

Global inequities in adverse pregnancy outcomes: what can we do?



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The Health Equity Leadership & Exchange Network states that “health equity exists when all people, regardless of race, sex, sexual orientation, disability, socioeconomic status, geographic location, or other societal constructs, have fair and just access, opportunity, and resources to achieve their highest potential for health.” It is clear from the wide discrepancies in maternal and infant mortalities, by race, ethnicity, location, and social and economic status, that health equity has not been achieved in pregnancy care. Although the most obvious evidence of inequities is in low-resource settings, inequities also exist in high-resource settings. In this presentation, based on the Global Pregnancy Collaboration Workshop, which addressed this issue, the bases for the differences in outcomes were explored. Several different settings in which inequities exist in high- and low-resource settings were reviewed. Apparent causes include social drivers of health, such as low income, inadequate housing, suboptimal access to clean water, structural racism, and growing maternal healthcare deserts globally. In addition, a question is asked whether maternal health inequities will extend to and be partially due to current research practices. Our overview of inequities provides approaches to resolve these inequities, which are relevant to low- and high-resource settings. Based on the evidence, recommendations have been provided to increase health equity in pregnancy care. Unfortunately, some of these inequities are more amenable to resolution than others. Therefore, continued attention to these inequities and innovative thinking and research to seek solutions to these inequities are encouraged.

Key words: healthcare deserts, health inequities, infant mortality, maternal mortality, pregnancy care, pregnancy research

Introduction

Striking inequities in maternal and infant healthcare exist in different settings. The most obvious inequities lie between high- and low-resource settings, which are generally attributed to deficiencies in

availability, accessibility, acceptability, and quality of care secondary to less available financial support for health and health systems. However, these inequities are not limited to low-income settings. Moreover, less financial support is not the only source

of inequities. Similar problems are present in subsets of individuals in high-resource settings. Not surprisingly, apparent causes include social drivers of health, such as low income, inadequate housing, suboptimal access to clean water, structural racism,

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and growing maternal healthcare deserts globally. These causes disproportionately affect birthing patients of color and indigenous populations.¹ An important question that has been addressed is the role that research plays in contributing to these disparities. In October 2021, the Global Pregnancy Collaboration (CoLab) sponsored a workshop on this topic documenting inequities and searching for causes and solutions.² This manuscript summarizes and updates the findings of the workshop and presents recommendations based on the concepts that were forwarded at the meeting. In this presentation, we used the gender-neutral headings preferred by the editors.

The problem

The global maternal mortality estimate ranged from 339 maternal deaths per 100,000 live births in 2000 to 223 maternal deaths per 100,000 live births in 2020—a reduction of 34.3% in mortality rate.³ However, striking disparities in pregnancy care and maternal mortality exist between high-income countries (HICs) and low- and middle-income countries (LMICs). More than 95% of maternal deaths occur in LMICs. Maternal mortality estimates in the world's lowest-income countries are 377 maternal deaths per 100,000 live births, which is 40 times higher than the maternal mortality estimates in Europe. Maternal deaths in sub-Saharan Africa and South Asia accounted for approximately 86% of the estimated global maternal deaths in 2020.

Both HICs and LMICs share many constraints and inequities that limit access to care. Of note, 3 of the most important contributors to inequities in pregnancy and neonatal care in both HICs and LMICs are structural healthcare access, such as geographic barriers and transportation infrastructure; social determinants of health, including economic strata and cultural beliefs; and structural racism. However, many low-resource settings (LMICs) face the additional challenges of limited healthcare infrastructure, insufficient number of healthcare providers, and inadequate training and research capacity. For example, in the 81 countries that account for 95% of all maternal deaths and 90% of all child

deaths worldwide, only 52% of births involved a skilled birth attendant, and only 54% of pregnant individuals underwent at least 4 antenatal visits.⁴

The importance of economic strata and ethnicity in the access to antenatal care (ANC)² was emphasized by Dr Barros and colleagues who reported that the inequities between the richest and the poorest birthing individuals and children are most strongly driven by low healthcare coverage among the poor⁵ and among minority ethnicities⁶ in LMICs.

Similar problems exist in “care deserts” in high-resource settings. Among HICs, indigenous populations (eg, Native Americans, Aborigines in Australia, or First Nations in Canada) have a 2- to 3-fold increase in maternal mortality,^{7–9} which may be attributed to geographic isolation. Kozhimanni et al¹⁰ reported that the incidence of severe maternal morbidity and mortality in the United States was higher among indigenous birthing individuals than among nonindigenous birthing individuals and was higher among rural residents than among urban residents (2.3% for rural indigenous individuals vs 1.8% for urban indigenous individuals) (risk ratio, 1.3; 95% confidence interval, 1.0–1.6). In addition, race and ethnicity contribute to inequities. In the United States, Black and Native American or Alaska Native birthing people have a 3-fold increased rate of maternal mortality than non-Hispanic White birthing people. Maternal education level and income level do not confer protection. Increased mortality is postulated to be due to the allostatic load secondary to structural racism. This is exacerbated by the resulting healthcare bias that influences the quality of obstetrical care.^{11,12}

Dr Eve Lackritz, formerly the acting clinical director of Rosebud Indian Health Service Hospital, reviewed the issues of maternal health among Native American birthing people who face the challenges of obstetrical care in remote, rural areas that are exacerbated by the underlying social, economic, and health problems of many native populations in the United States.² In general, Native American populations who live on reservations in remote areas often have fewer employment opportunities, have higher poverty rates, live in food

deserts, and have a high prevalence of associated chronic health conditions, including obesity, diabetes mellitus, hypertension, alcohol and drug use, intergenerational discrimination, and depression. These underlying health issues contribute to the important differences in pregnancy health and adverse pregnancy outcomes between Native Americans and Whites. Further contributing to the pregnancy risk for both Native American and White birthing individuals is the distance and limited access to emergency obstetrical and neonatal services inherent in rural areas. In rural areas, the availability of hospitals with emergency obstetrical services is already insufficient and continues to decline, mainly due to the economic and staffing constraints of maintaining surgical services in areas with relatively low demand. In the United States, between 2004 and 2014, the percentage of rural counties with hospital obstetrical services declined from 55% to 46%.¹³ Over half of all rural counties in the United States have no hospital with obstetrical care,¹³ thereby increasing the distance and time to emergency services. Problems of distance are further exacerbated by issues of race and ethnicity. A study in Montana revealed that 90% of White birthing individuals lived within a 2-hour drive to a level 2 facility whereas only 52% and 25% of Native American birthing individuals lived within a 2-hour and 1-hour drive to a level 2 facility, respectively.¹⁴ In rural counties that were not adjacent to urban counties, there was an increase in out-of-hospital births and preterm births.¹⁵ Although the disparity of maternal outcomes between rural and urban centers is increasing, Dr Lackritz pointed out that issues regarding the health of Native American birthing individuals, particularly in rural areas, are understudied. Research is needed to identify modifiable causes of maternal health in the context of understanding the complex and multifactorial nature of social and economic determinants of health, care seeking, underlying health conditions, and challenges to access healthcare.

Dr Polite Dube, regional performance-based financing and health technical advisor in Ethiopia, addressed the issues present in “fragile contexts.”² A fragile setting is defined by one of several

characteristics, including recognition by the United Nations that a significant investment is required to maintain peace and by flight across borders by ≥ 2000 individuals per 100,000 population who need international protection as immigrants. It is estimated that this will include more than 40% of the world's population by 2030.¹⁶ These areas have all the problems previously cited for low-resource settings. These are compounded by other issues, including military conflicts, religious beliefs, patriarchal societies with consequent gender inequities, and minimal levels of education. Data collection is especially problematic, with issues present in other low-resource settings exacerbated by risks to data collection staff, difficulty in reaching the population because of poor transportation infrastructure, and a very mobile population that is highly distrustful of investigators. These issues make it difficult to interpret the relevance of the collected data. Moreover, some data and information can be controversial, politicized, or unrepresentative of a group. Similar to other settings, researchers can contribute to the problem of not understanding the context in which they are working. Despite these impediments, research is crucial for effective policymaking, program monitoring, and evaluation in these areas. In addition, the need to be certain that interventions do not have harmful effects is important. However, a way to resolve these research issues without resolving the underlying issues leading to the fragile context is not evident. Dr Dube cited the need for innovative solutions and challenged the group to suggest such solutions.

Does research have a role in fostering inequities?

Thus far, our discussion has reported several factors leading to healthcare inequities. However, the question can be asked as to whether pregnancy research has a role in fostering inequity. Unfortunately, the answer is yes. It is well known that most maternal and fetal adverse outcomes occur more frequently in low-resource settings.^{17,18} However, most pregnancy research studies are from high-resource settings, and consequently,

the questions addressed are directed toward high-resource settings. Findings on pathophysiology, treatment, and epidemiology in high-resource settings that guide clinical care are applied with minimal modification to low-resource settings, sometimes with limited success.

Taking preeclampsia as an example, it is easy to demonstrate the inappropriateness of this extrapolation. It is well accepted that preeclampsia has a large immunologic component.^{19,20} For years, it has been considered that exposure to paternal antigen is protective.²¹ Pregnancy after the usual exposure to fetal blood in the first pregnancy,²⁰ extended exposure to the partner's semen by pregnancy deferred for a longer time,²² repeated pregnancy with the same partner,²³ and not using barrier contraception²² reduced the risk of preeclampsia. Most activities can be quite different in high- and low-resource settings.^{24,25} In addition, the underpinnings of the effect of immunology are determined by specific immunotypes of the mother and baby (ie, father), which vary in different populations.²⁶ Diet, activity, infectious diseases exposures (eg, malaria or HIV), and microbiome all contribute to preeclampsia and are quite different in high- and low-resource settings.

In addition, the foci of preeclampsia research indicate the bias toward questions relevant to high-resource settings. For example, the traditional pathophysiological model of preeclampsia states that failed remodeling of spiral arteries with subsequent reduced delivery of nutrients and oxygen results in syncytiotrophoblast stress and subsequent maternal syndrome.²⁷ However, pathologic evidence of this phenomenon is present only in approximately 20% of pregnancies complicated by preeclampsia, primarily in those occurring before 37 weeks of gestation or accompanied by fetal growth restriction. The remaining 80% did not show increased evidence of these changes.²⁸ Probably, as a reflection of this, most early predictors of preeclampsia are only useful for preeclampsia occurring before 37 weeks of gestation.²⁸ Later-onset preeclampsia has not been considered as important as early-onset preeclampsia in high-resource settings where perinatal mortality is almost exclusively in early-

onset preeclampsia, and later-onset preeclampsia can be managed by expeditious delivery. Unfortunately, this is not the case in low-resource settings, and 80% of preeclampsia cases occurring after 37 weeks of gestation contribute substantially to maternal and neonatal mortalities and morbidities. The examples provided are from low-resource settings. Nonetheless, many of these same issues and differences are present in some high-resource settings.

Furthermore, in even well-designed studies, limited care available in low-resource settings can influence the response to treatments that are quite successful in high-resource settings. A 2015 study on the use of antenatal steroids to reduce the effect of preterm birth in low-resource settings indicated an increased mortality among infants in the treatment group.²⁹ The suspicion that this was related to the quality of available care with, for example, antenatal steroids administered to term fetuses was supported by a 2020 meta-analysis conducted in better resourced centers³⁰ and a consequently large multicountry trial,³¹ which demonstrated a beneficial effect.

Dr Seye Abimbola, a health system investigator originally from Nigeria, raised another important point about research performed in low-resource settings. He pointed out that, all too frequently, resource investigators from HIC fail to adequately involve the local populations in research in low-resource settings.^{2,32,33} In many instances, the targets of research chosen by high-resource investigators are not based on current knowledge of the situation in the local setting. This raises the concern that decisions on research topics are more based on the needs of the investigators (eg, publication) than solving an important local problem. He suggested that the most appropriate research would be that requested by the local population.³²

All these findings indicate that much research in high-risk settings is directed largely at targets that may not be relevant to low-resource settings, despite our best intentions and efforts. In this case, we are contributing to epistemic injustice in research (ie, an unfairness in how we produce, use, and circulate knowledge).³³

Solutions: the path forward

Fortunately, the problems of health inequities, including maternal and infant health, have been recognized by international groups. In 2015, the United Nations set sustainable development goals to reduce maternal mortality to at least <70 per 100,000 live births and neonatal mortality to at least 15 per 1000 live births by 2030 worldwide.³⁴ There is an indication of progress, with global maternal mortality reduced to 38% between 2000 and 2017.³⁵ Nonetheless, maternal mortality remains disproportionately high in low-resource settings. Much remains to be done, as suggested below.

Modifications of clinical care to reduce inequities

Antenatal care. Most care providers believe that ANC is one of the strongest approaches to improving pregnancy outcomes. In the United Kingdom, increased availability of antepartum care through the National Health Service was correlated with reduced maternal and neonatal mortalities.³⁶ Dr Barros discussed how his group has tested this assumption quantitatively. The approach used to examine the effectiveness of ANC was not a simple yes/no as to whether there was ANC but rather a graded score (content-qualified antenatal care coverage indicator [ANCq] score) (Table³⁷). The ANCq score provides a measure of adequacy that considers not only the number of ANC visits but also their content. The ANCq covers all individuals in need of ANC rather than being restricted to pregnant individuals who have at least 1 ANC visit. The best care receives a score of 10, and the absence of any care receives a score of 0.³⁷ These findings support several previously demonstrated relationships, but in a graded manner. For example, if one divides women into wealth quintiles, the lowest ANCq scores are in the lowest quintile and increase with increasing wealth.⁵ However, a novel finding from Dr Barros' research was the association between birthing person's empowerment and ANC quality. There was a

TABLE

Scoring of the variables that compose the content-qualified ANC coverage indicator

Contact with ANC service	Points
Number of ANC visits	
0	0
1–3	1
4–7	2
≥8	3
ANC started in first trimester of pregnancy	
No	0
Yes	1
ANC content	
Skilled provider in at least 1 visit	
No	0
Yes	2
Blood pressure measured	
No	0
Yes	1
Urine sample collected	
No	0
Yes	1

Adapted from Arroyave et al,³⁷ 2021.

ANC, antenatal care coverage.

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clear and significant increase in ANCq scores with increasing maternal empowerment.⁵ These studies have been conducted in >100 countries, and the associations are consistent. However, the gap between the poorest and richest and least and most empowered pregnant persons in different countries varied widely, suggesting different targets for improving care in different settings. This approach unravels the vast inequities in ANC regarding poverty and pregnant person's empowerment. Not surprisingly, a very strong relationship was observed between an increasing ANCq and reduced infant mortality. Even after adjusting for several contributors to improved ANC, there was still a 30% reduction in infant mortality based only on the quality of care, as indicated by the ANCq score.³⁸ Another important conclusion of the

analyses was that, in all populations, higher ANCq scores were related to significantly decreased infant mortality gaps between the richest and the poorest.³⁸

In conclusion, the results of previous qualitative studies are confirmed by multicountry quantitative analyses, showing that improving ANC for disadvantaged pregnant persons reduces inequities in its coverage and can reduce infant mortality overall and the inequities in infant mortality. In addition, the authors suggest targets for improving care that are of different importance in different populations. A fascinating review of the history and application of ANC emphasizes that improvements are possible in all settings, including high-resource settings.³⁹ These include, among other changes, care in which the patient and family are more involved in

decisions and collaboration to facilitate high-tech and high-touch care. In addition, the number and content of visits will be reevaluated. Antepartum care via telehealth, largely instituted during the COVID-19 pandemic, is an encouraging approach to resolve many of these issues cost-effectively, but it needs further assessment for its ability to prevent maternal and neonatal mortalities.⁴⁰

Moreover, postpartum care has components that can influence inequities in care, but unfortunately, it is beyond the scope of this manuscript.

Collaboration and empowerment. Several presentations at the meeting addressed the importance of the involvement of patients in the direction and quality of clinical care and research.⁴¹ Dr Joyce L. Browne and Ms Koiwah Koi-Larbi discussed their experiences and insights from patient engagement in the transdisciplinary Pre-eclampsia adverse Outcome Triage studies, which aimed to improve the care for birthing individuals with pre-eclampsia in Ghana.^{2,42} Ms Scarlett Hopkins presented similar conclusions and recommendations based on her experience with an indigenous population in Alaska.² Drs Cornelia Graves and Ann Celi not only addressed the specific issue in US Black pregnant individuals but also provided general suggestions on improving the quality of care.² Ms Marieke J. Hollestelle presented an approach to solidarity and empowerment that could be useful in pregnancy care and research.²

Ms Koi-Larbi presented the importance of the patient as the first line of defense in recognizing problems and stimulating action to address the identified problems. This was based on her experiences and led her to form the advocacy group, Action on Preeclampsia, in Ghana.² Ms Koi-Larbi and Dr Brown have successfully worked to facilitate transdisciplinary collaboration between patients, care providers, and investigators. They concluded that strengthening local ownership increases relevance, acceptance, and trust, which are essential for more effective care and equitable conduct of research. They pointed out that this is particularly important in individuals most at risk (ie, those in vulnerable/

stigmatized/marginalized populations). They further pointed out the value of these behaviors in a research setting by not only increasing the success of the study but also emphasizing, as pointed out by Dr Abimbola, the role of individuals directing research to topics relevant to them.³² They described an approach that promotes transparency, cooperation, and recognition of the strengths and needs of all partners. It identifies ways to navigate power differences and differing opinions within research collaborations.

Ms Hopkins's conclusions about an Alaskan indigenous population largely mirrored those garnered from the Ghanaian population, in relation to involvement of the community in research priorities, structuring and conducting research, and dissemination of research findings. She raised the very important point of taking time to communicate with the participants or, as she stated, "taking time for tea."²

Drs Celi and Graves presented several specific suggestions to address the inequities in outcomes of US Black pregnant individuals, which nonetheless are likely generalizable.² They suggested that paying attention to the individual's living environment, social determinants of health, diet, housing, and structural racism can support patient empowerment. They pointed out that, similar to many lower-income countries, the United States has many maternity healthcare deserts with limited access to obstetrical care, especially in rural areas.⁴³ The issue of bias poses a challenge at both the system and personal levels. However, it can begin to be addressed by providing a more diverse workforce, increasing the number of care providers of the concurrent race.^{44,45} An early step toward this goal could occur at the level of perinatal community health workers and doulas.⁴⁶ In addition, they echoed the need for the involvement of pregnant Black persons in decisions and research related to their health.

Ms Hollestelle, a bioethicist, addressed the concept of "solidarity," defined as "...enacted commitments to accept costs (financial, social, emotional, or otherwise) to assist others with whom a person or

persons recognize similarity in a relevant respect."^{2,41,47}

This concept of solidarity, as defined above, has been actualized in several medical settings, usually with rare diseases, to positively affect studies and policies. This approach is valuable in pregnancy and, to a certain extent, is present in small settings. However, it is a difficult issue in pregnancy, which has not yet been executed in an organized manner and has not exercised the full ability to bring about change. The problems are as follows:

1. Pregnancy is short and full of changes and new activities.
2. Pregnancy is not a disease, and individuals are often unaware of potential health problems.
3. The patients and providers may not be aware that they can improve the outcomes.

The solutions are to a certain extent a "work in progress" but include empowerment of individuals and raising awareness about pregnancy and potential issues and the possibility of eliciting change from earlier in life (before pregnancy). Furthermore, people should have data available to them supporting these claims. The latter requires the help of many other relevant stakeholders who can provide access to knowledge and ways for individuals to contribute to knowledge generation. The importance of establishing such a concept for pregnancy was evident from many presentations.

Improved respectful maternal and newborn care. Dr Özge Tunçalp from the World Health Organization (WHO) Department of Sexual and Reproductive Health and Research, pointed out the importance of the quality of care at the time of labor and childbirth and how the experience of care is as essential as provision of care.^{2,48} Respectful and dignified maternal care is a right for all pregnant persons.⁴⁹ Research shows that about one-third of pregnant individuals globally experience mistreatment during childbirth,⁵⁰ including physical and verbal abuse,

discrimination, and nonconsented care—all of which are examples of human rights violations that deter individuals from future healthcare seeking.^{50–53} Younger age and lack of education were found to be prominent determinants of mistreatment.⁵³ This has implications for the newborn. For example, when individuals experienced physical abuse during childbirth, their newborns were more likely to be slapped.⁵⁴

Providing high-quality, respectful maternity care is recommended by the WHO.⁵⁵ The guideline includes recommendations on communication, companionship of choice during labor, oral fluid and food intake, continuity of care, mobility, and pain management. To better account for complex drivers of mistreatment, a set of reviews have been completed to inform context-specific strategies at the country level.^{56–59} It is clear that multifaceted strategies at the community, facility, and systems levels are needed to end mistreatment and improve respectful care for all.

Community healthcare and health facilities

Dr Zulfiqar A. Bhutta addressed the importance of improvements in healthcare delivery not only at the community level but also in the hospital setting.² In the last 40 years, neonatal mortality and maternal morbidity and mortality in low-resource settings have been decreasing. However, it seems that the rate of improvement for both is decreasing. The prevalence of these problems varies widely in different countries and even in different loci in the same country, tracking reasonably well with increasing poverty. Importantly, Dr Bhutta indicated that 50% of maternal deaths occur at home or in transit to the hospital in Pakistan.⁶⁰ Major efforts have been made to improve early contacts on the pathway to care. Improvement of community healthcare contacts in the last 20 years has been associated with a 25% reduction in neonatal mortality and maternal morbidity and mortality, and approximately 25% of this is accomplished through patient education and interaction.¹⁵ In a recent study, attempts were made to further improve

care at the community health level. These included efforts to improve monitoring, referral, and early treatment among public sector community health workers in rural Pakistan. The study aimed to improve the outcomes in patients with preeclampsia. The components of the program were successful. For example, more than 98% of pregnant individuals had blood pressure and urine protein checked during community care visits. However, the occurrence of the primary outcome, which was a composite of neonatal and maternal morbidity, was not reduced.⁶¹ It seems that the failure to improve outcomes was largely related to care delivered in the hospital. Dr Bhutta proposed that this indicates a further important target to improve pregnancy outcome should care be provided in health facilities. In some cases, the technology available, including that used in the research-based studies at the community level, is beyond the training of care providers and the capability of the facility.⁶² Another area that must be considered is the role of social problems, which is considered beyond the scope of medical intervention, including education. Progress in further reducing adverse maternal and infant outcomes must be directed toward personal, community, and systemic targets.

Research modifications to reduce inequities

Dr Abimbola emphasized and several other presenters supported that research will be most effective if directed at the perceived needs of the population being studied. These needs can be identified by the potential participants in research projects, but they do not always direct most of the research toward those needs. It is obvious that the research directed at these appropriate target areas should be emphasized. An additional approach, and one likely to have more influence, relates to the importance of “passion” as a driving force in research. Investigators are passionate about topics that are important to them, as is evident in the examples provided by high-resource investigators. By extension, the answer to directing

research to targets important to low-resource settings is to increase research by investigators in such setting. We must improve not only physical infrastructure but also human infrastructure in low-resource settings. We must train not only skilled investigators but also research leaders who will determine research directions and priorities in low-resource settings.

The value of health services research. Prof Sten H. Vermund discussed his extensive experience with efforts to reduce mortality and morbidity among mothers and babies worldwide.² His initial observations from the United States were not encouraging. For example, he indicated that there had been a 3-fold increase in congenital syphilis as the budget for disease prevention was reduced in 2016. This indicates the importance of maintaining successful programs. He discussed efforts to reduce maternal and infant morbidities and mortalities in low-resource settings, demonstrating the power of health services research (how to deliver care) to improve outcomes.

In 2000, it was predicted that there would be a massive increase in infant deaths from HIV/AIDS and related diseases in Africa. The prediction was for close to a doubling of infant mortality before age 5 years in children from several African countries by 2020. Fortunately, the President’s Emergency Plan for AIDS Relief was made available, which provided an opportunity to blunt these increases. This was largely accomplished through determining with health services research how to effectively modify maternal/infant care. The first step was screening the population at large, the second step was assisting wanted pregnancies through family planning, and the third step was treating mothers with infection to prevent transfer to the infant. Initial efforts addressed these issues, and initial data evaluation suggested success. However, examining the data more carefully was less encouraging. Although 90% of pregnant persons with HIV were identified, proceeding through the steps to effective therapy beyond this, offering intervention, uptake to intervention, and adherence to therapy, both mother and infant receiving therapy resulted in only

30% of infants receiving adequate treatment. Only 25% of pregnant persons were retained in care, and only 25% of infants received initial screening. The analysis revealed that pregnant individuals did not proceed from postpartum care to the HIV early intervention clinic for mothers and infants with HIV. A process assessment indicated that this was not only because of an additional visit after discharge but also because the individuals providing care in the HIV clinic could not adequately instruct pregnant individuals because they did not speak the local dialect. Based on this, the process was changed. Individuals were walked from the site of delivery at postpartum discharge to the HIV early intervention clinic where the need for follow-up and therapy was explained by care providers in their local dialect. In the next year, the percentage of babies with appropriate early evaluation doubled.⁶³ Many challenges remain to be addressed. Prof Vermund presented other problems whose solutions were evident through implementation analysis and strongly emphasized the major importance of the study of processes through health services research.

Improvements in research infrastructure. Research projects in low-resource settings must not only answer relevant questions but should also result in a lasting infrastructure at the research site. As much as possible, biomarker measurements should be performed at the site of research. Sample collections should result in local biobanks, and high-resource centers should, when appropriate, share their samples with low-resource settings. It is mandatory for studies to be designed in such a way that successful modifications of care persist beyond the study and that there are lasting gains to research infrastructure and clinical care.

Improved data acquisition

An important contributor to the inequity of care is that reliable, transportable, and sharable data are rarely available in low-resource settings. Almost all statistics on maternal and neonatal morbidities and mortalities in low-resource settings are estimates. In our experience with statistics from a low-income country, we received

very different figures for maternal mortality from 3 different agencies. The problem is related to several issues. One is out-of-hospital deliveries, and their outcomes are recorded sporadically, at best. Furthermore, the limitations of time for data entry lead to the worst problems having the worst data. It is not possible to assess the magnitude of a particular problem or its underlying causes using unreliable data. Similarly, the success of an intervention cannot be determined without reliable baseline and follow-up data. CoLab is currently participating in a trial of a computer tablet-based mobile data entry program. This is designed to replace the paper-based system present in virtually all hospitals worldwide. Considerable effort was expended in acquiring these data.

However, despite these efforts, it is difficult to use these data to improve service provision and to share or to combine these data easily with past and future data and data from other settings as the recording is unstandardized and paper based. Drs Christopher W.G. Redman and Ali Kashan reported on a system to try to overcome these problems that will be piloted in several healthcare facilities in the Kilimanjaro Region, Tanzania.² This platform is based on the District Health Information Software 2 platform, an open-source administrative system widely used in low-resource settings that does not require a license fee. The goal is to provide a portable system that (1) can be used to record data on pregnancy and birth at any healthcare facility or home delivery, (2) easily stores electronic records that are saved at local servers, (3) allows data entry online or offline to deal with Internet connectivity problems, and (4) is accessible for data sharing or comparing different results at different times for longitudinal data and determining results of interventions.

Improving human infrastructure: training of investigators in low-resource centers

One of best ways to resolve inequities in the relevance of research to the needs of low-resource settings is to have research conducted by individuals from this setting. This approach and avoiding gender and racial inequities in the research team

are crucial for pertinent research in high- and low-resource settings. For sustainability, this requires not only investigators with research skill but also research leaders. Dr Leslie Myatt of CoLab presented an approach that this group felt would address this issue.² They proposed taking advantage of the several early career training opportunities (eg, in the United States, Building Interdisciplinary Research in Women's Health) designed to provide academic leaders in high-resource settings. Research leadership training would be conducted in centers that could provide not only excellent mentors but also an infrastructure with well-developed programs in research education/training. The infrastructure should include organized courses in mentoring, responsible conduct of research, grant and manuscript writing, trial design, etc. The trainees would spend 6 months in a high-resource setting learning research leadership skills through hands-on exposure and course work. In addition, they will work with their local HIC mentor and an "at-home" mentor to develop a project that will be conducted on their return to the home site. With the advent of remote learning, simulation, and models of in situ training in LMICs, alternative models with a lower risk of brain drain could also be considered. Part of this experience will involve submitting this project for appropriate extramural funding. Because the program requires exposure to HIC training methods, the plan includes some training abroad. This is chosen as a brief 6-month exposure to maximize pertinent at-home training and to discourage loss of intellectual capital from the site of origin.

At the termination of the HIC-led experience, the trainees are expected to return to their home setting. At this point, training in the home environment will continue with the goal of setting up relevant training for other investigators. The trainees will maintain contact with the mentor through regularly scheduled electronic contact and annual visits by the mentor to the trainee. The trainee with the help of several CoLab members with experience in training programs and course development will work to establish not only

courses addressing topic listed above but also topics identified by the consortia as particularly relevant to their settings and needs. Continuing but decreasing contact with CoLab will oversee the development and maintenance of these programs.

Identifying mechanisms by which inequities contribute to adverse pregnancy outcomes. The obvious and best solutions to inequities are correcting them directly and through addressing their underlying social determinants, which are the targets of current investigations. However, the mechanisms by which the stress of inequities results in adverse outcomes may provide answers to complement these investigations or minimize the effect of the stressor. Dr Tracy L. Bale provided a glimpse of potential future directions for research on this linkage. Dr Bale provided fascinating evidence of objective hints of how stress can have a specific biological effect years after an insult.² In a study of individuals with sexual trauma years before, it was found that the markers of hypertension and diabetes mellitus were most common in individuals who experienced abuse prepubertally and that markers of depression and posttraumatic stress syndrome were more common in those whose abuse occurred during adolescence.⁶⁴ In addition, these differences in the manifestation of the exposure were linked to a different pattern of proteins in the extracellular vesicles from the 2 groups. As it is increasingly evident that these vesicles are involved in cellular communication, the functions of these proteins could provide insights into the mechanisms by which stress can alter outcomes. One of the fascinating findings was a striking increase in skin-related proteins, particularly “Merkel cells” that are related to the translation of physical signals to tactile perception in the skin.⁶⁵ Interestingly, these cells mature during adolescence in humans. These data raise many interesting possibilities for linkages that would be premature to explain at this time. However, it does support the concept that stress operates through mechanisms that can be

manipulated. This is further supported by other works on placental genes^{66–71} and the vaginal microbiome.^{72–74}

Conclusions and recommendations

An overview of pregnancy care worldwide indicates substantial inequities. These inequities are present not only in low-resource settings but also in “health-care deserts” and particular populations in high-resource settings. The answer to the question of whether research contributes to inequities is a resounding yes. The opinion of experts on the resolution of these inequities is hopeful in many areas but not in all areas.

Here, we provide a list of recommendations to resolve inequities. Moreover, we admit that the resolution of some inequities requires major transformations in society and in the structure of the healthcare system.

Recommendations

Modifications of clinical care.

1. Antenatal care must be emphasized and facilitated.
2. Respectful inclusion of individuals and communities in solutions to areas in which care must be modified is mandatory.
3. Attempts must be made to provide care providers whose backgrounds and ethnicities are similar to the individuals for whom care is being provided.
4. All pregnant individuals in all resource settings deserve respectful care, particularly during labor and delivery. This requires that the pregnant person be able to articulate their experiences and be heard.
5. Attention to the quality of clinical services at community and system levels is mandatory to improve care.
6. Future modifications should begin to consider the role of postpartum care.

Modifications of pregnancy research.

1. The importance and value of studying the delivery of care (health services and health policy research) must be emphasized and applied to assess clinical care and its delivery.

2. Local populations (individuals and communities) should be included in research priorities and agenda, setting the design and conduct of studies.
3. Improvements in and strengthening of research infrastructure and capacity must be a target for and sustained in all research studies in low-resource settings.
4. An important target for infrastructure improvement is human resources. Innovative training to strengthen research competencies and provide research leadership from settings in which improvement in care is required should be instituted and supported.
5. In a world in which data analysis of large valid data is increasing exponentially, efforts must be made to improve the collection of harmonized data in all settings, including low-resource settings.
6. Research to determine how the recognized issues leading to bad outcomes act to cause these effects is of great value. These findings can help identify new targets for therapy in areas that currently seem insoluble.
7. Future studies should address the contribution of postpartum care to inequities.

We present these suggested steps as solutions to the issues currently beyond our control to stimulate innovative ideas of others toward a solution for these problems. ■

CRediT authorship contribution statement

James M. Roberts: Writing – review & editing, Supervision, Project administration, Conceptualization. **Seye Abimbola:** Writing – review & editing. **Tracy L. Bale:** Writing – review & editing. **Aluisio Barros:** Writing – review & editing. **Zulfiqar A. Bhutta:** Writing – review & editing. **Joyce L. Browne:** Writing – review & editing. **Ann C. Celi:** Writing – review & editing. **Polite Dube:** Writing – review & editing. **Cornelia R. Graves:** Writing – review & editing. **Scarlett Hopkins:** Writing –

review & editing. **Ali Khashan:** Writing — review & editing. **Koiwah Koi-Larbi:** Writing — review & editing. **Eve M. Lackritz:** Writing — review & editing. **Sten H. Vermund:** Writing — review & editing. **Michael G. Gravett:** Writing — review & editing, Writing — original draft, Supervision. ■

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