ANTENATAL CARE:

A SUCCESS STORY? THE (IN)EFFECTIVENESS OF ANTENATAL CARE IN REDUCING MATERNAL MORALITY AND PROMOTING MATERNAL HEALTH IN DEVELOPING COUNTRIES

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Antenatal care (ANC) is considered a success story in low- and middle-income countries (LMIC), as its uptake is very high. This paper aims to assess its effectiveness to reduce maternal mortality and promote maternal health in LMIC. Facility-based deliveries attended by skilled personnel are required. Focused on counseling, ANC could lead to facility-based delivery, but socioeconomic and cultural factors, and the quality and accessibility of services determine its uptake. A package of evidence-based interventions during ANC reduces maternal mortality and morbidity. ANC provides a platform to address social problems such as gender violence as well. Despite the opportunities ANC represents, challenges are found at client, workforce and health system levels.

Introduction

The 2014 Millennium Development Goal (WHO) Report estimates that 83% of women in low-and middle-income countries (LMIC) received at least one antenatal care (ANC) visit by skilled health personnel during their pregnancy in 2012 compared to 65% in 1990 (1), leading to ANC uptake called a success story (2). ANC provides the opportunity to reach many pregnant women and, arguably, should be put to the most effective use possible (3). Upon closer inspection however, major discrepancies exist between and within countries, resulting from determinants that appear quite similar across contexts (4, 5). Moreover, it is questionable whether ANC should have been given the praise it received, as it has proven to be ineffective in predicting or preventing maternal mortality (6).

In this paper we will describe the relevance of ANC in relation to maternal mortality and maternal health, as well as examine the factors that influence its utiliza-

So What?

ANC can contribute to improved maternal health and reduced maternal mortality if aligned with the socioeconomic and cultural realities of women in LMIC. However, both quality and accessibility of ANC need improvement. Health system strengthening and workforce improvement therefore remain a priority to ensure that the most vulnerable, the poor and rural women, will benefit from ANC services. tion in order to assess whether ANC can truly be qualified as a success story in LMIC. Although maternal and neonatal health and mortality are closely linked, notably while discussing ANC, this paper will focus specifically on issues in relation with maternal health and mortality.

What is Antenatal Care?

ANC is an "umbrella term used to describe the medical procedures and care that are carried out during pregnancy" p. 1 (6). The British Ministry of Health introduced ANC in 1929 as a prophylactic care program. Visits were intended to start in early pregnancy with 4-week intervals; 2-week intervals from 28 weeks to 36 weeks, and weekly from then on. This model was widely adopted and nearly universal in high-income countries (HIC) (7), even though there were substantial differences between countries with regard to the number and content of ANC (3).

The model remained unchanged until 2001, when the World Health Organization (WHO) commissioned a randomized controlled trial (RCT) with nearly 25,000 women in four different countries at varying stages of development (8). The RCT compared the standard eight-visit ANC model with a new model consisting of five goal-oriented ANC visits and found that pregnancy outcomes were similar. For pre-eclampsia, however, an increased risk could not be ruled out. The WHO subsequently adopted the new model of 'focused ANC', and a minimum of four ANC visits is now the recommended ANC frequency (9).

The content of ANC is dictated by evidence-based interventions such as tetanus immunization, detection and treatment of sexually transmitted diseases, iron and folate supplementation, and in case of an HIV-positive mother, an antiretroviral course for the prevention of mother-to-child transmission. The focused ANC (FANC) model stresses the importance of counseling and the writing of a birth and emergency plan (2, 10).

The Determinants of ANC

ANC coverage is usually expressed as the percentage of women who have had at least one ANC visit, which is very high at 83% in 2012. However, only 52% of the pregnant women in LMIC received a minimum of four ANC visits in 2012 (compared to 37% in 1990) (1). Why is it that nearly 50% of women in LMIC do not receive adequate ANC?

The meta-synthesis of Finlayson and Downe (2013), which included 21 qualitative studies involving 1,230 women in 15 countries, studied ANC uptake and identified three key themes (11). The first theme, "pregnancy as socially contingent and physiologically healthy" emphasizes cultural and contextual aspects. Resistance to risk-averse care models is observed in women who regard their pregnancy as a healthy physical state, and as such do not see a need for a check-up with health professionals. Moreover, in some cultures, health-seeking decision-making is beyond the pregnant woman's control. Instead, husbands, mothers-in-law, or tribal elders decide whether or not women attend ANC. This is further compounded by traditional or cultural beliefs about pregnancy disclosure. Respondents in South Africa think it wise to wait until several periods are missed before determining that they are pregnant. In rural Pakistan women are embarrassed by their pregnancy as it demonstrates their sexual activity. In several parts of Africa and Southeast Asia women believe that they are vulnerable to witchcraft in early pregnancy. Going to public places, notably to an ANC clinic, is perceived as a public declaration of pregnancy and is thus undesirable.

Theme two, "resource use and survival in conditions of extreme poverty", relates to the direct and indirect costs of ANC visits (payments for drugs and transportation or loss of income), as well as the dangers and difficulties during travel (fear of attack, bad road conditions, etc.). Even though ANC itself might be free, the poorest simply can't afford any additional expenses, as all their money is required for basic survival.

The last theme, "not getting it right the first time" refers to supply challenges. Pregnant women perceive that ANC is not worth the effort because clinics are understaffed and under-resourced. Sometimes, procedural rules are inhibitive, for example denying women access to delivery facilities when they don't have an ANC card, and may serve as a reason why women might attend one ANC appointment only. Disrespectful, humiliating, or even abusive behaviors of health staff are critical barriers to ANC use as well.

Authors conclude that there might be a misalignment between the current ANC program design that is centralized and risk-focused, and the socioeconomic and cultural realities of some women in LMIC. The standard ANC design is based on premises such as 'pregnancy is potentially risky', 'pregnancy is a positive life event', and 'women have sufficient resources to make rational health choices'. The meta-synthesis, however, found that pregnancy is regarded as a healthy physical state, might be socially risky because of the belief in witchcraft or the shame associated with sexual activity, and (in)direct financial costs can impede seeking ANC. The same misalignment is found on the supply side as well. Whereas the program design is based on ANC being affordable (or even free), positive or irrelevant staff attitudes, and fully resourced clinics, the reality is that unexpected costs arise, staff attitudes are highly important, and clinics often lack drugs, medical material, and equipment.

Simkhada et al. (2008) systematically reviewed the literature on factors affecting ANC utilization in LMIC and conclude that women's social, political and economic status needs to be taken into account (4). Based on 22 quantitative, 4 qualitative, and 2 mixed methods studies, the authors identify 7 themes. Under the theme of "socio-demographic factors", women's education is identified as the best predictor of ANC visits. Studies also found that ANC use increases with the husband's educational level, with being married, and with the age at the time of marriage. Specifically, those 19 years and older are more likely to make use of ANC than those who are younger at the time of marriage. Women pregnant with a first child are generally more likely to use ANC, as is the case for women with birth intervals of more than 3 years. In 'unwanted' pregnancies, women tend to start ANC later and visit less frequently. Nine studies show a significant role for religion, ethnicity, and caste. In India, Muslims are more likely to use ANC than women practicing other religions. Women from lower castes in India and from marginalized groups in other countries are less likely to use ANC.

Other themes that Simkhada et al. identify are: "availability" of health care services, including opening times and waiting times; their "accessibility", with urban women being more likely to use ANC than rural women, the latter experiencing significant distance and transport barriers; and "affordability". Significant economic relationships are found in 21 studies, varying from household wealth, socio-economic status of the women (paid employment, employment outside the home), and expenses related to ANC service use, including costs of drugs and laboratory tests. "Women's position in the household and society", their autonomy and decision-making power influences ANC use, as does "women's knowledge, attitudes, beliefs and culture". Women exposed to mass media with knowledge about family planning, danger signs in pregnancy and dietary knowledge, as well as women who have prior experience with miscarriage or neonatal death are more likely to use ANC. Fear of witchcraft and the shame associated with pregnancy are also deterrents. In the final theme, "characteristics of health services", supply side barriers, such as poor quality of care and negative attitudes of health personnel, are identified.

Studies that examine the determinants of delivery care show that factors influencing delivery in health facilities are similar to factors affecting ANC uptake. Gabrysch and Campbell (2009) found only two previous reviews on determinants of delivery service use in LMIC, of which Thaddeus and Maine (1994) reviewed the whole range of determinants and Say and Raine (2007) specifically focused on place and socio-economic status (12-14). Thaddeus and Maine's seminal work "Too far to walk" presented the 'three delays model' in which factors affecting delays in decision-making to seek healthcare, delays in arrival at the health facility, and delays in adequate healthcare provision were identified for the period between the onset of obstetric complications and their outcomes. They found that quality of care was a more important barrier to healthcare seeking than cost (13). Say and Raine (30 studies in 23 countries) found a wide variation in the relationship between determinants and the use of maternal healthcare services, mainly because of contextual variety and methodological challenges, as not all studies equally controlled for potential confounders (14).

Gabrysch and Campbell's own extensive review that includes over eighty studies found that determinants had not changed significantly over time, and the study was appropriately called "still too far to walk" (12). They conclude that studies had concentrated on sociocultural and economic accessibility variables and neglected factors affecting physical accessibility and perceived

need/benefit. They warn against drawing conclusions when not every possible factor influencing service uptake is considered. For example, studies in Ghana and Nigeria conclude that promotion of female education would be the most effective measure to reduce maternal mortality, while accessible quality health care was not considered (15, 16). Berhan & Berhan (2014) is the most recent meta-analysis of determinants for birth in health facilities. They found that urban women were 9.8 times more likely to use services than rural, and use increased for women with secondary education or higher versus primary or no education (OR = 5.7; 95% CI, 3.77-8.6). However, the meta-analysis only deals with socio-demographic factors and half of the 24 selected studies took place in Ethiopia, which makes results less generalizable (17).

There are many determinants that affect use of ANC, notably the use of 4-visit ANC. Determinants may be interlinked in the sense that educated women may be living in urban areas where more health services are offered, more knowledgeable to appreciate ANC services, and more likely to have paid jobs and the decision-making power to seek care. Determinants have differential effects across countries or among different areas within a country, emphasizing the importance of context. Quality of services is still insufficiently measured (12), and while it is important to address women's autonomy or education, it won't solve any problem if health services are not accessible or inadequate.

How does ANC contribute to the reduction of maternal mortality?

In 2013, approximately 289,000 women died "during pregnancy, childbirth, or within 42 days after termination of the pregnancy from causes (excluding accidental or incidental causes) related to - or aggravated by- pregnancy or its management" p. 29 (18), of which 99% lived in developing countries (19). The estimated lifetime risk for maternal mortality in 2015 was 1:33 in high-income countries versus 1:41 in low-income coun-

tries, with the highest risk in Chad (1:18) (19), thereby representing the largest discrepancy of all statistics in public health (5). The most recent WHO systematic review on global causes of maternal deaths by Say et al. (2014) reviewed 23 studies published in the period 2003-2012. They found that nearly three quarters of all maternal deaths were due to direct obstetric causes and 27.5% to indirect causes. The top 3 causes of death were hemorrhage (27%), hypertensive disorders (14%) and sepsis (10.7%) (20). These direct causes for maternal mortality, together with the clustering of mortality around delivery, illustrate the need to focus on intra-partum care, i.e. all women should have access to skilled attendance (by a midwife, doctor, or nurse with midwifery skills to attend to uncomplicated deliveries at labor and birth (21), and timely referral to emergency obstetric care (EOC) (5, 22, 23). This chapter looks into the main causes of maternal mortality and how ANC addresses them. It examines the pathways of the association of ANC uptake with facility-based delivery and its challenges.

ANC is a relatively cheap intervention that can be planned over a 9-month period and provided to women in practically any geographic area. Providing access to appropriate care during labor and delivery, however, is a much more complex endeavor, requiring highly skilled personnel and a functional health system providing basic and EOC services (22). This has led to programs focusing on ANC rather than delivery care (24), but how effective is ANC in reducing maternal mortality? ANC has been routinely delivered in developed countries for nearly a century (25). Its effectiveness, however, has only been challenged in the 1980s -1990s (26). Cochrane (1972) states that ANC, by some chance, escaped critical assessment and that ANC should be subjected to RCTs (cited in Carroli 2001 (10, 27)).

In 1996, McDonagh confirms that many of the antenatal procedures comprised screening tests that rarely

complied with established effectiveness criteria, and that results from RCTs were available for nutritional supplementation only (6). She defines risk factor as a link in a chain of associations leading to illness and identifiable prior to the event it predicts. This requires good medical history taking, which has been a challenge. To detect pre-eclampsia, blood pressure must be taken. Not only are there many systematic and random errors made in blood pressure recording, the natural history of the pre-eclampsia is not known, and the positive predictive value of taking BP was estimated to be 40% only (28). Many other screening tests had low predictive power as well (as low as 13%), and even ultrasounds in the UK produced over 50% false positives (Tew 1990, cited in McDonagh (6, 29)). It resulted in many women being referred unnecessarily, overburdening the health system, and causing unnecessary stress and cost to women.

Rooney reviewed the effectiveness of ANC for the WHO in 1992 and questions the beneficial associations between ANC and maternal morbidity and mortality. The decline in the latter since the 1930s could be partially attributed to improved obstetric care and, in places where ANC is lacking, delivery services are likely to be poor and information systems unreliable (7). Rooney was unable to identify studies in LMIC that adequately controlled for confounding factors, which is essential as outcomes of ANC attendance (vs. non or late attendance) are likely to be confounded by socioeconomic factors, education, knowledge, distance etc. She points out that ANC, like other screening programs suffers from 'inverse care laws', i.e. those at highest risk are least likely to make use of preventive services (7).

Carroli et al. (2001) updated and expanded the Rooney's review and provided an overview of evidence-based interventions that aim to prevent, detect, and treat causes of maternal mortality and serious morbidity to be included in ANC. Regarding hemorrhage, ANC's role

is limited: detection of women at risk and ensuring that they deliver in an adequately equipped facility, detection of signs and symptoms, combined with immediate referral, and reduction in anemia prevalence. Folate and iron supplementation are recommended for the latter. With regard to hypertensive disorders of pregnancy (HDP), authors repeat findings articulated by McDonagh: the lack of consistent patterns in disease etiology, identification, and treatment (except for caesarian sections) make it challenging to effectively address HDPs, even though it is hypothesized that calcium supplementation could reduce HDP. With regard to sepsis, the last of the top 3 causes of maternal death, most effective interventions take place in the intra-partum period. Tetanus vaccination is an exception: the 2-dose vaccination provided in the ANC period has been one of the most successful interventions against puerperal sepsis (10).

In recent years, interventions during ANC addressing indirect causes of maternal mortality have demonstrated effectiveness. Early detection and treatment of plasmodium falciparum malaria in pregnant women and antiretroviral therapy (ART) of HIV-positive pregnant women can reduce maternal mortality.

Preventing malaria in expectant mothers is of great concern, especially in parts of the world where it is endemic. Annually, 25 million pregnancies are affected by malaria in Africa alone (2). Malaria can lead to severe anemia in pregnancy, which increases the risk of mortality associated with haemorrhage during delivery. The highest malaria infection rates are found in the second trimester. ANC is therefore crucial to detect malaria with rapid tests, to treat with artemisinin-based combination therapy, and to prevent through intermittent presumptive treatment and the use of insecticide treated bed nets (30). Although Carroli et al. did not find convincing evidence regarding the effectiveness of intermittent prophylaxis for malaria during pregnancy, a 2006 Cochrane Review found significant reductions in maternal anemia in intervention groups. In 2012 McGready et al. (31) demonstrated a significant decline in maternal mortality through systematic screening and treatment of falciparum malaria during pregnancy. Over a 25-year period the maternal mortality ratio in Thai-Burma border camps dropped from 499/100,000 to 79 (p<0.05), of which nearly 40% was caused by infection of non-puerperal sepsis and falciparum malaria.

With high prevalence and infection rates of HIV, ANC has gained popularity as a means to detect and treat HIV in pregnant women (20, 24). In populations where HIV prevalence is higher than 15%, half of the pregnancy-related deaths are related to HIV (32). In a systematic review from 2003-2014, Holtz et al. (33) find that ART reduces maternal mortality. The effect is greater if ART is started at an earlier stage of the pregnancy, with CD4 counts >350 cells/mm2, and when the disease is less advanced. The so-called B+ regimen, which the WHO recommends since 2012, starts all HIV-infected pregnant women on a single-pill fixed-dose triple ART, regardless of CD4 cell count, from their first ANC visit and for the rest of their lives (34). Authors state that this seems to be the right approach to reduce HIV-related maternal mortality. They warn, however, for a risk of increased mortality in the 30-day period after ART initiation, notably in women with advanced HIV. They advise intensive follow up and vigilance in this period.

Generally, interventions shown to be effective in pregnancy relate to chronic maternal conditions (anemia, HDPs, and infections) rather than acute, such as hemorrhage and obstructed labor that emerge close to delivery (10). As the greatest dangers arise in the intra-partum period, the contribution of ANC to maternal mortality reduction is therefore in encouraging women to deliver in adequate health facilities with competent staff (24). This is why, in the model of FANC, so much attention is given to health promotion, birth preparation, and emergency plans (22).

Studies have demonstrated that pregnant women attending ANC services are more likely to deliver in a health facility with skilled birth attendance (21, 35-37). Different causal pathways explain this association. The information and quality of care that pregnant women receive during ANC could make them opt for facility-based delivery (38).

In a cross-sectional cross country analysis of 19 sub-Sahara African countries, Nikiema et al. (2009) researched the health information pregnant women receive during ANC to predict delivery in a health center. It is hypothesized that increased knowledge about danger signs and potential complications in pregnancy and delivery will increase use of delivery services. This means that women need to receive advice and remember it. The study found, however, that less than 50% of the women reported having received health information and the ones that did, remembered it in varying degrees (recall from 6% in Rwanda to 72% in Malawi). Recall increased with the number of ANCs received, as was the likelihood of receiving health information, which doubled with 3 ANC visits (OR=1.9) and nearly tripled with 5 (OR=2.72). Disturbingly, women considered high risk did not consistently receive more health information. Rural women were less likely to have been advised (OR=.70) whereas they are more likely to be more distant from EOC services. Teenagers and uneducated women received less health information as well (OR=.84 and OR=.65 respectively). Authors looked at the interaction between the number of ANC visits (with and without health information) and institutional delivery. They concluded that women were more likely to deliver in a health facility with every additional ANC visit; the effect was even greater when women received health information (e.g. OR=1.6 for 2 visits compared to OR=3.82 for 5 or more visits, and OR= 2.34 and OR=4.81, respectively, with health information) (38).

The "psychological factor" plays a role as well. Getting familiar with health personnel during ANC lowers the threshold of getting into health facilities during the intra-partum period (37). For many women and girls, ANC services are their first point of contact with official health services. If this has proven to be a positive experience, it will be more likely that they opt to continue using these services for delivery, notably if delivery will be assisted by the same health care provider who provided ANC (2).

Another causal pathway is found in the change of health habits as a result of regular use of ANC services that aim to reinforce using skilled birth attendance for delivery (36). Studies evaluating curative services found that targeting maternal behavioral change may have a large impact in settings with high rates of modifiable risk factors (39, 40).

That said, much depends on the quality of services that women receive. Ensuring the use of up-to- date clinical protocols and standards based on evidence is essential (21). Barber (2006) found that women receiving most of the ANC procedures prescribed by national protocol were more likely to deliver in a health facility (OR=2.29 (1.18-4.44)), but no significant association was found with women who received 75% or less of the content (35).

How does ANC contribute to Maternal Health?

With the acceptance of the FANC as the new ANC model, WHO moved away from the risk detection approach aimed at reducing maternal mortality to a focus on improving maternal health, which is both required to improve newborn health and an end in itself.

Campbell and Graham (2006) include ANC as an essential component to an effective strategy to reduce maternal mortality outside the intra-partum period. On top of medical interventions, advice giving is recommended regarding care-seeking for normal deliveries, planning of maternal and neonatal emergencies, recognition of dangers signs, warmth and exclusive breastfeeding, contraception, and birth spacing. Obstetric, medical, and social histories need to be recorded to not only detect pre-existing and medical conditions, but to identify social problems such as violence (22).

Sexually transmitted infections (STIs) can cause serious maternal morbidity and perinatal morbidity and mortality, but have hardly any impact on maternal mortality (24). Systematic screening and treatment for syphilis is part of FANC as it shows high cost:benefit ratios, notably in LMIC where prevalence might be twice as high as in industrialized countries (5-15%) (10). A study in Zambia found that untreated syphilis resulted in abortions, stillbirth, low birth weight, prematurity or congenital syphilis in 58% of the affected pregnancies (41).

Pregnancy may aggravate pre-existing health conditions. For one, it engenders haemodilution, a normal process in which iron is depleted regardless of iron supplementation. Iron levels return to normal quickly after the pregnancy, which is the reason why universal iron supplementation is no longer recommended. In LMIC, however, two-thirds of women suffer from anemia, and as anemia is often the underlying cause of mortality, iron and folate supplementation remain recommended for the FANC (6). Other factors aggravating anemia include malaria, intestinal parasites, sickle cell disease, infections, blood loss, or poor socioeconomic conditions (42).

ANC represents a strategic entry point for the prevention of mother-to-child transmission (PMTCT) of HIV. HIV is associated with stillbirth, ectopic pregnancy, and spontaneous abortion (10). Early detection of HIV during ANC visits facilitates taking preventive measures to avoid or lower the risk of vertical trans-

mission during pregnancy, delivery, or breastfeeding. In 2013, approximately 210,000 children were infected with HIV in sub-Saharan Africa (43), of which over 90% occurred by vertical transmission (40). If infected infants are not treated, half die before they are 2 years old; however, adequate interventions can reduce mother-to-child transmission to 5% instead of the 20-45% if no antiretroviral (ARV) prophylaxis is utilized A systematic review and meta-analysis of 44 (44).studies by Wetstein et al. (2012) looks into ARV prophylaxis coverage in 15 sub-Sahara African countries (45), where 90% of the PMTCT need is (44). They found that the 'opt-out' approach to HIV- testing was successful: 93.7% of the women were tested compared to 57.6% when the patient would request to be tested (opt-in). Overall, 70.3% of pregnant women receive some ARV prophylaxis, with better uptake when the male partner is involved and when women deliver at a health facility. Uptake on continuous ARV treatment is very low: of the 22.3% eligible women (based on CD4 count) an estimated 61.1% started treatment. Authors conclude that coverage needs to be improved if the UNAIDS goal of eliminating all pediatric HIV infections by 2015 is to be achieved (45). The B+ regimen that starts all HIV-infected pregnant women on lifelong ART extends protection from mother-to-child transmission to future pregnancies from the moment of conception, which is not unimportant in environments where fertility rates are high (34).

HIV-infected pregnant women are also more exposed to opportunistic infections like tuberculosis (TB) than HIV negative women, and the risk of active TB increases during pregnancy (10). Nguyen et al. systematically reviewed tuberculosis care for pregnant women (2014). The 35 studies selected for review, of which 20 were carried out in LMIC, show that diagnosis during pregnancy is often delayed, as TB symptoms resembled pregnancy symptoms. Both TB prophylaxis and treatment seem safe and effective for pregnant women and their babies, provided that early initiation and effective follow-up are guaranteed. However, this early practice was lacking, perhaps why TB prophylactic treatment showed a low compliance rate (46). TB is the third leading cause of death among women of reproductive age (15-44 years) and can cause infertility and poor reproductive health outcomes (47). With approximately 510,000 women dying from TB in 2013, and 3.3 million contracting TB, integrating TB care in ANC would improve TB diagnosis and treatment (46, 48).

Through social history taking, ANC provides an opportunity to bring up sensitive issues affecting maternal and neonatal outcomes, such as gender-based violence (GBV). However, abused women start their ANC late, often in the third trimester only (49). Heise et al. give a global overview of GBV and its reproductive health consequences. Violence compromises women's mental and physical health, and may result in adverse pregnancy outcomes. Direct consequences on reproductive health are increased risk of unwanted pregnancies, STIs, and HIV, as women subjected to domestic violence are often unable to request the use of condoms or other forms of contraception. Sexual and physical violence is associated with chronic pelvic pain, irregular vaginal bleeding, sexual dysfunction, and premenstrual distress. Indirect consequences include a variety of risky behaviors, such as (excessive) drug and alcohol use, less contraceptive use, and promiscuity. Physical or sexual abuse during pregnancy has been linked to increased risk of antepartum hemorrhage, miscarriages, abortions, stillbirth, fetal distress and growth retardation, low birth weight of the infant, and neonatal death (50).

Gender-based violence is a public health priority, and health professionals need to be well trained in identifying the signs and symptoms in pregnant women during routine ANC. Health professionals can create a safe/secure environment during ANC visits, where women feel free to disclose these sensitive issues, receive (community) support, counseling, and information regarding legal assistance from organizations advocating for women (51).

Female genital mutilation (FGM) is a traditional practice that is common in about 28 African countries, and in certain parts of Asia. An estimated 100 to 140 million women and girls have undergone FGM, and about 2 million girls are at risk of undergoing FGM annually (52). The WHO defines FGM as "partial or total removal of external female genitalia or other injury to the female genitalia whether for cultural or any other non-therapeutic reasons" p.1 (53). The antenatal period is an excellent opportunity for the healthcare team to counsel, to promote health, and to educate women, their partners and family, regarding the health consequences of FGM, the risks of re-infibulation in case of multiple deliveries, and to discourage women to request re-stitching after delivery. This is also the ideal moment to encourage women to advocate for the elimination of FGM in their communities, where the practice is deeply rooted, to prevent future generations of women and girls from undergoing the same procedures (51).

Discussion

In our quest to find out whether ANC truly has been the success story some claim it to be, we found reason to answer both positively and negatively.

Even though ART treatment and rapid detection and treatment of malaria during the ante-partum period have demonstrated effectiveness, ANC might not be the best approach in reducing maternal mortality, as most deaths occur in the intra-partum period. However, as easy as it might be to criticize the success of ANC with regard to reduction of maternal mortality, it is much harder to produce evidence to support its (in)effectiveness. Maternal deaths, even with high ratios in the hundreds per 100,000 live births, are often too small in number to produce significant results, unless an unrealistically high sample size could be secured (6). The study would have to be prospective in order to ensure that all maternal deaths are properly registered, a process complicated by home deliveries, abortions, weak existing maternal death registration, and the misclassification of many maternal deaths (5, 54). Not only would such a study be very laborious and costly, with numerous potential confounders, it would be hard to control for interaction between variables and contextual variation might make generalization challenging (7). Furthermore, even if ANC were ineffective, how ethical would it be to take away a health service that is so widely accepted and used?

Several studies have focused on ANC contributing to a reduction of maternal mortality through indirect causal pathways aimed at health facility delivery. Indirect effects of health education and personal experience may be difficult to assess. They are important, however, in raising awareness regarding the importance of skilled birth attendance during the intra-partum period (55), which is considered to be the priority strategy to reduce maternal mortality (56). Even though it is suggested by some that ANC would rather be a marker of facility-based delivery (37), others claim that some features of ANC, such as the lower costs and the fact that women can plan their visits, which result in a much higher uptake of ANC than facility-based deliveries, make ANC sufficiently distinct for it to be considered a predictor for professionally assisted delivery (2, 37). It is reported that women who have had one ANC visit are six times more likely to deliver with a skilled birth attendant (SBA), and women who had more than four visits, compared to women with fewer visits, are 3 times more likely to deliver with an SBA (24).

Moreover, ANC might be the only service provided for women, thus the only opportunity to reach them, so there are practical reasons to keep ANC (6). ANC transcends basic healthcare by providing a solid ground for counseling and health promotion (22, 24). Adopting healthy habits and building a healthy environment for women and their babies, through breastfeeding, postnatal care, family planning, and birth spacing, as well as learning how to recognize danger signs during pregnancy and to be prepared for emergencies are all essential components in the new model of FANC (10, 22).

Unfortunately, health promotion and counseling are often not provided during ANC, and/or women are not able to remember the messages (38). Moreover, counseling appears to be very time consuming: whereas prior to the introduction of FANC a minute and a half was dedicated to counseling, now counseling would take on average an additional 30 minutes. This does not take into account informing and counseling of women for additional services such as TB or violence. Additionally, health staff would need to be trained to provide effective counselling (57).

Significant dose-response effects have been observed with regard to the number of ANC visits and the health information provided, other ANC content delivered, and facility-based delivery attended (35, 37, 57). Furthermore, a 2010 Cochrane meta-analysis that included 7 RCTs involving over 60,000 women showed that even though most outcomes were not significantly different in the FANC model compared to the traditional ANC model, there was evidence that perinatal mortality might have increased with the reduced visits model in LMIC (58). All the above-mentioned considerations taken into account, it might be wise to conclude that for LMIC a reduction of ANC visits should not be a priority (58), especially not in countries where the average number of ANC visits is not more than four visits anyway (57).

ANC has become the platform to provide other health services related to improving maternal and neonatal morbidity and well-being. In that light, efforts to include interventions addressing GBV need to be encouraged. Interest in GBV and pregnancy only developed in the last few decades, whereas violence in pregnancy is more common than several recognized maternal health conditions that are currently being screened for (59). Ganatra et al. showed that more pregnant women die from domestic violence (15.7%) than from sepsis (13.2%) or eclampsia (8.3%), and was bested only by postpartum hemorrhage (30.6%), the acknowledged number one cause of maternal mortality (60). Currently, deaths by injuries and accidents fall outside the scope of the ICD10 definition for maternal mortality (18). ICD11, however, might take suicide into account as in some countries suicide rates among pregnant women are very high, especially when the pregnancy is unwanted (20).

FGM, another prevalent form of GBV, requires sensitive attention as well. Even though women might understand that it is a harmful medical practice, underlying sociocultural and belief systems, as well as the role of the women in the society, make it challenging to address this issue effectively. Health facilities known to refuse re-infibulation after delivery, for example, may even cause women to avoid using their services, possibly leading to much greater harms to the woman and her child (52).

This brings us to the complicated field of the determinants for service utilization. There are many factors determining the use of ANC. At the demand side, the most important seem to be education and location, with uneducated poor and rural women being significantly disadvantaged (4, 17). Apparently there is a disconnect between the current ANC model and the socioeconomic and cultural realities of pregnant women, with many women regarding pregnancy as a healthy state instead of a risky undertaking requiring medical follow-up; some women simply do not have the means to access ANC even when offered for free (11). Sociocultural and economic accessibility variables are well researched, but factors affecting accessibility

and perceived need/benefit are neglected (12). Quality of care, however, seems to be one of the strongest facilitators of facility-based delivery (13). Health system strengthening is therefore crucial for effective delivery of reproductive health services. More investments need to be made in health workforce improvement through training and motivation strategies. Effective support and supply of health facilities, as well as reliable and timely health information are necessary to (further) improve quality of care (61). For policy relevance, supply-side challenges such as service accessibility and quality are more amenable to change than sociocultural factors such as women's autonomy, and whereas addressing those factors are important, how much good will autonomy do if there is no health center in the vicinity that can provide basic and emergency obstetric services (12)? More efforts could be made to include the community. Many of the health information, education and promotion activities could be provided by community health workers, for example (62). This would lessen the burden of counseling during ANC as well.

Addressing maternal mortality is not only important from a health perspective, it is important for economic and social development at both the individual and national levels as well. At the family level a mother's death affects children's health, education, and welfare, effects that can be carried on inter- generationally (63, 64). At macro-level, maternal deaths lead to loss of productivity, which, globally, has been estimated to represent 15 billion USD per year (63).

Maternal deaths are just the 'tip of the iceberg'. For every maternal death, 30 women suffer debilitating physical and mental disabilities, such as fistula, infertility, damage to reproductive organs and nervous systems, chronic pain, depression, and social isolation. The total number of women suffering illnesses and near misses after delivery is estimated to be 10-20 million per year (23, 65). Demographic transition with reduced fertility rates in notably India and Nigeria that accounted for a third of all maternal deaths in 2015 (19) are reducing global maternal mortality figures. Yet the epidemiological transition brings other challenges, such as the burden of noncommunicable diseases in pregnancies, which needs further exploration (20).

Conclusion

Although ANC might have started as a more ritualistic intervention, in time it has developed into a solid service with evidence-based interventions. ANC is widespread and widely accepted, as coverage data demonstrates. Attending ANC to enhance SBA attendance and facility-based delivery is the ultimate aim of the FANC, for which counselling is essential. Accepted FANC measures to reduce maternal mortality and morbidity include the detection and treatment of STIs (especially syphilis), anemia (through iron and folic acid supplementation), malaria, HIV, and TB. To qualify ANC as being truly effective, evidence-based interventions need to be correctly applied to as many pregnant women as possible. Significant improvements are therefore required with regard to its quality and accessibility. It is essential that the most vulnerable, the poor and rural women, will benefit from its services. Concerted efforts will need to be made to strengthen health systems and to improve socioeconomic situations in developing countries. Moreover, serious attention should be given to the improvement of women's position in society, promoting gender equality, education, and legal recourse, to address determinants of ANC use generally, and gender-based violence specifically.

The refocusing of ANC from maternal mortality reduction to maternal health facilitates providing health services that have a great impact on maternal and neonatal morbidity, as well as neonatal mortality. It allowed for a flexible adaptation to new realities when HIV became the major indirect cause of maternal mortality. For the immediate future, this flexibility is required to take into account the burden of noncommunicable diseases in pregnancies, as developing countries are facing the double burden of noncommunicable diseases and deaths caused by infectious diseases and reproduction related causes.

Even though the FANC might bring advantages of burdening women with less ANC visits, a note of caution needs to be given with regard to LMIC where perinatal mortality seems to have increased. Moreover, ANC visits have become more time-consuming because of counseling, and health staff are not adequately trained to provide this service.

As ANC provides the entry point to offer services to many women whose first contact with formal health services is their very first antenatal care visit and because of its high uptake, we tentatively conclude that ANC has been a success. Further quality and accessibility improvements need to be made in order to reach its full potential, however.

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