populations. Each article's inequity findings were extracted and reported, along with frequencies of inequities. Our sample included 66 studies. The majority of the studies investigated MAR outcomes by race/ethnicity and found that historically marginalized populations had poorer outcomes. LGBTQ + populations were less likely to use MAR or seek infertility care. Most studies found positive correlations with MAR use with income and education. The least commonly studied inequities in our sample were sex and/or gender and rural/under-resourced populations; findings showed that men and people from rural/under-resourced populations were less likely to access MAR. Studies that examined occupational status had varying findings. We suggest that future research be targeted toward: (1) standardizing and diversifying race/ethnicity reporting regarding MAR, (2) the use of community-based participatory research to increase data for LGBTQ + patients, and (3) increasing access to infertility care for men.

Keywords Medically assisted reproduction · Healthcare inequities · Scoping review · Infertility

# Introduction

Infertility affects one in five women in the USA, according to the CDC [1]. Studies have shown that infertility impacts women in a variety of significant ways; one such study found that women with infertility had a 32% increased relative risk of mortality of any cause than women without infertility [2]. With the exception of advancing age and increasing BMI, it was found that infertility rates were comparable across various races/ethnicities, educational backgrounds, and household income brackets [3–5]. However, the rates at which women seek treatment for infertility correlate with socioeconomic

status, higher education, and whether or not they were insured [5]. Treatments for infertility have been collectively referred to as medically assisted reproduction (MAR), encompassing assisted reproductive technology (ART), in vitro fertilization (IVF), and intrauterine insemination (IUI), among others [1]. Studies show that historically marginalized patients are less likely to seek treatment for infertility compared to their white counterparts [6]. Healthcare inequities research seeks to identify potential barriers to MAR access and is necessary to increase accessibility to successful treatment for future patients with infertility.

Healthcare inequities are defined as systematic differences in access to healthcare between populations due to specific characteristics pertaining to each group [7]. Inequities in healthcare are often associated with demographic characteristics including gender, socioeconomic status, education level, geographic location, race, and ethnicity [7]. In general, research indicates that certain social inequities majorly influence the health, well-being, and quality of life of affected patients with infertility [8]. Within MAR research, many studies focus on health factors linked to infertility [9]. In conjunction with these existing studies,



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further research on healthcare inequities can help elucidate barriers to accessing care.

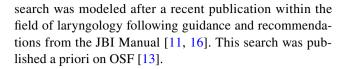
To our knowledge, this scoping review was the first of its kind to investigate research into healthcare inequities for people seeking care for infertility. A scoping review design was chosen due to the ability of scoping reviews to compile large bodies of literature and subsequently identify knowledge gaps within that literature. This design is helpful in identifying specific research questions that may be further pursued by systematic reviews [10]. In this study, multiple databases were used to evaluate studies pertaining to MAR, specifically as it relates to healthcare inequities. The purpose of our study was to identify which areas of MAR research concerning healthcare inequities may be inadequate, so that more targeted research in those areas can be pursued in the future.

#### Methods

We conducted a scoping review to identify the state of inequities research related to MAR and to determine where gaps exist. We conducted our study in accordance with best practice recommendations according to the Joanna Briggs Institute (JBI) methodology for scoping reviews [11]. For standardization of reporting, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR) [12]. We used a pilot-tested methodology incorporating standardized search strategies, inclusion/exclusion criteria, and data extraction materials. Our entire methodology and protocol were uploaded to Open Science Framework (OSF) to ensure transparency and reproducibility of results [13]. This study did not constitute human subject research and was not subject to Institutional Review Board oversight.

#### Literature Search

In July 2022, we performed a database search of MEDLINE (via PubMed) and Ovid Embase databases to identify published articles on health inequities related to MAR. According to the JBI Manual, two online databases should be used to search for articles pertaining to the review topic [11]. A 2016 study showed that use of these two specific databases together retrieved over 97% of citations included within 120 systematic reviews [14]. Published articles pertaining to inequities within the topic of MAR were obtained using PubMed's (MeSH) and Embase's (Emtree) list of vocabulary. Search terms were created using the National Institute of Health's (NIH) list of health inequity populations, which encompass the following: race and ethnicity, sex, gender, LGBTQ + identity, under-resourced/rural populations, education level, income, and occupational status [15]. Our



## **Research Question**

Our scoping review was focused on the following research question: Among patients needing MAR, what research has been published on inequities, and how has that research changed over the past six years (2016–2021)? We set out to answer sub-questions which included (1) did studies investigating similar inequities in MAR have concordance of findings and (2) to what extent has Sexual and Gender Minorities been researched since the NIH's 2016 addition? The purpose of our scoping review was to identify the state of research into inequities within MAR. Additionally, we sought to provide recommendations for future research.

# **Training**

We used two different resources for training of investigators which were delivered in person and/or on video. Prior to conducting this study, all authors were trained on the purpose and methodology of conducting a scoping review according to the JBI Reviewers' Manual 2020 [11]. The Cochrane Learning Live webinar provided supplemental information on scoping reviews as well [17].

#### **Selection Process**

After identifying citations from our systematic search, we uploaded our results into Rayyan, a platform used for conducting title and abstract screening [18, 19]. Two authors (A. H. and K. R.) first removed duplicates from the initial search and then conducted title and abstract screening according to inclusion criteria described below. The authors conducted screening in a masked, duplicate fashion. Conflicts in decisions between investigators were resolved through discussion, with a third investigator (R. B.) available for adjudication. Rationale for exclusion of studies was recorded and presented in the PRISMA flow diagram.

## **Inclusion and Exclusion Criteria**

The *population*, *concept*, and *context* framework provided by the JBI manual was used to develop criteria for inclusion in this scoping review [11]. Our *population* included literature with one of the following study designs: cohort studies, retrospective database reviews, cross-sectional analyses, literature reviews, qualitative studies, scoping reviews, systematic reviews/meta-analyses, clinical trials, and case—control studies. The *concept* of our scoping review consisted



of research focusing on health inequities related to MAR. To increase sample validity and feasibility, our review only included literature published in English [20, 21]. The *context* was addressed by limiting our inequities to the NIH's list of health disparity populations [15]. Studies included in this analysis were published between 2016 and 2021. This restriction was based on the NIH's classification of Sexual and Gender Minorities as a health inequity population in 2016 [22]. Finally, we limited the scope of our review to publications with study populations from the United States due to inconsistent connotations regarding inequities across cultures [23].

Criteria for exclusion in our data analysis included studies which (1) were published prior to 2016 or after 2021, (2) were published in a non-English language, (3) were unrelated to MAR, (4) were related to fertility preservation (e.g., cryopreservation), (5) did not analyze one of the health inequities listed, (6) non-human studies, and (7) were published as a letter to the editor, correspondence, or commentary. These study designs were excluded as they do not consistently report original research. The PRISMA flow diagram shows the reasons for exclusion throughout the screening and data extraction process.

# **Data Charting**

We used a pilot-tested Google Form to extract data from studies including title of the study, author name, PubMed Identifier, publication year, years analyzed, study design, number of subjects enrolled, and setting (e.g., single institution, multi-institution). Data points were based on recommendations from the JBI Reviewers' Manual 2020 [11].

As a calibration exercise, two researchers (A. H. and K. R.) extracted data from five identical studies. Findings were then reconciled through discussion with a third author (R. B.) available to resolve disagreements as necessary. Following completion of this calibration exercise, the authors then completed extraction from the full sample obtained in the screening process. Full sample data extraction was completed in a similar fashion. Findings for each inequity were summarized in a table including the author name, publication year, setting, number of participants, conditions examined, inequities examined, and a brief summary of the findings from each study.

## **Use of Language**

We used standard language based on the American Medical Association's (AMA) Advancing Health Equity: A Guide to Language, Narrative and Concepts to provide equity-centered, person-first language [24]. If an included study did not adhere to this guide, efforts were made to standardize language without losing original author intent.

The following race-conscious terms adopted from the AMA were used throughout this study: Black, white, Hispanic/Latina/Latino/Latinx, Native peoples/Indigenous peoples/American Indian and Alaska Native [24]. The term "historically marginalized" was used to refer to groups who have been oppressed, excluded, and segregated [24].

The AMA defines "sex" and "gender" as separate concepts. "Sex" refers to the assignment at birth as either a male or female "Gender" refers to the emotional, psychological, or social behaviors which define someone as a man, woman, both, or neither [24]. Studies which did not delineate between sex or gender were coded under both terms. We used the acronym LGBTQ+as a general term to describe all of the sexual orientations as well as sex and/or gender identities [24].

# **Data Summary and Presentation**

Our findings were summarized using Stata 17.0 (StataCorp, LLC, College Station, TX, USA). We described frequencies and percentages of (1) which inequities were found, (2) study designs (e.g., cross-sectional analyses, cohort studies, etc.), and (3) settings of each study (e.g., National database, regional database, etc.). The frequency of studies investigating research into Sexual and Gender Minorities since 2016 was also assessed.

# **Results**

#### **General Characteristics of Included Studies**

Our literature search initially yielded 5318 articles. After 917 articles were identified as duplicates and removed, the titles and abstracts of 4401 unique results were screened, with 96 included studies remaining. Among these, 30 studies did not meet inclusion criteria and were therefore excluded from data extraction. Sixty-six studies were included for full-text review and extraction. The PRISMA flow diagram—designated Fig. 1—demonstrates the study selection process and provides brief reasoning for exclusions. Table 1 outlines the frequencies of the inequities examined, study designs, and study settings. The most common inequity examined within our sample was race/ethnicity (45/66; 68.2%), followed by income status (30/66; 45.5%), and education (22/66; 33.3%). The least common inequities examined included sex and/or gender (4/66; 6.1%), occupational status (5/66; 7.6%), and rural/under-resourced populations (5/66; 7.6%). Table 2 summarizes the main findings of included studies with respect to inequities examined. Figure 2 demonstrates the frequencies of the top three most commonly examined inequities.



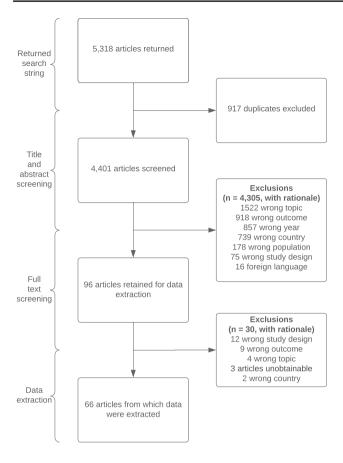


Fig. 1 PRISMA flowchart

Table 1 Frequencies and percentages of inequities among included trials

Inequities examined	Frequency $(n=66)$	Percentage (%)
Race/ethnicity	45	68.2
Sex or gender	4	6.1
LGBTQ+	15	22.7
Income	30	45.5
Education	22	33.3
Rural/under-resourced	5	7.6
Occupational status	5	7.6
Study design		
Cohort study	18	27.3
Cross-sectional analysis	22	33.3
Literature review	10	15.2
Retrospective database review	13	19.7
Qualitative study	1	1.5
Secondary RCT analysis	1	1.5
Systematic review/meta-analysis	1	1.5
Study setting		
National database	20	30.3
Multiple institutions	8	12.1
Single institution	38	57.6



# Race/Ethnicity

Within the included studies, 45 examined race/ethnicity. The majority of these examined negative outcomes following MAR such as in vitro fertilization, intrauterine insemination, and intracytoplasmic sperm injection, among others. Low live birth rates following MAR were found in Black [6, 34, 40, 46, 50, 51, 61, 63, 65, 69, 73, 76, 77, 88, 90], Asian [6, 40, 50, 51, 61, 63, 69, 73, 77], Hispanic [6, 34, 51, 57], and Middle Eastern/North African women [75]. Low intrauterine/clinical pregnancy rates were seen in Black [6. 51, 65, 69, 85, 88], Asian [6, 51, 65, 69, 85, 88], Hispanic [6, 51, 69], and American Indian/Alaska Native [33] women. Two studies found high spontaneous abortion rates in Black women [6, 73]. Low implantation rates were seen in both Asian [57] and Black [76] women. Humphries et al. found an association between increased risk of pregnancy loss and Hispanic, Black, and Asian race/ethnicity [51]. American Indian/Alaska Native women had low delivery rates [33]. Salem et al. found low fertilization rates after intracytoplasmic sperm injection in Middle Eastern/North African women [75]. One study found that BIPOC women undergoing ART were more likely to give birth to a low gestational age or extreme preterm infant [85]. Another study found that Black women using ART were more likely to have preterm or low birth weight infants [34]. In contrast, two studies found that race and ethnicity were not associated with blastocyst formation rate [56] or spontaneous abortion rates [88]. Six studies found that race and ethnicity were not associated with other aspects of infertility treatment, such as financial strain, duration of treatment, receiving medical evaluation, or having treatment declined [35, 39, 41, 47, 52, 72].

In addition to investigating outcomes following MAR, the included studies evaluated the likelihood of seeking infertility treatment. Four studies found that ART use was highest in white women [27, 28, 43, 73], while three studies found that Asian women had the highest rate of use [38, 84, 89]. Seven studies found that Hispanic women were less likely to seek out infertility treatments or use ART [6, 35, 38, 45, 54, 83, 84]. Some studies found Black women [6, 26, 38, 54, 83, 84], Asian women [6, 35], American Indian/Alaska Native women [38], or Pacific Islander women [38] to have lower rates of infertility treatments. Two studies found that Black women were more likely to discontinue IVF treatments [29, 76].

#### Sex/Gender

There were four studies that examined sex and/or gender findings in our sample. Rangel et al. found that female surgeons were more likely to use ART than male surgeons [74]. Although multiple health organizations recommend both individuals in a couple struggling with infertility be

Table 2 Characteristics of included studies

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Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Adashi & Dean, 2016 [25]	Literature review	Single institution	Infertility treatment	Income	Women with higher household incomes were more likely to use infertility treatments.
Anyalechi et al., 2021 [26]	Cohort study	Multiple institutions $n = 660$ $2011-2012$	In vitro fertilization	Race/ethnicity E	Black women were more likely to have tubal factor infertility, but they were offered IVF for treatment at similar rates to white women. However, Black women were less likely to be offered IVF treatment for non-tubal factor infertility.
Arocho et al., 2019 [27]	Retrospective database review	National database n=47,076 1995–2017	Donor insemination	Race/ethnicity, income, education, 1 LGBTQ+	The majority of donor insemination users were (1) non-Hispanic white, (2) had a college degree or more, and (3) reported a household income of more than 400% of the poverty line. Sexually marginalized women made up slightly less than half of donor insemination users.
Badreldin et al., 2021 [28]	Cohort study	Single institution $n=82$ $2005-2016$	In vitro fertilization	Race/ethnicity Vace/ethnicity	Women who used IVF were more likely to be non-Hispanic white individuals.
Bedrick et al., 2019 [29]	Cohort study	Single institution <i>n</i> = 669 2001–2014	In vitro fertilization	Race/ethnicity, income	Black women were more likely to discontinue IVF treatment and returned for treatment more slowly. Income was not associated with treatment discontinuation or time to return for treatment.
Bell, 2016 [30]	Literature review	Single institution n = 58 2008-2010	Infertility	Income, LGBTQ+	Women in same-sex relationships struggled to access infertility treatment due to insurance company requirements of medically evidence-based infertility diagnoses. High socioeconomic status women did not face the same issues as low socioeconomic status women who struggled to maintain infertility care due to miscommunication with their physicians or inability to pay for follow-up appointments.



Table 2 (continued)					
Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Cheng et al., 2019 [31]	Literature review	Single institution	Assisted reproductive technology	LGBTQ+	In the past, sexually marginalized individuals have been denied access to ART. Today, barriers for transgender patients in accessing ART include a lack of LGBTQ-centered information on fertility clinic websites, as well as financial or emotional support systems. One study found that most transgender patients could not access ART due to negative experiences with the provider.
Collins & Chan, 2017 [32]	Cross-sectional analysis	National database $n = 4792$ $2004-2007$	Infertility treatment	Race/ethnicity, income, rural/under-resourced, education	Compared to white women, Asian women were more likely to have ethical concerns with IUI, IVF, and gestational carrier use, while Black women were more likely to have ethical concerns about IUI alone. Black Asian, and Hispanic women were more likely to have ethical concerns about donce gg use. Women from lower-income households were more likely to have ethical concerns with IUI, while women with higher education levels or living in metropolitan areas were less likely to have ethical concerns with IUI, while women with higher education levels or living in metropolitan areas were less likely to have ethical concerns with IUI.
Craig et al., 2018 [33]	Cohort study	Single institution $n = 663$ 2007–2012	Intrauterine insemination	Race/ethnicity	Pregnancy and delivery rates after IUI treatment were lower among American Indian/Alaskan Native patients compared to white patients; however, Black, Asian, and Hispanic patients' pregnancy rates did not differ. Equivalent associations were found among patients taking oral fertility medications.
Crawford et al., 2017 [34]	Cohort study	National database $n = 4,327,279$ 2000–2010	Assisted reproductive technology	Race/ethnicity, education	Black and Hispanic women who used ART gave birth to fewer neonates compared to white or Asian American/Pacific Islander women. Black women who used ART were most likely to have a preterm or low birth weight neonate. The majority of women who used ART were more likely to have have a preterm or low birth weight neonate. The majority of women who used ART were more likely to have higher education levels.



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Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
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Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Dimitriadis et al., 2017 [35]	Cohort study	Single institution n = 1495 2004-2013	Intrauterine insemination	Race/ethnicity	Asian and Hispanic women waited significantly longer periods before seeking infertility treatment.  No differences were observed between races and the duration of IUI treatment, or the average number of IUI cycles completed to achieve pregnancy.
Domar et al., 2018 [36]	Cross-sectional analysis	Single institution n = 383 2010–2014	In vitro fertilization	Income	A quarter of patients interviewed attributed their discontinuation of IVF to their inability to afford the out-of-pocket treatment costs.
Downing et al., 2021 [37]	Retrospective database review	National database <i>n</i> = 201,873 2012–2016	Assisted reproductive technology	LGBTQ+	Heterosexual couples using ART had higher risks of preterm birth and low birth weight. In contrast, no difference in outcome risks was seen among same-sex couples using ART compared to same-sex couples not using ART.
Ebeh & Jahanfar, 2021 [38]	Cross-sectional analysis	National database $n = 67,554$ 2017	Assisted reproductive technology	Race/ethnicity, education	Asian women were more likely to use ART than non-Hispanic white women; Black, American Indian/ Alaska Native, Pacific Islander, and Hispanic women were less likely to use ART. Women with at least a college degree were also more likely to use ART.
Elliott et al., 2016 [39]	Cohort study	Single institution $n = 111$ 2015	Infertility treatment	Race/ethnicity, income, education, occupational status	Race and employment status were not associated with financial strain due to infertility treatment. Men with less than a college degree or an income less than \$100,000 were more likely to experience financial strain. Patients spent an average of one-fifth of their household income on infertility treatments.
Engmann et al., 2020 [40]	Secondary analysis of RCTs	Multiple institutions <i>n</i> = 1650 2014–2015	Reproductive medicine trials	Race/ethnicity, income, education	Black and Asian women, women with a high school diploma or less, and women with lower incomes were more likely to be non-adherent to protocols in reproductive medical trials. Non-adherence correlated with a lower probability of live birth.



Table 2 (continued)					
Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Farland et al., 2016 [41]	Cohort study	Single institution $n = 7422$ 1989–2009	Infertility	Race/ethnicity, income	Infertile women with lower incomes were less likely to report having had an infertility evaluation.  No significant differences were found for infertility evaluations in association with race.
Galic et al., 2021 [42]	Cross-sectional analysis	Single institution $n = 1460$ $2018-2019$	Infertility treatment	Race/ethnicity, income, education	Black patients were more likely to report that their physician did not understand their cultural background. Latinx and Asian patients reported increased concern about the side effects of infertility treatment, such as miscarriages and birth defects. Patients with lower incomes reported more concerns about financial costs of treatment, and patients with higher education levels were more likely to attribute their infertility to stress or age.
Goossen et al., 2019 [43]	Cross-sectional analysis	Multiple institutions $n = 1004$ 2019	Infertility	Race/ethnicity	White veterans were more likely to receive treatment for infertility, despite BIPOC veterans being more likely to self-report infertility.
Greenfeld & Seli, 2016 [44]	Literature review	Single institution	Assisted reproductive technology	LGBTQ+	Fertility treatment centers are becoming more welcoming to LGBTQ + patients. Studies have shown better functioning and less parenthood-related stress within same-sex couples compared to heterosexual couples. Higher relationship satisfaction was found in gay couples who used ART.
Greil et al., 2020 [45]	Cross-sectional analysis	National database $n = 1218$ 2004–2007, 2008–2010	Infertility treatment	Race/ethnicity, income, education, occupational status	Women who are (1) unemployed, (2) of Hispanic ethnicity, or (3) had lower levels of education were less likely to have fertility tests completed. Financial stress and full-time employment were associated with higher levels of depressive symptoms, while higher education levels were associated with lower levels of depressive symptoms.



Table 2 (continued)

Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Hansen et al., 2016 [46]	Cross-sectional analysis	Multiple institutions $n = 900$ 2015	Ovarian stimulation, intrauterine insemination	Race/ethnicity, income, education	Black women had lower odds of live birth after treatment, but not of conception or pregnancy. Lower incomes were associated with lower live birth rates, and education status did not have an association with pregnancy outcomes.
Hariton et al., 2021 [47]	Cross-sectional analysis	Single Institution n = 8660 2015-2020	In vitro fertilization, autologous oocytes	Race/ethnicity, income, rural/ under-resourced, education	Being declined IVF-AO was not associated with race/ethnicity or geographic location of residence. However, annual income of less than \$50,000 per year and those having a master's or professional degree were more likely to report being declined.
Harris et al., 2017 [48]	Cross-sectional analysis	National database $n = 510$ 2009–2013	Assisted reproductive technology	Rural/under-resourced	Over one-quarter of reproductive age women in the USA were found to live in an area that does not have local access to an ART clinic.
Heyward et al., 2021 [49]	Retrospective database review	Single institution 2013–2020	Frozen embryo transfer	Race/ethnicity	Black women had significantly lower live birth rates after IVF, while there was no difference between white and Asian women. Spontaneous abortion rates were similar among races. Also, Black women had significantly lower live birth rates after natural cycle and programmed frozen embryo transfer.
Hill et al., 2017 [50]	Cohort study	Single institution n = 2956 2009-2013	In vitro fertilization	Race/ethnicity	Black and Asian women had lower live birth rates in unadjusted models. When models were adjusted for age, BMI, and other infertility-related factors, live birth rates were similar among different races/ethnicities.
Humphries et al., 2016 [51]	Systematic review/meta-analysis	Multiple institutions $n = 24$	In vitro fertilization	Race/ethnicity	The majority of studies found lower clinical pregnancy and live birth rates for Black, Asian and Hispanic women using IVF, as well as increased risk for pregnancy loss.



Table 2 (continued)					
Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Insogna & Ginsburg, 2018 [6]	Literature review	Single institution	Infertility	Race/ethnicity, income	Black, Hispanic, and Chinese American patients were much less likely to seek infertility treat- ment, despite Black and Hispanic patients having higher rates of infertility. These populations had lower clinical pregnancy and live birth rates following IVF; Black women had higher spontaneous abortion rates. Financial barriers were shown to play a large role in these populations' access to infertility treatment—one study saw a fourfold increase in ART use in Black women with at least partial insurance coverage.
Insogna et al., 2020 [52]	Cross-sectional analysis	Multiple institutions $n = 242$ 2018–2019	Infertility treatment	Race/ethnicity, income, education, occupational status	The majority of patients, regardless of race/ethnicity or educational level, sought care before 1 year when struggling with infertility; some differences were found when races were compared, but none was statistically significant. Over half of the patients reported treatment cost as a barrier to care. Hispanic patients were less likely to report that time off work was a barrier to care, compared to white patients.
Jacobson, 2018 [53]	Cross-sectional analysis	Single institution $n = 444$	Surrogacy	LGBTQ+	Most fertility clinic websites did not have content about surrogacy services for gay men. Fertility clinic websites with content for gay men made it easily accessible on the home page half the time. In contrast, the majority of surrogacy agency websites displayed content featuring gay couples.



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Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings

Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Janitz et al., 2019 [54]	Retrospective database review	National database n=1824 2002, 2006–2010, 2011–2013	Infertility treatment	Race/ethnicity, income, education	Black and American Indian women were less likely to seek medical help to get pregnant, compared to Asian and white women. Hispanic women were less likely to seek infertility care than non-Hispanic women, but this was not significant. Women who sought treatment for infertility were more likely to have 16 or more years of education and higher household incomes.
Jin & Dasgupta, 2016 [55]	Retrospective database review	National database <i>n</i> = 923 2011, 2014; 2013, 2015	Assisted reproductive technology	LGBTQ+	Only a quarter of fertility clinic websites had reproductive education materials for same-sex couples in 2014; this percentage increased to almost 40% by 2015. Information for transgender individuals, however, was presented on less than 5% of the websites.
Khunte et al. 2020 [56]	Retrospective database review	Single institution <i>n</i> = 1134 2013–2016	Infertility treatment	Race/ethnicity	Race was not independently associated with blastocyst formation rate after controlling for BMI and other confounding variables.
Kotlyar et al., 2021 [57]	Cohort study	National database <i>n</i> = 148,572 2014–2016	Assisted reproductive technology	Race/ethnicity	Asian women without prior ART history were more likely to use ICSI, though implantation rates and overall ART success rates were lower, regardless of prior ART history. Hispanic women had lower live birth rates, despite having more embryos transferred during treatment.
Lee, 2017 [58]	Qualitative study	Single institution n = 54 2013-2015	Assisted reproductive technology	Income	Patients often paid out-of-pocket for ART treatments due to lack of insurance coverage. Interviews showed that finances were at the forefront of many patients' concerns regarding ART.



Table 2 (continued)					
Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Lee et al., 2019 [59]	Cross-sectional analysis	Single institution $n = 1427$ 2016	Assisted reproductive technology	Race/ethnicity, sex or gender, income, education, LGBTQ+	The majority of participants supported placing age limits on IVF use; 70% supported placing limits on women, while 57% supported placing limits on men. People who identified as Black, sexually marginalized, or those with a college degree were less likely to support IVF age limits on women. Income was not associated with support for or against age limits.
Leung et al., 2019 [60]	Cohort study	Single institution $n = 156$ 2010–2018	Assisted reproductive technology	LGBTQ+	Significantly more oocytes were retrieved from transgender patients compared to cisgender patients during treatment cycles, even after the use of testosterone for hormone replacement therapy.
Ligon et al., 2019 [61]	Cohort study	National database $n = 44,696$ 2013–2015	In vitro fertilization	Race/ethnicity	Black and Asian women using IVF had lower live birth rates, though this was independent of ovarian reserve biomarkers.
Lindheim et al., 2019 [62]	Cross-sectional analysis	Single institution $n = 78$ 2017	Assisted reproductive technology	Income, LGBTQ+, occupational status	Couples in the USA using ART were less likely to financially plan for treatment, or take on extra employment in order to afford treatment. Couples sought out ways to better manage the financial strain, such as undergoing fewer cycles. Gay couples faced more barriers to ART—including lack of benefits and discrimination—which was associated with country of residence.
Liu et al., 2021 [63]	Retrospective database review	Single institution <i>n</i> = 899 2008-2015	Assisted reproductive technology	Race/ethnicity	There was a high concordance of race between oocyte recipients and donors. Regardless of donor race, cycles with Black recipients had lower live birth rates. Hispanic recipients with Hispanic donors had higher live birth rates, but had lower birth rates with non-Hispanic donors. The lowest live birth rates were seen for non-Asian recipients and Asian donors.



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Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Mehta et al., 2016 [64]	Literature review	Multiple institutions	Male factor infertility	Income, education	Infertile men had high out-of- pocket treatment expenses and often reported limitations to treat- ment due to cost. Couples with college educations and higher incomes were more likely to seek out expensive, higher intensity fertility treatments. College edu- cation was independently related to improved odds of pregnancy and treatment success.
Mikhael et al., 2021 [65]	Cross-sectional analysis, cohort study	Single institution <i>n</i> = 194 2015–2018	Infertility treatment	Race/ethnicity, rural/under- resourced	Both Black and Asian women had lower odds of achieving intrauterine pregnancy, while Black women alone had lower live birth rates following ART. The average travel distance for women to fertility clinics for treatment was 143.1 miles; telehealth was not associated with negative outcomes.
Monseur et al., 2019 [66]	Cohort study	Single institution <i>n</i> = 11,396 1999–2017	Intrauterine insemination	LGBTQ+	Heterosexual couples undergoing intrauterine insemination with autologous or donor sperm had increased pregnancy rates associated with double insemination; this effect was not seen in Iesbian couples or single patients. Lesbian couples and single women had sufficient success with single insemination, possibly due to better fertility statuses.
Nazem et al., 2019 [67]	Cohort study	Single institution n = 800 2006–2018	Ovarian induction, intrauterine insemination	LGBTQ+	Pregnancy outcomes were similar between lesbian and heterosexual groups. Multiple gestation rates were higher in lesbian women undergoing ovulation induction compared to lesbian women undergoing natural cycles.
Negris et al., 2021 [68]	Cross-sectional analysis	Single institution <i>n</i> = 1460 2018–2019	Emotional stress	Race/ethnicity, income, education	Black and Latinx women were most likely to believe that emotional distress can reduce fertility treatment success, or cause a miscarriage. Lower household incomes and lower educational levels were found to be associated with similar beliefs.



Table 2   (continued)					
Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Okeigwe & Marsh, 2018 [69]	Literature review	Single institution	In vitro fertilization	Race/ethnicity, income, education	Black and Asian women had decreased odds of pregnancy and live births compared to white women. White women with higher education and higher income had more access to treatment.
Öztürk et al., 2021 [70]	Cross-sectional analysis, qualitative study	Single institution $n = 12$ 2018	Infertility treatment	Income, rural/under-resourced	All study participants reported increased financial strain due to treatment costs. Some patients considered the financial burden of treatment to be more stressful than the treatment itself. Three participants reported that living in rural areas created a barrier to accessing fertility treatment.
Peipert et al., 2019 [71]	Cross-sectional analysis	Single Institution n=37 2017	Infertility treatment	Race/ethnicity, sex or gender, LGBTQ+	Increased access to fertility care for single men, single women, lesbian, gay, transgender, and Jewish individuals was observed after grant awards were given by charity foundations.
Persily et al., 2020 [72]	Retrospective database review	National database $n = 7519$ 2011–2017	Infertility treatment	Race/ethnicity, income, education	Men who had received infertility testing were more educated and had higher household incomes. Race was not associated with receiving infertility testing in men.
Quinn & Fujimoto, 2016 [73]	Literature review	Single institution	Assisted reproductive technology	Race/ethnicity, income, education	Non-Hispanic white women with higher levels of education and household income were more likely to report using fertility services. Multiple studies have shown that Black women have lower live birth rates and higher spontaneous abortion rates after IVF, while Asian women were found to have lower cumulative birth rates. Some studies showed that the cost of one IVF cycle in the USA could exceed half of the average patient's annual disposable income.



Table 2 (continued)					
Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
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Author(s) Rangel et al., 2021 [74]					
Rangel et al., 2021 [74]	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
	Cross-sectional analysis	Multiple institutions $n=850$ 2020–2021	Assisted reproductive technology	Sex or gender, occupational status	Female surgeons were more likely to use ART than male surgeons, and more likely to have major pregnancy complications than female non-surgeons regardless of ART usage.
Salem et al., 2017 [75]	Cohort study	Single institution <i>n</i> = 390 2006–2014	In vitro fertilization, intracyto- plasmic sperm injection	Race/ethnicity	Middle Eastern/North African women had lower odds of fertilization rates after intracytoplasmic sperm injections, as well as lower odds of live birth rates compared to white women.
Seifer et al., 2020 [76]	Cohort study	National database n = 122,721 1999-2000, 2004-2006, 2014-2016	Assisted reproductive technology	Race/ethnicity	White women had more ART cycles than Black women, although Black women have increased ART use over the years. Discontinuation of ART was most frequent among Black women. Black women had lower clinical intrauterine gestation, implantation, and live birth rates, despite having a greater number of embryos transferred during an initial ART cycle.
Shapiro et al., 2017 [77]	Retrospective database review	National database n=851,100 2004-2013	Assisted reproductive technology	Race/ethnicity	Using ART was inversely related to fertility rates. Autologous ART produced lower live birth rates among Asian and Black women. Third party ART resulted in relatively low live birth rates among Black women.
Stephen et al., 2016 [78]	Retrospective database review	National database n = 2325 1995, 2002, 2006–2010	Assisted reproductive technology	Income, education	Women with lower education levels were less likely to have used ART. Income did not have a significant association with ART usage.
Stevenson & Silva, 2017 [79]	Cross-sectional analysis	Single institution $n = 144$ 2010–2011	In vitro fertilization	Race/ethnicity	White women had lower perceived stress scores related to ART than non-White women.



Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Strasser & Dupree, 2020 [80]	Literature review	Single institution	Infertility treatment	Sex or gender, income	Though multiple health organizations recommend that both members of an infertile couple be evaluated, male partners do not receive an evaluation a quarter of the time. About one-half of men in one study reported increased financial stress due to fertility treatments. Another study found that men may spend between 24 and 79% of their annual income on fertility treatments.
Thakker et al., 2021 [81]	Retrospective database review	National database n = 12,456 2011–2017	Infertility	Race/ethnicity, income, education	Race was associated with the use of infertility care. Unevaluated women were more likely to have less education and have lower household incomes.
Thompson, 2016 [82]	Literature review	Single institution	In vitro fertilization	Income	IVF was disproportionately used more often by wealthier people in the USA.
Tierney, 2020 [83]	Retrospective database review	National database $n=26,015$ 2006–2018	Infertility treatment	Race/ethnicity	Hispanic and Black women were less likely to seek ART, compared to white women.
Tierney & Cai, 2019 [84]	Retrospective database review	National database 2010–2017	Assisted reproductive technology	Race/ethnicity, education	White women had higher total fertility rates attributable to ART than Black and Hispanic women. Black and Hispanic women used ART less often than white women, while Asian women used ART more often. Women with more than a 4-year degree were two times more likely to use ART.
Willson et al., 2021 [85]	Cohort study	Single institution n = 2050 2008-2018	In vitro fertilization	Race/ethnicity	Both Black and Asian women were less likely to achieve an intrauterine pregnancy after IVF. With single-child deliveries, BIPOC women were more likely to have lower gestational ages at time of delivery, as well as extreme preterm births. No differences were found in moderate to late preterm deliveries, or in modes of delivery between groups.



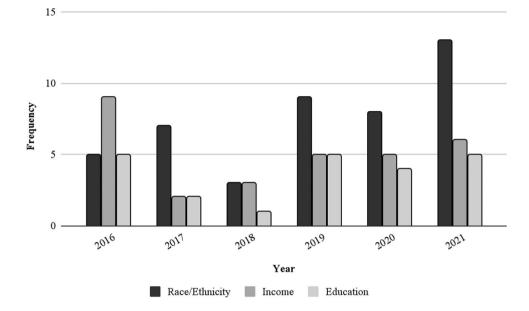
Table 2 (continued)

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Author(s)	Study design	Setting and no. of subjects	Condition	Factors examined	Findings
Wiltshire et al., 2019 [86]	Cross-sectional analysis	Single institution $n = 158$ 2017	Infertility	Race/ethnicity, education, LGBTQ+	Black women remained neutral considering negative and positive infertility treatment beliefs, while those with a history of infertility therapy were more likely to agree with negative treatment beliefs. There was no significant difference in treatment beliefs based on education level or sexuality.
Wu et al., 2017 [87]	Cross-sectional analysis	National database $n = 379$ 2016	Infertility	LGBTQ+	Over half of Society for Assisted Reproductive Technology member fertility clinics included LGBTQ+content on their websites. However, clinics located in the Midwestern and Southern United States were significantly less likely to do so.
Zhou et al., 2020 [88]	Cohort study	Single institution $n = 926$ 2009–2015	Infertility treatment	Race/ethnicity	Black recipients had fewer fertilized oocytes and a similar number of transferred embryos compared to white recipients, but Black recipients had significantly lower pregnancy and live birth rates. No association with race was seen with spontaneous abortion rates. Hispanic recipients had significantly lower pregnancy rates, but similar live birth rates. Asian recipients had significantly more fertilized oocytes, but similar pregnancy, live birth, and spontaneous abortion rates.
Zhou et al., 2021 [89]	Cross-sectional analysis	National database n=8.755,271 2018–2020	Infertility treatment	Race/ethnicity, income	Before the COVID-19 pandemic, ART usage was highest among Asian women and those with higher incomes. The recovery of ART usage after the pandemic was faster among Asian women, while overall usage rates were similar among other racial groups and incomes.

Abbreviations: ART assisted reproductive technology, BIPOC Black, Indigenous, and people of color, ICSI intracytoplasmic sperm injection, IUI intrauterine insemination, IVF in vitro fertilization with autologous oocytes



Fig. 2 Frequency of inequities examined over time



evaluated, Strasser and Dupree found that men were only evaluated a quarter of the time [80]. Private funding in the form of grants helped increase access to fertility care for single men and women [71]. In one study, participants supported limitations to IVF treatment due to age, disproportionately in favor of restricting access for women compared to men [91].

## **Income**

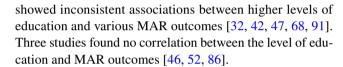
Of the included studies, 23 found that income was positively correlated with access to treatment and/or decreased financial strain [6, 25, 27, 30, 36, 39–42, 45, 47, 52, 54, 58, 64, 69, 70, 72, 73, 80–82, 89]. Two studies reported no correlation between income and limitations to treatment [29, 78]. One study found that lower incomes were associated with lower live birth rates [46].

## **Rural/Under-resourced**

Regarding location, three studies found that living in rural areas created a barrier to accessing treatment [48, 65, 70]. One study found that those living in a metro area were less likely to have ethical concerns about infertility treatment and one study found no correlation to MAR being associated with geographical region [32, 47].

# **Education**

In our sample, 22 studies examined education level and its varying associations to infertility treatment. Of the included studies, 14 found that higher levels of education were positively associated with receiving MAR treatment [27, 34, 38–40, 45, 54, 64, 69, 72, 73, 78, 81, 84]. Five studies

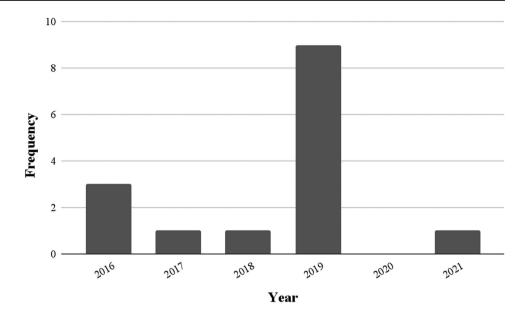


#### LGBTQ+

Since the NIH's classification of Sexual and Gender Minorities as a health disparity population in 2016, 15 articles within our sample investigated LGBTQ+inequities in MAR, illustrated in Fig. 3. In regards to the findings of the studies, barriers to accessing MAR were common themes. Three studies found that fertility clinic websites were lacking in educational content focused on LGBTO + fertility issues [31, 53, 55]. One study found that over half of fertility clinics partnered with the Society for Assisted Reproductive Technology displayed LGBTQ + content on their homepage; however, these clinics tended not to be found in the Midwestern or Southern United States [87]. Other barriers discussed in our studies were difficulties with insurance approval for treatment [30], negative experiences with treatment providers [31], and lack of benefits and discrimination [62]. In contrast, one study found that access to infertility treatment was increased for LGBTQ + patients through funding from charity foundations [71]. Regarding MAR outcomes, three studies found more positive outcomes for LGBTQ + patients compared to their heterosexual and cisgender counterparts [44, 60, 66]. Downing et al. found no differences in outcome risks between same-sex couples using ART and those not using ART [37]. Similarly, Nazem et al. found that pregnancy outcomes did not differ between same-sex and heterosexual couples [67]. One study by Arocho et al. found that sexual minority women made up less than half of patients who use donor insemination [27]. Lee et al. found that sexual minorities are less likely



Fig. 3 Frequency of studies investigating sexual and gender minorities inequities since 2016



to support age limitations on IVF use for women [91]. One study found that there was no association between sexuality and negative or positive MAR beliefs [86].

# **Occupational Status**

Of our included studies, five examined occupational status. Rangel et al. found that through both non-assisted conception and ART, female surgeons were more likely to have major pregnancy complications than non-surgeons [74]. Greil et al. found that women who were unemployed were less likely to undergo fertility testing; meanwhile, employed women undergoing MAR were more likely to have depression symptoms [45]. One study found that white patients were more likely to report that taking time off work would be a barrier to accessing MAR [52]. Lindheim et al. found that couples undergoing ART in the USA were less likely to take on extra employment in order to afford care [62]. One study found that occupational status was not associated with financial strain due to infertility treatment [39].

# Discussion

Our findings identified several limitations for patients who use or attempt to access MAR. Included studies in our sample frequently evaluated race/ethnicity, income, and education inequities and their association with MAR. However, research into MAR inequities, with respect to sex and/or gender and those in rural/under-resourced areas, are in need of ongoing investigation. We will further discuss the areas in which research is deficient and explore the significance of these gaps.

Race/ethnicity is associated with significant inequities in infertility treatment. In our review, the majority of studies evaluated race and ethnicity. The gaps within this line of research are numerous and complex, and though our study has highlighted some, there are likely more that have yet to be researched. Additional research is greatly needed in many areas; however, only a few are described here. First, our review identified gaps in access to healthcare, and additional research is needed to determine the extent and nature of inequities in infertility treatment. A usable system for race and ethnicity documentation is critically necessary for standardization, in order to facilitate the conduct of essential studies. The Society for Assisted Reproductive Technology (SART) does not require practitioners to document race/ethnicity; thus, this data is missing for a substantial proportion of patients [92]. A 2021 study estimated that information regarding racial and ethnic demographics is missing for over 47% of patients within the SART database [93]. Turner et al. conducted an investigation of race/ethnicity reporting in clinical trials which found that only 44% of studies reported any race/ethnicity data over the twodecade study period [94]. They also found a lack of crosstabulation of race and ethnicity reporting, to better capture the diversity of these populations [94]. For example, Asian populations are difficult to properly study, owing to the complex heterogeneity of this group. Women from Asian backgrounds are often all grouped together within one category, which limits data analysis. However, placing Asian women into specific categories runs the risk of sample sizes too small for adequately powered or meaningful analyses [94]. More research is needed to evaluate the collection of patients' race/ethnicity information. Also, a majority of studies on inequities in infertility treatment focus solely on



Black and white patient differences. Studies are needed to better understand the extent, nature, and causal factors contributing to these inequities in other racial/ethnic groups.

The LGBTQ+community experiences significant barriers to healthcare across a range of health conditions including mammography screening [95], cervical cancer screening [96], and abortion care [97]. These barriers are complicated by LGBTQ+hesitancy in seeking care due to a variety of reasons such as (1) lack of cultural awareness and sensitivity by providers and (2) fear of discrimination by providers [98, 99]. A systematic review examining culturally competent care for the LGBTQ+community seeking infertility treatment found many studies in their sample emphasized the need for patient-reported suggestions to improve competency in providers [100]. The call for patient-reported suggestions highlights the need for increased uptake of community-based participatory research to meaningfully engage historically marginalized populations while empowering them to be an active participant in the creation of research questions and outcomes to improve accessibility and adherence to care [101]. Current suggestions to improve accessibility include the use of gender-neutral language on forms and signs, the inclusion of all partners for the patients undergoing treatment regardless of their sex, and the breakdown of cis- and heteronormative expectations in healthcare settings [100]. Although some research has been done to explore ways to create more culturally sensitive care, studies examining the implementation of these suggestions and their success are pertinent to ensuring these changes are widespread.

Overall, the studies within our sample generally focused only on women with sex and/or gender inequities being sparsely investigated. Although Chandra et al. found that men and women of reproductive age have similar rates of infertility—it was found that male partners do not receive an evaluation a quarter of the time—despite multiple health organizations recommending that both members of infertile couples be evaluated [80, 102]. When infertile males were evaluated, one study noted an imbalanced diagnostic process where male infertility is usually only based on seminal analysis. However, female infertility diagnoses explored a broader variety of potential causes [103]. Furthermore, coverage for male factor infertility treatment is also largely excluded from healthcare laws in comparison to females, which disproportionately places the responsibility for reproductive treatment on female partners [104]. In order to provide more equitable access to infertility diagnosis and treatment, Coward et al. recommend further evaluation into defining the population of infertile men and the inequities in accessing treatment [105]. Future policy changes to increase insurance coverage for male infertility diagnosis and treatment, and to create guidelines to increase access to infertility evaluation, is dependent on understanding the full scope of the problem.

Rural and under-resourced populations were seldom investigated in our sample. Brodeur et al. found that almost

25 million women in the USA live in areas that do not have nearby access to an ART center and that male infertility specialists are also difficult to come by [106]. Due to a lack of fertility specialists, Chin et al. found that women in rural or under-resourced areas were likely to visit a general practitioner or an OB/GYN for fertility concerns, and were more likely to receive treatments limited to less invasive options such as oral medications [107]. To help improve treatment inequities in under-resourced areas, the American Society of Reproductive Medicine recommended improving education and awareness on the signs and symptoms of infertility and the treatment options, which can help guide patients into their options and allow them to advocate for themselves [108]. For example, the Walking Egg Project aims to bring affordable infertility care to under-resourced populations worldwide. Their project initiative is multidisciplinary in nature and emphasizes the role of education around reproductive health and proper training for providers, in order to create a decreased disease burden and greater understanding of the needs of under-resourced populations [109]. Although investigation into the use of technology to bridge the gap in access for rural and under-resourced populations has seen significant improvement, there is still a lack of research on how to increase access to ART. These gaps are in part due to the nature of the intervention, which requires a significant amount of treatment cycles, numerous phlebotomy-based tests and imaging procedures, and visits to the fertility specialist, creating logistic challenges for patients in under-resourced areas [48]. A recent pilot study—run in collaboration with the Walking Egg Project—investigated the possibility of a simplified culture system for IVF that would reduce the requirement for specialized equipment and decrease costs [110]. The multidisciplinary efforts of this research can allow for collaborative decisions to create individualized treatment plans that patients can commit to and is suitable for their lifestyle, making MAR more accessible.

# **Strengths and Limitations**

In regard to the strengths of our paper, the protocol was written a priori and was strictly followed. To ensure reproducibility and transparency, our protocol and extracted data was uploaded to OSF [13]. All screening and data extraction were performed in a masked, duplicate fashion. Investigators were trained using materials from Cochrane and the JBI, and sample extraction was done to achieve high inter-rater reliability. Our study had several limitations. First, our sample was composed primarily of cross-sectional analyses and findings may not remain relevant over time. Furthermore, it is possible that we did not capture all available literature regarding inequities in MAR due to our inclusion criteria being limited to studies that were in English, completed in the USA, and published between 2016 and 2021. However, Bramer et al. found that



searches of both EMBASE and PubMed were sufficient to retrieve 97.5% of the relevant studies [14].

## **Conclusion**

Our study showed that race/ethnicity, income, and education were the most frequently investigated inequities regarding MAR, while sex or gender, rural/under-resourced populations, and occupational status were the least frequent. We identified research gaps in each of these areas and recommend the following for future research: (1) standardizing and diversifying race/ethnicity reporting regarding MAR, (2) increasing access to infertility care for LGBTQ+populations by providing more inclusive care, (3) increasing access to infertility care for men, and (4) increasing access to MAR for rural/under-represented populations by identifying logistic challenges.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s43032-023-01236-6.

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**Data Availability** Our entire methodology and protocol were uploaded to Open Science Framework (OSF) to ensure transparency and reproducibility of results, alongside all of our data. The link to this data is provided in the reference list (number 13).

Code Availability N/A.

# **Declarations**

Ethics Approval N/A.

Consent to Participate N/A.

Consent to Publication N/A.

Conflict of Interest No financial or other sources of support were provided during the development of this manuscript. Dr. Vassar reports receipt of funding from the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, the US Office of Research Integrity, Oklahoma Center for Advancement of Science and Technology, and internal grants from Oklahoma State University Center for Health Sciences—all outside of the present work. All other authors have nothing to report.

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