CHAPTER 08

Summary, discussion and implications of main findings, and future perspectives

General aim of the thesis

Although some progress has been achieved over the past two decades, Ethiopia is one of the sub-Saharan African countries most affected by the burden of chronic undernutrition. Both political and agroclimatic changes have contributed to food insecurity for decades creating malnutrition across generations. The Sustainable Development Goal (SDG 2) targets the intergenerational cycle of chronic undernutrition and its consequences by their focus on optimizing maternal and child nutrition. The preconception period and the first 1,000 days of life, i.e., from conception to 2 years of age, are critical intervention windows to optimize maternal and child nutrition. Despite a large body of evidence on undernutrition among under five children in low-and-middle income countries like Ethiopia, less is known on the first 1,000 days including pregnancy, as well as what are important determinants of a healthy first 1,000 days when looking at the pre-pregnancy conditions. Therefore, the current thesis aims to shed light on the window of opportunity in the pre-pregnancy period and during the first 1,000 days to improve maternal and child outcomes to contribute to breaking the vicious circle of chronic undernutrition and its consequences. We summarized the aims and main findings as reported in the previous chapters below.

Summary of the chapters

In chapter 1, we provided an introduction to maternal and child nutrition with special emphasis on the first 1,000 days of life. Concepts and presently used models to understand and study this period are introduced in this chapter. Additionally, the aims and the specific research questions, and a brief overview of the **KI**lite-Awlaelo **T**igray **E**thiopia (KITE) cohort are provided. This thesis used the KITE birth cohort data established in Kilite-Awilaelo Health and Demographic Surveillance Site (KA-HDSS) in the Tigray region of northern Ethiopia.

In chapter 2, we identified specific socioeconomic characteristics, reproductive and obstetric conditions, psychosocial factors, and food and dietary habits associated with pre-pregnancy nutritional status as a critical step towards improving maternal and child health outcomes. Firstly, a high prevalence of pre-pregnancy undernutrition (36.2%) was found as measured by pre-pregnancy body mass index and/or mid-upper arm circumference. In addition, lower women empowerment, lower dietary diversity, food insecurity, not being from a model household, and regular fasting driven by religious beliefs and habits in the community were associated with lower pre-pregnancy nutritional status.

In chapter 3, preconception and prenatal determinants of gestational weight gain were investigated. In our study population, most of the women (64%) did not gain adequate

weight during pregnancy according to IOM guidelines. Higher pre-pregnancy body mass index, higher women empowerment, hemoglobin levels measured at prenatal booking and better dietary diversity were associated with higher gestational weight gain. Adequate prenatal care was also linked with gaining higher weight during pregnancy. Additionally, our results indicated that optimizing dietary diversity, pre-pregnancy body mass index, women's economic empowerment, and providing adequate prenatal care would result in respectively 55.2%, 51.6%, 50.1%, and 41.4% probability of gaining adequate gestational weight. Furthermore, the results suggest that preventing illness during pregnancy and refraining from fasting for religious purposes may positively impact the probability of gaining adequate gestational weight.

In chapter 4, we related maternal nutritional status before and during pregnancy to adverse birth outcomes. This analysis revealed a high prevalence of adverse birth outcomes; preterm birth (15.6%), low birth weight (16.0%), and small for gestational age birth (20.3%). Our findings showed that lower pre-pregnancy weight was not directly associated with adverse birth outcomes, but indirectly through lower gestational weight gain. Whereas lower gestational weight gain was associated with higher risk of the adverse birth outcomes. Short maternal stature, defined as ≤153.0 cm, did not directly influence adverse birth outcomes but did exert an indirect influence through lower pre-pregnancy weight and gestational weight gain. The indirect influence of short maternal stature was attenuated and was no longer significant among women with normal pre-pregnancy weight and adequate gestational weight gain indicating that optimizing maternal nutrition prior to and during pregnancy can compensate the influence of short maternal stature.

In chapter 5, we studied the role of maternal distress in the perinatal period on adverse birth outcomes. Perinatal maternal distress refers to high symptoms of anxiety, depression, and/or stress during the perinatal period, i.e., the period between 22 weeks of gestation and the end of the first week postpartum. Next we also examined if perinatal maternal distress was an independent risk factor or a mediator in the pathway of socioeconomic adversity to adverse birth outcomes. Socioeconomic adversity was defined as poor economic status, food insecurity, women's disempowerment, intimate partner violence, lack of social support, and stressful life events. In our study population, 21.4% of the women had high symptoms in one, 12.5% in two, and 9.2% in three of the domains of distress. Our results also revealed that perinatal anxiety, depression, stress, and total distress scores were all associated, albeit modestly, with low birth weight, and small for gestational age birth, but not with preterm birth. Furthermore, mediation analyses demonstrated that perinatal distress may be a mediator in the pathway of socioeconomic adversity to adverse birth outcomes.

In chapter 6, we looked at postpartum weight change in relation to pre-pregnancy weight and gestational weight gain. At 18-24 months after delivery, women had on average 0.4 kg higher body weight when compared to their pre-pregnancy weight. The range was -3.2 to 5.5 kg, indicating a large interindividual variation. Whereas 18% of women shifted to normal weight compared to the pre-pregnancy period, still about one-third (33.2%) of the women were underweight at 18 to 24 months postpartum. Of whom 5.1% were not underweight before pregnancy. Lower gestational weight gain, food insecurity, and high symptoms of perinatal distress were associated with postpartum undernutrition.

In chapter 7, concluding the assessment of events in the first 1,000 days of life, we evaluated growth outcomes of the children born in the study. The overall prevalence of stunted growth in early childhood in our study population was 37.8% (95% CI: 33.9, 41.8). Lower maternal stature, pre-pregnancy body mass index, gestational weight gain and birth weight were associated with higher risk of stunted growth in early childhood. Moreover, experiencing at least one pregnancy complications, pre-lacteal feeding, and respiratory illnesses were linked with stunted growth. The population attributable fraction of short maternal stature, low pre-pregnancy body mass index, and inadequate gestational weight gain combined was 64% indicating eliminating these three risk factors might reduce stunted growth by 64%.

In chapter 8, we discussed the pertinent findings of this thesis and their implications, followed by methodological considerations and future perspectives. Finally, we provided concluding remarks and lessons learned in general terms.

Discussion and implications of the main findings

Is the pre-pregnancy period a missed opportunity to improve maternal nutrition?

Pre-pregnancy nutritional status may impact maternal nutrition and health status over the entire perinatal period. In view of this challenge, looking at the pre-pregnancy period and identifying the main factors influencing pre-pregnancy nutritional status is a key step towards improving maternal nutrition and health. Therefore, firstly, we indeed showed a high prevalence of pre-pregnancy undernutrition (36.2%) indicating the pre-pregnancy period is a largely missed opportunity to improve maternal and fetal outcomes. Secondly, most clear impact was seen from factors that may contribute to identify appropriate nutrition-sensitive, such as health extension package implementation, and nutrition-specific interventions, such as diet diversity that could be used as a part of the preconception care package or separate intervention.[1]

As described in **chapter 2**, pre-pregnancy nutritional status was positively impacted by implementing a health extension package.[1] Health extension package is a health promotion and disease prevention program consisting of 16 components, including maternal health, family planning, nutrition, proper and safe waste disposal, and food hygiene and safety measures. Selected households that can implement the package and can serve as a change agent by influencing their neighbors are trained and certified as model households after implementing the program in the community. Being a woman from a model household can be, therefore, used as a proxy for improved health literacy, maternal health service utilization, dietary practices, hygiene, and environmental sanitation as shown by previous studies.[2–4] These may be translated into improved nutritional status. Overall, promotion of such a health extension program may be an excellent approach to improve pre-pregnancy nutritional status in a cost-effective manner, especially in areas where access to health care is limited.[5] Implementation of the health extension package, however, was not common (24%) in the area and needs to be expanded further.

In addition, we found a positive association between women's empowerment and pre-pregnancy nutritional status,[1] which is seconded by some studies.[6,7] Aubel *et al.* defined empowerment as the ability of individuals or groups to improve capacities, critically analyze situations, and take actions to improve those situations. Hence, the results in this thesis suggested that empowered women may have better access to income, better decision-making regarding their health, higher control over finances, improved mobility, and less domestic violence. These may translate to better health-seeking behavior, improved dietary practice,

and maternal nutrition.[7,8] For instance, a study in Benin showed empowering women could improve maternal dietary quality.[7] Of note, empowered women did not exceed 12% in our study area. Tailored public health interventions aiming at empowering women need to take into account the deeply rooted societal norms that have a negative impact on maternal nutrition. Perhaps, strengthening the health extension package may also play a role in empowering women at least on the health literacy domain.

Having access to affordable and nutritious foods is an important prerequisite to improve dietary quality and preconception nutritional status. In our study population, a substantial number of the women were from food insecure households (36.9%) and had inadequate diversity of diet (47.7%). Additionally, both higher food insecurity and lower dietary diversity scores were associated with lower pre-pregnancy nutritional status as described in chapter 2 of this thesis.[1] Though there are no studies that assessed nutritional status before pregnancy, a number of studies showed similar findings during pregnancy.[9–11] Thus, reforming agriculture to increase productivity with adequate emphasis on nutrition-sensitive agriculture such as agricultural diversification may be one of the policy interventions. Also, protein-energy and multiple micronutrient supplementation and fortification of staple foods may have positive impact as recommended by WHO.[13]

Besides the inadequate food intake and diversity of diet because of limited access to food, some dietary habits may be exacerbated by religious behaviors. The high prevalence of regular fasting (~70%) observed in our study population was associated with lower pre-pregnancy nutritional status in this thesis.[1] Although no previous study examined the impact of fasting on pre-pregnancy maternal nutrition, another study in Ethiopia associated fasting with poor maternal nutritional status after pregnancy.[13] Fasting is defined as abstaining from animal-source foods such as meat, dairy products and egg as a part of religious observances. In Orthodox Christianity, a religion which an overwhelming majority of the population in our study area follows, more than half of the days in an entire year are fasting times. They may negatively impact both nutrient dietary intake and diversity of diet. This argument is supported by a study in Ethiopia that showed a lower energy and micronutrient intake among children during the fasting period compared to the non-fasting period.[14,15] As family members share the same dish in Ethiopia, the finding reflects the impact of fasting on women of reproductive age before pregnancy as well. Hence, the finding informs the necessity for involving opinion leaders in general and religious leaders in particular in nutritional programs. Empowering women towards a healthy dietary practice may also play a role in improving maternal nutrition. The house-to-house visits by health extension workers and prenatal care visits could be important channels for nutritional communication to mobilize the community at large.

In conclusion, the pre-pregnancy period is largely missed window as an opportunity to improve maternal nutritional status. Health extension package implementation, women empowerment and (religious) fasting were the most relevant factors that need to take the attention of concerned bodies to improve the outcome.

Which period is more important to improve maternal nutrition: the pre-pregnancy or pregnancy period?

This thesis showed that many women (64%) did not gain the recommended amount of weight during pregnancy.[16] Almost 90% of the women who did not achieve adequate gestational weight gain were underweight before pregnancy. A recently published review also showed 67-98% of underweight women do not gain adequate weight during pregnancy in low-income sub-Saharan Africa countries which is in line with our finding.[17] These results show that the pregnancy period is not used to compensate the opportunity missed before pregnancy and to improve maternal and child outcomes in low-income countries. Additionally, the findings indicate interventions during pregnancy may not be able to augment weight gain for underweight women in low-income countries where a prenatal booking is delayed. In support of this argument, we observed that higher pre-pregnancy weight was not associated with higher gestational weight gain within the recommended range among underweight women whereas this was the case among their normal weight counterparts. From a policy perspective, the findings signify the importance of the pre-pregnancy period to improve maternal nutrition and the benefit of starting public health interventions in the preconception period. At this intervention point, focusing on the most impactful factors like fasting, health extension package and women empowerment is important. Also, there is a need for a mechanism to identify women early during the course of pregnancy so that interventions aimed at improving maternal nutrition could start early and achieve the intended target by directing more priority to underweight women.

Pre-pregnancy nutritional status may not be the only factor at play. Identifying other factors influencing maternal nutritional status during pregnancy may offer insights to guide interventions directed at improving the outcome. In this thesis, higher women empowerment was associated with higher gestational weight gain,[16] as it did with pre-pregnancy nutritional status. The empowered women may have better opportunities with regard to jobs, education, income, access to food and better bargaining power on the household resources. Thus, better empowerment may translate into better diet diversity, nutrient intake, and nutritional status as reflected in higher gestational weight gain. Therefore, integrating gender perspectives in policies, programs and nutritional interventions may be one of the strategic

approaches to empower women and improve their nutrition and health. Establishing structural arrangements at the institutional level may be required to realize the gender mainstreaming and women empowerment. Equally important is solving societal attributes and structural factors contributing to lower women empowerment like the social norms that let women be dependent on their husbands.

Furthermore, this thesis showed a positive association between adequate prenatal care and gestational weight gain.[16] In agreement with this finding, previous studies show a positive relationship between having at least four prenatal care visits and adequate weight gain during pregnancy, although total prenatal care visits without taking the time of booking into account does not show adequacy.[18] The association could be due to the fact that prenatal care offers an opportunity for nutritional communication, micronutrient supplementation like iron-folic acid, and diagnosis and treatment of illnesses. Integrating preconception care into the existing health system might also benefit women and their children. It could be even leveraged to serve as a strategic delivery platform for nutrition-specific interventions.

To conclude, it seems that the pre-pregnancy period is indeed the most important period to improve maternal nutritional status with heath extension package implementation, religious fasting, and women empowerment being the most impactful factors. During pregnancy, women empowerment and adequacy of prenatal care utilization had most impact on gaining higher weight other than the already known dietary quality.

Is maternal nutrition prior to or during pregnancy more important in terms of optimizing birth outcomes?

As described in **chapter 4**, lower pre-pregnancy weight did not have a direct association with higher risk of adverse birth outcomes. However, it was related with higher risk of adverse birth outcomes indirectly through lower gestational weight gain. In support of our finding, a prospective study in Vietnam showed an association between low pre-pregnancy weight and adverse birth outcomes.[19] Conversely, another prospective study in Gambia did not find a significant association among all the participating women but, interestingly, it did among underweight women,[20] which is in line with our findings. The difference between our finding and those in the Gambian study could be related to the protein energy supplement provided to the women in the latter. Furthermore, lower gestational weight gain was linked with higher risk of adverse birth outcomes which is consistent with the literature.[21–26] As illustrated in **chapter 2** of this thesis, almost all underweight women did not gain the recommended weight during pregnancy.[16] As a result, 31.0% of the women in our study

population were underweight and did not achieve adequate gestational weight gain. These findings clearly suggest that in settings where maternal undernutrition is high and prenatal care booking is delayed, birth outcomes cannot be improved by interventions covering the pregnancy period only. Overall, our study offers additional insights regarding the importance of focusing on the preconception period to improve birth outcomes which is first not receiving adequate attention in low-income countries and secondly is especially relevant for underweight women. Not only needs the pregnancy period better attention, it should also be extended to encompass the preconception period.

Can adequate pre-pregnancy weight and gestational weight gain compensate the influence of short maternal stature on birth outcomes?

As illustrated in **chapter 4** of this thesis, short maternal stature, reflective of chronic undernutrition in early life, was indirectly associated with adverse birth outcomes through low pre-pregnancy weight and low gestational weight gain. Although we are not aware of studies that looked at the indirect effect through low pre-pregnancy weight and gestational weight gain, there are studies that showed a direct association between short maternal stature and adverse birth outcomes.[27,28] Interestingly, the indirect influence of short maternal stature was attenuated among women with adequate pre-pregnancy weight and gestational weight gain. These results show that the impact of chronic undernutrition in early life reflected as short maternal stature can be compensated with sufficient pre-pregnancy weight and gestational weight gain, at least to prevent adverse birth outcomes. Further, our findings highlight the necessity for nutritional interventions to offer a priority to short stature women so that the prevention of adverse maternal and child health outcomes would be possible as indicated elsewhere.[29] When short stature and being underweight coexist, the impact on birth outcomes may even be far higher.[30] In our study, 25.2% of the women were both short stature and underweight. Therefore, important improvements could be made for a substantial part of our population.

Is perinatal distress an independent predictor or a mediator in the pathway of socioeconomic adversities to birth outcomes?

Although several studies showed an independent association between perinatal distress and adverse birth outcomes,[31–34] little is known on the mediation role of distress in the link between socioeconomic adversity and adverse birth outcomes in low-income settings. Perinatal distress, as described in **chapter 5** of this thesis, may be a mediator in the pathway between socioeconomic adversity and small birth size. That is, socioeconomically

disadvantaged women (food insecure, not empowered, not having adequate social support, etc) may experience distress that activates the hypothalamic-pituitary-adrenocortical axis, resulting in higher cortisol levels. The placental 11β-hydroxysteroid dehydrogenase-type 2 (11b-HSD2) enzyme protects the fetus from glucocorticoid exposure by converting cortisol to inactive metabolites. However, chronic prenatal exposure to distress may drain the ability of the 11b-HSD2 to protect the fetus from cortisol resulting in intrauterine growth retardation. [35,36]

Our findings may, therefore, highlight the relevance of targeted screening and management of distress, focusing specifically on women experiencing socioeconomic adversity. In low-income countries like Ethiopia, the screening and management of perinatal distress can be facilitated by integrating mental health better within primary maternal health care services.

What changes in maternal nutritional status has been achieved after pregnancy compared to the preconception period?

Our study population's poor pre-pregnancy nutritional status remained high (33.2%) 18 to 24 months after pregnancy, as described in **chapter 6** of this thesis.[37] As lactating women, their poor nutritional status will impact their children's growth and development. Further, in Ethiopia, the inter-pregnancy interval is short, and these women will probably enter the subsequent pregnancy with poor nutritional status. Lower gestational weight gain was one of the strongest determinants of poor nutritional status after pregnancy. Also, pre-pregnancy weight was detrimental to gestational weight gain, as depicted in **chapter 3** of this thesis.[16] These findings show that maternal nutritional status during the pre-pregnancy, pregnancy, postnatal, and inter-conception periods are interconnected. To summarize, the results suggest it is essential to promote nutrition and health throughout the women's reproductive course. As we showed in **chapters 2, 3, and 6**, ensuring food security, empowering women, improving prenatal care, avoiding religious fasting, implementing health extension package, etc., may be some of the intervention areas.

Which preconception, prenatal and postnatal factors are the main drivers of stunted growth at the end of the first 1,000 days?

Lower maternal stature, pre-pregnancy body mass index, and gestational weight gain, as described in **chapter 7** of this thesis, were associated with a higher risk of stunted growth in early childhood. These findings are partly or fully supported by similar prospective studies in low-and middle-income countries.[30,38–40] The probable explanation may be shared

genetic factors and the adverse effects of maternal undernutrition on intrauterine fetal growth manifested as lower birth size. Such adverse effects on birth outcome could be related to lower immunity and increased risk of infection, especially in low-income countries where unhealthy environments and suboptimal child feeding are common. Recurrent infections may then lead to stunted growth by suppressing dietary intake, disrupting absorption of essential nutrients, and using the available nutrients and energy for an immune response where they could have been used for growth. In support of this argument, this thesis also found an association between respiratory illnesses and stunted growth in early childhood (**chapter 7**). Therefore, maternal nutritional interventions starting from the preconception period may improve child outcomes, as seen in some studies.[41–43] Furthermore, such interventions targeting children, especially those born small in size, may also improve growth and health.

Notably, if all the participating women had normal pre-pregnancy weight, and achieved adequate gestational weight gain, 36% of the stunted growth in early childhood might have been prevented. If the women were not short stature as well, stunted growth might have been reduced by 64% (**chapter 7**). Unfortunately, there is no quick fix nutritional intervention to compensate for intergenerational effects of short maternal stature. Several generations may be required to remove the effects of chronic undernutrition in early life, as reflected in short maternal stature.[40] So, the focus should be on risk factors amenable to short-term nutritional interventions, like low pre-pregnancy weight and inadequate gestational weight gain to optimize birth outcomes and postnatal growth, which is a primary requirement for the reduction of the intergenerational burden.

Quite the opposite of our expectation, the contribution of eliminating inadequate gestational weight gain (11%) was almost half of the contribution of eliminating low pre-pregnancy weight (23%) in terms of preventing stunted growth (**chapter 7**). These results may be partly explained by the fact that almost half of the women who did not achieve adequate gestational weight gain were underweight before conception. The findings may also suggest the need for preconception interventions in contexts with a high prevalence of pre-pregnancy undernutrition. Apart from nutrition, eliminating respiratory infections and possibly others like gastrointestinal infections might decrease the prevalence of stunting in early childhood by 34%. These findings highlight that, for the nutritional interventions to be effective in low-income countries like Ethiopia, we must combine them with infection prevention and control measures.

In conclusion, our findings revealed that the 50% reduction in stunting cannot be achieved by improving health and care during pregnancy alone. Hence, optimizing pre-pregnancy

maternal nutritional status, and prevention and control of respiratory infections and possibly others may be essential to achieve further improvements in child growth and development.

Methodological considerations and future perspectives

In our cohort study, we tried to overcome limitations of studies reported in the literature. Use of self-reported pre-pregnancy weight or weight measured at prenatal booking is common in many studies. First, recording self-reported weight is not practical in most low-income countries like Ethiopia because weighting is not common, as scales are not easily accessible. As women in low-income countries do not start prenatal care in their early pregnancy, weight measured at the first prenatal booking could be a highly biased proxy for pre-pregnancy weight. In this thesis, actual weight was measured before pregnancy as part of a prospective cohort study. Although there is a probability of a change in weight in the time between the weight measurement and conception, the likelihood of any drastic changes is low. Yet, future studies may consider finding ways to measure weight closer to the moment of conception, for instance, when an intervention such as pre-pregnancy nutritional supplementation is offered.

Furthermore, we used body mass index, mid-upper arm circumference, gestational weight gain, and birth weight as anthropometric indicators of nutritional status. Future studies may consider additional measures like the child's birth length and head circumference and assessments in the cognitive domain to have an even more complete overview. These additional measurements would allow assessing cognitive development next to physical growth. Although our data allowed the assessment of weight and height up to 18-24 months, a longer follow-up would help evaluate the consequences of chronic undernutrition in early life. It may provide additional insights into adequate growth and development requirements later in childhood. Such data could inform to what degree growth trajectories in early childhood can be altered.

Estimating the nutritional and dietary attributes of the participants in our cohort was a subject of much debate. A detailed assessment is time-consuming, but missing information may limit the strength of evidence. In this thesis, we assessed dietary diversity through a 24-hour dietary recall method. The daily dietary intake varies, and a single-day dietary recall method may not perfectly capture the usual dietary practice. Therefore, assessing dietary intake over multiple days, like the three-day dietary recall method, may offer better insight into the future's dietary quality. When affordable, considering biomarkers of dietary intake and nutrient status to measure the biological effects of specific dietary components, and to assess the impact of diet on perinatal outcomes, may provide an even more complete picture. Today,

little is known about the nutritional contents of the common dishes in Ethiopia. Investigating the nutritional composition of common dishes in Ethiopia may enhance our understanding of nutrient intakes and help health professionals in their nutritional counseling. This information will help women make an informed decision about their dietary practice and child's feeding.

Modern obstetric care revolves around the accurate estimation of gestational age, but this is not always feasible in low and middle-income countries. We used the last menstrual period (LMP), fundal palpation, and/or ultrasound to estimate gestational age. However, ultrasound dating, the most realistic measure to determine gestational age, was unavailable in most women. In addition, LMP is vulnerable to inaccurate recall and digit preference, and because of the assumption that ovulation occurs on day 14, it often over/underestimates gestational age and introduce random error. Future studies that rely entirely on a gold standard ultrasound scan for gestational age dating may offer a better impression by reducing bias. Finally, our examination of the influence of perinatal distress as an independent risk factor or a mediator of the pathway linking socioeconomic adversity to adverse birth outcomes, such as small for gestational age, could have benefitted from a collection of bio-specimens. As we could not do so, we could not measure biomarkers such as cortisol or norepinephrine, validated markers of distress, and possibly critical surrogate markers of changes in oxygen and nutrient supply to the fetus linked to adverse birth outcomes. Future studies assessing distress objectively are warranted.

Finally, recent literature shows that besides the massive impact of environmental factors, also genetics may contribute to maternal nutritional status, adverse birth outcomes, and child growth. Maternal and paternal genetics and paternal origins of health and disease are thought to influence birth outcomes and child growth. The complex interaction of environmental and genetic factors may also be at play. Therefore, future studies in low-income countries like Ethiopia should be encouraged to consider the assessment of maternal and paternal genetics and nutritional status. For instance, epigenetic studies may help uncover the underlying mechanisms linking chronic undernutrition in early life and perinatal outcomes. Though our results show that adequate pre-pregnancy weight and gestational weight gain can compensate for the influence of short maternal stature on adverse birth outcomes, the possibility there could be other uncompensated effects of chronic undernutrition in early life that deserve the attention of future studies. Another suggestion for future research is to investigate if adequate gestational weight gain can compensate for the influence of pre-pregnancy underweight on birth outcomes. Such studies may require a larger sample size so that the subgroup analysis would be adequately powered.

We observed a high prevalence of undernutrition before, during, and after pregnancy in our cohort that collected data in northern Ethiopia starting from preconception until the end of the first 1,000 days of life. The need for effective nutritional interventions is undeniable to improve maternal and child nutrition and health. There is a need for clinical trials with well-defined nutritional interventions that may help assess the best intervention strategy to break the perpetual cycle of intergenerational undernutrition. For instance, protein-energy and multiple micronutrient supplementations may be relevant for our study population in terms of improving maternal nutritional status and birth outcomes. In addition, introducing preconception care into the existing health system and evaluating its contribution to maternal nutrition and health, birth outcome, and child growth may be needed. Unfortunately, it is not universally integrated in the existing health system yet in several low-income countries like Ethiopia.

Concluding remarks and lessons learned

Based on the evidence in the current thesis, we believe that the pre-pregnancy, pregnancy, and postpartum period are clearly still missed opportunities to optimize maternal nutrition status, birth outcomes, and child growth. Multifaceted factors were found to affect maternal and child nutrition. Therefore, nutrition should be part of a life-course approach that regards maternal and child nutrition within women's and their children's overall health. To this end, selected nutrition-sensitive and-specific interventions may play a role in breaking the intergenerational cycle of undernutrition and its consequences. The nutrition-sensitive interventions may include strengthening the health extension package, women empowerment, and screening and managing perinatal distress, focusing specifically on women experiencing socioeconomic adversity. Similarly, preconception nutritional supplements, promoting maternal dietary quality, and optimizing sociocultural factors such as religious fasting may be some of the nutrition-specific interventions. Given that many factors from different domains are at play, intersectoral collaboration is also needed to solve the grave problem of undernutrition and its consequences.

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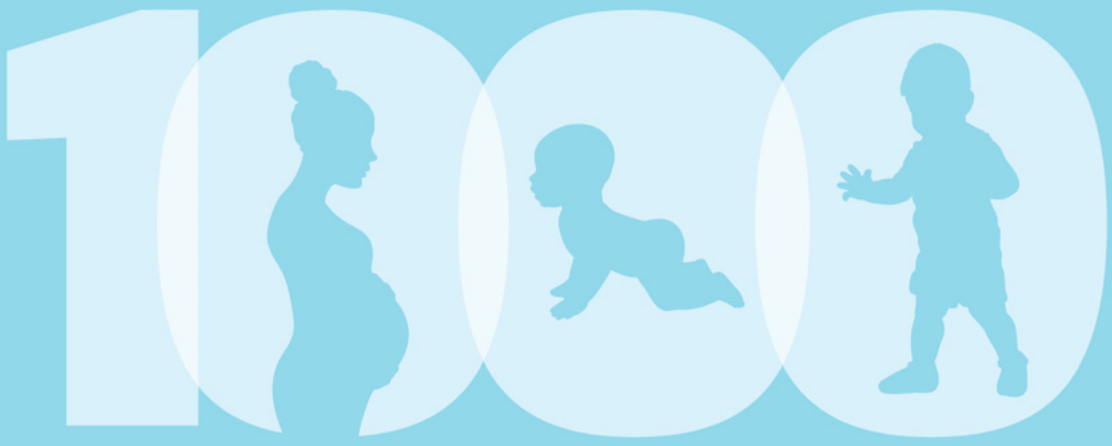
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