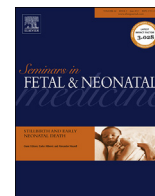




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Pregnancy subsequent to stillbirth: Medical and psychosocial aspects of care



Megan E. Fockler^{a, b, *}, Noor Niyar N. Ladhani^{a, c, d}, Jo Watson^{a, b}, Jon F.R. Barrett^{a, c, d, e}

^a Women and Babies Program, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

^b Lawrence S. Bloomberg Faculty of Nursing, University of Toronto, Toronto, Ontario, Canada

^c Division of Maternal–Fetal Medicine, Department of Obstetrics and Gynaecology, University of Toronto, Toronto, Ontario, Canada

^d Maternal Fetal Medicine, Sunnybrook Health Science Centre, Toronto, Ontario, Canada

^e Clinical Trials Services/The Centre for Mother, Infant and Child Research, Toronto, Ontario, Canada

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Pregnancy after stillbirth presents unique challenges for families and healthcare providers. Medical surveillance and interventions must be optimized to improve outcomes and provide individualized support for families. A key component of acceptable care is psychosocial support that is delivered in a timely and sensitive manner by care providers with knowledge about the pervasive impact of stillbirth. With the lack of existing evidence to guide care, there is an urgent need for global leadership and research to address knowledge gaps.

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1. Introduction

It is estimated that 2.6 million third-trimester stillbirths occurred worldwide in 2015, with most occurring in low- and middle-income countries [1]. Stillbirth has a pervasive impact on women, families, health systems, and communities. This impact continues into the subsequent pregnancies. After perinatal loss, the majority of women become pregnant again, with rates of pregnancy as high as 80% within the first 18 months [2,3]. It is important that healthcare providers understand the impact of stillbirth on subsequent pregnancies in order to promote the health and wellbeing of the fetus, neonate, woman, family, and community.

2. Pregnancy care systems

2.1. The good news: the value of specialized care

There is increasing evidence that informed, sensitive, and specialized care may have a powerful positive influence on women who are pregnant following stillbirth. Women report increased satisfaction when given the option of primary care or regular input from knowledgeable and specialized providers, including

obstetricians, nurses, and midwives [2,4–6]. In our Subsequent Pregnancy Program at Sunnybrook Health Sciences Centre in Toronto, Canada, we also find that families need individualized care plans and knowledgeable navigation throughout pregnancy and the postpartum period by a known interprofessional team.

2.2. The current system: a call for change

There is increasing evidence that women experiencing pregnancy after stillbirth have unique care needs. Existing obstetrical management practices do not sufficiently address these needs and families are not satisfied with traditional models of hospital antenatal care [3,5–8]. In a pregnancy after stillbirth, many women seek reassurance through interactions with providers, but report that interactions often fall short of their expectations [3,5,9]. Many parents encounter providers who are unaware of their history and the relevant impact of stillbirth, have dismissive attitudes to worries and concerns, and make insensitive and inappropriate comments [3].

Whereas some authors reported positive evaluations of specialist programs and support, including telephone contact, increased and flexible appointments, individualized preparation for birth, parent education, and postnatal support [3], others noted that specialized care is inconsistent [5,6,9]. Additionally, whereas targeted support appears to improve experiences for families, the contribution of different interventions to the overall success of programs is not clear [3].

* Corresponding author. Women and Babies Program, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, M4N 3M5, Toronto, Ontario, Canada.

E-mail address: megan.fockler@sunnybrook.ca (M.E. Fockler).

2.3. Moving forward: challenges for care providers

Counseling regarding management of a subsequent pregnancy is a great challenge, as little evidence is available to guide providers in this setting. Understanding and addressing the unique needs of families is important for care providers, but current guidance is lacking, as are evidence-based care pathways [2,3,5,10–12]. Guidelines that address individual risk factors, local conditions and resources, and the psychosocial needs of families are necessary [10,11,13].

3. Preconception counseling and the inter-pregnancy interval

There is no recommended regimen for the right inter-pregnancy interval after a stillbirth. Women should generally be encouraged to pursue pregnancy if and when they feel the time is appropriate [9,14].

Parent groups and practitioners have encouraged preconception counseling. At this time, a review of the index event can be conducted, a thorough history can be ascertained, and expectations in the subsequent pregnancy can be established. There is often a significant amount of anxiety that comes with attempts at conception following a stillbirth, and visits during the inter-pregnancy interval, reassurance of management plans, and surveillance are helpful for parents [15].

4. Risk of recurrent stillbirth

There is conflicting evidence regarding the risk of subsequent stillbirth. Whereas some authors have suggested that there is a low risk for recurrence when the index stillbirth is truly unexplained [16], others have shown increased risk of stillbirth in subsequent pregnancies, ranging from two- to ten-fold over the general population [17,18]. Much of this depends on the etiology of the index stillbirth, the degree of investigation of the index event, and level of intervention to correct medical disorders. Retrospective studies provide varying data on the risks of recurrent of stillbirth and are limited by inconsistency in defining the index stillbirth [19].

Increased recurrence risks have been shown in women with first trimester losses, early and late stillbirths, and intrapartum deaths. These risks remained significant among women perceived as otherwise low risk, indicating that unless there is an obvious, non-reproducible cause of the initial stillbirth, there is a baseline risk of recurrence that requires attention in the subsequent pregnancy [20]. Other studies showed these risks to be most pronounced among women for whom the index stillbirth was in the extreme preterm period or post term [21].

A recent meta-analysis [22] echoed the results of individual studies. Pooled data from cohort and case–control studies showed a five-fold increase in the odds of stillbirth in subsequent pregnancies. The higher risk of recurrence may be among those with placental or growth-related issues in the index pregnancy. Indeed, when looking at recurrence based on etiology, it has been shown that women who sustain a pregnancy loss due to placental factors or due to prematurity are at highest risk of recurrence [23]. We find that women who fall into these categories, especially when placentally mediated, are often categorized as having unexplained or unexplored stillbirths.

An increased rate of gestational diabetes in the subsequent pregnancy, reduced birth weight, earlier deliveries, increased risks of fetal distress, and increased rates of obstetric intervention were also all shown in subsequent pregnancies [16]. One challenge for providers when assessing recurrence risk is that the finding of low recurrence for unexplained stillbirths, as some authors have suggested, may not be applicable when the “unexplained stillbirth” is

actually one whose etiology has not been thoroughly explored. Furthermore, the increased risk of poor subsequent obstetric outcomes could be due to underlying medical issues or iatrogenic from increased interventions.

It is important to note that many families are not reassured when considering their recurrence risk [15] and that their appraisal of threat to the pregnancy is often not connected to a determined medical risk [4,24]. Management of the subsequent pregnancy requires a balance of evidence-based recurrence risk with the acknowledgement that certain interventions will be required due to case-specific issues as well as parental anxiety.

The risks of recurrent stillbirth are mitigated by the resolution of certain modifiable risk factors. In high-income countries, these are usually smoking and obesity, whereas in lower-income countries this includes the provision of adequate antenatal and intrapartum care [25,26]. Because of the inherent medical and psychosocial complications and considerations, these pregnancies should be treated as high risk and commensurate with the specific care needs of the families involved [3,20,27].

5. Screening in the subsequent pregnancy

When a woman is seen prior to, or during, a subsequent pregnancy, a thorough history and exploration of the events of the stillbirth is helpful in considering the etiology and the risk of recurrence. The most valuable information regarding the cause of stillbirth is collected at the time of the event. At this time, a genetic survey, autopsy, autoimmune, and diabetes screening should be performed, in the hopes of identifying a possible cause. Thorough investigation of a woman's health and obstetrical history allows providers to anticipate and provide necessary care, including targeted supports and referrals [2,11]. Placental pathology merits consideration in all cases.

Women with an unexplained pregnancy loss after 10 weeks of gestation may warrant testing for antiphospholipid antibody syndrome (APLS). The laboratory criteria include the presence of one of the antibodies (lupus anticoagulant, anticardiolipin antibody, or anti- β_2 glycoprotein) on two occasions at least 12 weeks apart [28]. APLS predisposes to vascular thrombosis and increases risk of fetal death and growth restriction. When present, obstetrical outcomes are improved through treatment with anticoagulation and low-dose aspirin [28].

Biochemical markers in the first trimester may play a role in predicting the risk of stillbirth. The FASTER trial [29] showed an increased rate of stillbirth [odds ratio (OR): 2.15; 95% confidence interval (CI): 1.11, 4.15] and spontaneous loss prior to 24 weeks (2.50; 1.76, 3.56) where the PAPP-A (pregnancy-associated plasma protein A) taken during first trimester screening was below the 5th percentile in pregnancies unaffected by chromosomal abnormalities. A prospective study looking at prediction of risk of stillbirth at greater than 24 weeks based on first-trimester testing showed lower PAPP-A levels in women who sustained stillbirth in general, especially when for presumed placental reasons [30].

Failure of normal invasion of spiral arteries and subsequent risk for placental dysfunction may be displayed by abnormal uterine artery Doppler studies. It is not yet certain at which gestation this should commence or at what frequency they should continue [18].

First-trimester uterine artery Doppler studies may help identify pregnancies at risk for poor perinatal outcomes. A recent prospective study [31] assessing risk of adverse outcomes, including stillbirth, with low PAPP-A and abnormal uterine artery Dopplers found an association with low sensitivity. In the second trimester, a recent randomized controlled trial showed an increased risk of stillbirth with elevated uterine artery Doppler resistance [32]. Similarly, a meta-analysis of studies looking at the prediction of

stillbirth by abnormal second-trimester uterine artery Doppler found an association of three-to four-fold in high-risk pregnancies [33]. More work is needed to apply these models specifically into the previous stillbirth population and aid in the identification of women at risk in subsequent pregnancies.

In our Subsequent Pregnancy Program, all women with a previous stillbirth have a thorough history and examination to assess for any previously unidentified causes. Those with a history of unexplained or unexplored stillbirth will have APLS testing if appropriate, a PAPP-A measurement if first-trimester screening is done, a second-trimester uterine artery Doppler study, and additional surveillance as indicated. In addition, we maintain Doppler surveillance throughout the third trimester as indication of placental function and fetal circulation.

6. Medical management

6.1. Medical treatment

When the cause of the previous stillbirth is well established, treatment of the underlying cause, if applicable, is beneficial to reduce risk of recurrence. This is most frequently applicable for the stillbirths that are thought to be placentally mediated – for example, when associated with fetal growth restriction, or occurring in women affected by severe or early-onset pre-eclampsia. Even with stillbirths of unknown or unexplored causes, placental insufficiency is often the underlying cause.

The use of low-dose aspirin to prevent pre-eclampsia is well established [34], and this has been extrapolated to reduce the risk of recurrent stillbirth. A meta-analysis [35] showed that early initiation reduced the risk of perinatal death in women at risk for placental insufficiency. There is conflicting evidence about the benefit of low-molecular-weight heparin in the absence of APLS or other thrombophilias [36]. Treatment plans should be established on a case-by-case basis taking into account the circumstances surrounding the previous loss and the wishes of the family.

6.2. Antenatal surveillance

Women with a history of stillbirth, especially of placentally mediated etiology, are at risk of placentally mediated morbidity including pre-eclampsia, small for gestational age, intrauterine growth restriction (IUGR), and abruption [37–39]; risk of fetal distress, chorioamnionitis, preterm birth, and neonatal morbidity has also been shown [40,41]. Complications are considered to be due to a vasculopathy leading to impaired uteroplacental perfusion although chronic inflammation may also play a role with conditions such as chronic histiocytic intervillitis and villitis of unknown etiology reported to be recurrent [42,43].

The subsequent pregnancy will typically be fraught with anxiety and stressors, and antenatal surveillance may be beneficial to families. Indeed, women often request increased surveillance in the subsequent pregnancy [3,44]. However, increased procedures and tests may worsen stress in the pregnancy. Increased surveillance may also lead to more interventions. Indeed, subsequent pregnancies have higher rates of induced labour and elective cesarean section (CS) [16], although some of these interventions may be warranted. A South African study [45] examining indications for delivery in subsequent pregnancies showed that more than 30% of those deemed low risk for a recurrent stillbirth developed indications for early delivery such as IUGR, pre-eclampsia, and preterm premature rupture of the membranes. An open discussion of the risks and benefits of these requests is beneficial as a mutually acceptable care plan is devised [11,46].

Fetal movement monitoring is a low-cost test that may identify

placental dysfunction [47] and has been shown to reduce stillbirth rates when combined with consistent messaging and appropriate medical follow-up [48]. Women should be properly supported and educated about normal variations in movement to minimize anxiety caused by this surveillance.

The availability of flexible appointments, opportunity to contact healthcare professionals between appointments, and more frequently scheduled antenatal visits have all been shown to be beneficial in reducing maternal stress and should be offered [2,7,12]. Providers should understand that a woman's perception of threat to her pregnancy might not be associated with a determined medical risk [24].

In our Program, fetal growth is usually monitored closely, and wellbeing is monitored with ultrasound and/or fetal heart rate monitoring in the third trimester. This regimen is determined based on history, screening findings in the current pregnancy, and parental preferences. A survey of Australian obstetricians [37] showed that 87% recommended ultrasound studies in the third trimester, and 72% recommended regular fetal heart rate monitoring. Overall, the exact regimen should be tailored to the woman's obstetric history and preferences. More research in this area is urgently needed [49].

6.3. Mode and timing of delivery

Mode and timing of delivery should be determined through a conversation with the family, balancing the risks of prolonging the pregnancy with issues around late prematurity and early term deliveries. Providers should openly discuss the possible stresses women may experience, including procedures and tests [8] but also complications of early delivery such as neonatal jaundice and breastfeeding challenges [12,46,50]. In our Program, we offer visits to the birthing unit prior to delivery in an attempt to help parents better understand the process and decrease their stress response. We also offer an antenatal consultation with a lactation consultant to help parents anticipate infant feeding norms and needs.

Robson [37] showed that 93% of obstetricians caring for women with a previous stillbirth recommended early induction of labour (IOL). It is our experience that families almost universally accept and indeed request this. IOL may have significant emotional benefits for parents [12,46]. The stillbirth rate does increase after 39 weeks, and many experts advocate for delivery by this time in the subsequent pregnancy [12].

However, there is conflicting evidence of its efficacy. Gebhardt [45] retrospectively compared outcomes of IOL at 39 weeks versus 40 weeks in women with a history of unexplained or unexplored stillbirth. Those who were induced at 39 weeks had a higher rate of CS (50% vs 22.8%, respectively; $P = 0.02$). Furthermore, those planned for induction at 40 weeks had a higher chance of undergoing spontaneous labour (OR: 6.92; 95% CI: 1.96, 32.31). There were no antenatal deaths or neonatal morbidities in their study population ($n = 92$). Where fetal complications were identified, such as IUGR, timing of delivery was based on the clinical scenario. In contrast to these findings, a large cohort study ($n = 230,528$) looked at the risk of CS with IOL at 39 weeks and found no increased risk [51]. A meta-analysis looking at IOL in all women at term or post term showed a reduction in the CS rate among women who had been induced earlier ($n = 31,085$) [52].

A woman may doubt her body's ability to successfully carry and birth her baby, and she may request earlier birth planning and interventions [3,44]. In our experience, IOL before term or even before the gestation at which the stillbirth occurred is often practised and indeed requested by families. We also find that one of the most challenging periods for families is the time beyond 35 weeks, when reassurance is sought that their fetus will survive to term,

especially for women who have previously had late gestation stillbirths. During this timeframe, ongoing and sensitive support by known providers is crucial.

Requests for elective CS delivery are often discussed, although there is not much published in the literature to suggest that women request them at a higher rate. Robson, however, showed that 35% of obstetricians recommended elective CS in women with a history of stillbirth [37]. The circumstances and timing of the previous stillbirth need to be considered when counseling women on the risks and benefits of this request. With elective CS becoming more commonplace, some providers, after counseling about the risks, may choose to perform CS.

Providers need to consider the evidence, mental wellbeing of the woman, and potential risks of late preterm birth. Ultimately, timing and mode of delivery is a choice to be made between the woman and her care provider in order to balance the possible risks of these interventions with anxiety and the real or perceived risks of recurrent stillbirth.

7. Mental health considerations

7.1. Grief, fear, and vulnerability

Pregnancies subsequent to stillbirth are often characterized by heightened grief, fear, vulnerability, stress, guilt, and worry [53–55]. Providers should acknowledge this reality, attempt to normalize possible concerns and worries, and provide safe spaces for women to discuss their hopes and fears and to ask questions [4,24].

7.2. Anxiety, depression, post-traumatic stress

In addition to normal grief and worry, numerous adverse psychological sequelae are associated with pregnancies after stillbirth, including depression, post-traumatic stress, and anxiety [54,56,57]. Prenatal depression and anxiety are predictors of postpartum depression; high pregnancy anxiety, depression, and psychological distress have been associated with negative obstetrical, neonatal, and postpartum outcomes [5,57,58].

Anxiety is the most widely measured and reported state in pregnancies following stillbirth. Women report increased levels of anxiety and depressive symptoms [2,56,59], and are reported to exhibit significantly elevated rates of anxiety and depressive symptoms throughout pregnancy and the postnatal period [53,56,57,59]. Some women, such as those with low income, a history of trauma, and poor social supports, are at increased risk [59,60]. Anxiety often increases with specific experiences and at particular times, such as during routine appointments, when presenting for ultrasound, and especially around the gestational age of the previous loss [3,4,53].

Women and families are often able to adopt unique ways of coping during pregnancies after stillbirth and in the period after the birth of a live baby [53]. With this in mind, care providers should promote family strengths and provide proper screening, targeted follow-up, referrals, and aggressive treatment as appropriate [2,55,57,59,61].

8. Psychosocial considerations

8.1. Social isolation

Many families experience isolation from their normal support networks in pregnancies after stillbirth [3,5,13]. Some parents report insensitive comments from others [15,62], highlighting that their experiences may be unacknowledged and minimized [63].

Some women delay telling close family and friends about the pregnancy [3,4,62,64]. Cultural and intergenerational considerations, including the expectations to suppress outward grief, grieve privately, and stigma surrounding stillbirth, may increase isolation and have an adverse impact on the family [13,62,65,66].

8.2. Family-centered care

In subsequent pregnancies, stillbirth often continues to have a pervasive impact on families. Whereas some couples report a negative impact of grief on their relationships, especially surrounding blame and differences in coping mechanisms, others report positive changes in their relationship, with improved communication, emotional closeness, and mutual support [56].

Partners' needs are often inadequately addressed in pregnancies subsequent to stillbirth. Some male partners report intense feelings of grief, increased concern related to the outcome of the pregnancy, a heightened sense of risk, and being overlooked by healthcare providers and society [8,13,15].

Providers should evaluate the parental support system and support family health [6]. When desired by women and their families, providers should include partners, siblings, and grandparents in appointments, teaching sessions, and discussions about fears and concerns, and provide opportunities for questions and timely and individualized connections to mental health and community supports [15,62].

8.3. Peer support

In pregnancy after stillbirth, peer support is valued by many families and should be facilitated by providers whenever possible, whether in person or online [2,3,5]. In our Program, we find that peer support counteracts some of the social isolation families may encounter and normalizes certain experiences in subsequent pregnancies. It is also low cost.

8.4. Emotional support

Families tend to rely on providers for increased emotional support in pregnancy, yet quality and availability of such support varies widely [2–6]. A lack of understanding of the impact of stillbirth on subsequent pregnancies reduces capacity to provide adequate emotional and psychological support [3].

Women report increased satisfaction when providers openly acknowledge their previous loss, use their stillborn babies' names, and commit to forming trusting, respectful relationships while demonstrating empathy and compassion [2,3,5,8]. Providers should ask families what would be helpful and supportive [2,3].

8.5. Continuity of care

Women describe increased satisfaction when they have consistent providers through their pregnancy and in the postpartum period. It is important for all members of the care team to be aware of the history before meeting with the family and of heightened anxiety levels. Timely access to known providers is beneficial [3,5,7]. In our experience, families may feel significant and long-lasting distress when repeatedly met with providers who are unaware of their history.

9. Preparation for childbirth and parenting

9.1. Antenatal education

Preparing for birth after a previous stillbirth is difficult. Many

families will not attend antenatal education or preparation for parenting classes. Parents report that traditional antenatal education content is not appropriate and causes some worry and distress [5,13]. Women pregnant after stillbirth may not understand the physiology of birth, may be fearful of the birth process, and may doubt their ability to successfully have and parent a baby [3,4,67].

Focused education may be more appropriate for families [2,5], and may help to improve preparation for childbirth and parenting [5,67]. Parents may request assistance with writing a 'birth plan' and touring the area where they will give birth [67].

9.2. Attachment

There is conflicting evidence about the impact of stillbirth on parental–fetal attachment during the subsequent pregnancy and postnatally [2,54]. Women may delay or avoid preparing for the babies' arrival and resist attachment to the pregnancy, have restrained excitement, and avoid discussing or thinking about 'the future' [54]. Many families will benefit from open discussions with providers about the possibility of a difficult attachment process and the potential for conflicting emotions, such as joy and grief or hope and fear, during pregnancy and after the birth of a subsequent child [54,63]. Providers should ask women about their preparations for the baby and acknowledge the unique challenges of pregnancy and parenting after previous stillbirth [2].

9.3. Parenting considerations

Conflicting evidence exists about the specific role of stillbirth on attachment and parenthood, but parenting challenges after the birth of a healthy child, including isolation, guilt, hypervigilance, and exaggerated concerns about subsequent children have been reported [2,3,13,54,55].

During pregnancy, providers must be informed about the possible postpartum and long-term impact of stillbirth on families and provide safe spaces for discussion, appropriate referrals, and education [54,57]. When we first started our Program, we were not prepared for the enormity of the impact of a subsequent live birth on many families. Indeed, we found that additional surveillance, support, and monitoring are necessary, but they fall short of meeting family needs if stopped at birth. Pregnancies after stillbirth represent only one time-period in the pervasive story of stillbirths. Many families will benefit from ongoing community and in-home supports, and knowledgeable providers are poised to offer and connect families to these crucial supports during pregnancy.

10. Economic considerations

Families pregnant after stillbirth often have increased health-care utilization, including more diagnostic procedures and antenatal visits [4,10,13,65]. Overall, the direct and indirect medical, psychological, and societal economic impact of stillbirth is poorly understood, especially in low- and middle-income countries [10,55,65,68]. More emphasis on describing the pervasive costs of stillbirth, including those for subsequent pregnancies, is needed. It has been suggested that the majority of the economic cost of stillbirth is derived from the costs of providing care in subsequent pregnancies [10]. Such evidence could inform appropriate policy and clinical decision-making and help to evaluate the social and financial impact of specific interventions to reduce the financial impact of stillbirth in subsequent pregnancies [10,65,68].

Further evidence that the overall cost of stillbirth, in part due to financial considerations in subsequent pregnancies and beyond, may be higher than for live births could help to prioritize reductions in stillbirths worldwide [65,66]. This may be of particular

importance for low- and middle-income countries, where extremely limited resources must be prioritized and offered to those who most benefit from them [10,66].

11. Conclusion

Providers should understand the medical and psychosocial impact of stillbirth on subsequent pregnancies and provide timely, multidimensional, sensitive, and individualized care. The development of standardized care pathways and guidelines may assist providers and reduce current care discrepancies. The lack of evidence base, especially in low- and middle-income countries, impedes holistic care of families. More interdisciplinary research is urgently needed, as is continued leadership in bringing stillbirth prevention and care onto the global health agenda.

11.1. Practice points

- Women with a history of stillbirth are at risk of stillbirth and other obstetrical complications in their subsequent pregnancy.
- Underlying medical conditions should be explored and managed prior to and during the subsequent pregnancy.
- Traditional antenatal schedules and models of care are not acceptable to families; providers should tailor education, support, and care in partnership with families, taking their wishes into account.
- Mode and timing of delivery can be planned with families based on the nature of the previous stillbirth in the context of the current pregnancy.
- Families need knowledgeable, sensitive, and holistic navigation and care from known providers during the pre-conception, prenatal, intrapartum, and postpartum periods.

11.2. Research directions

- Increased knowledge of recurrence risk and optimal medical management, including mode and timing of delivery, based on the etiology of the index stillbirth.
- Examination of family preferences about mode and timing of delivery in pregnancies after stillbirth.
- Specific surveillance and intervention strategies and their associated obstetrical, family satisfaction, and cost/benefit outcomes.
- Effects of a previous stillbirth on attachment, parenting, and subsequent child health outcomes? What mitigates the impact?
- Specific care provision in resource-poor settings and among socially disadvantaged groups.

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