

# Building Biosocial Collaboration in the HeLTI–South Africa Trial

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## 21.1 Introduction

While the Developmental Origins of Health and Disease (DOHaD) as a field has been built on extensive physiological and epidemiological observational studies, there is recognition that the evidence base requires a shift to human intervention trials if it is to have any policy traction [1]. As intervention studies become more commonplace in the field of DOHaD, it is also essential to integrate a multidisciplinary perspective and social science approaches. Indeed, DOHaD is proving to be a productive and creative ground for biosocial collaboration between scientists and social scientists (including psychologists, anthropologists, sociologists, and science studies scholars), with recognition that integrating social science in interventions ensures that there is ongoing attention to assumptions embedded in research frameworks; maintenance of complexity in the face of the temptation to reach for the silver bullet; a retained sensitivity to socio-political and historical context; and active brokerage of new experimental forms of engagement with the communities of actors involved [2–4]. Such contributions are especially important given that DOHaD intervention studies will most frequently use complex public health interventions, where traditional methods are unable to capture the complexity of how context impacts intervention (and vice versa). New methods are required for understanding non-linear relationships and explaining results [5].

This chapter summarises lessons from the established literature on biosocial collaboration in trial contexts and considers their application in DOHaD intervention trials. Using the case study of the Healthy Life Trajectories Initiative (HeLTI), we illustrate the dynamics of a biosocial approach in action and discuss the benefits of building research infrastructures in DOHaD such that diverse disciplinary perspectives are given equal standing.

## 21.2 From Observation to Intervention: Time for Pragmatism?

As discussed in the introduction to this volume, DOHaD was formalised as a field with the consolidation of both physiological and observational studies of developmental programming that showed consistent associations between early life factors and adult health and disease outcomes, for example the relationship between birth size (lower birth weights) and adult non-communicable disease outcomes [6]. At the time the DOHaD Society celebrated its 10th World Congress in 2019, the field had expanded significantly to study a much wider range of associations, including the effects of early-life factors on mental health outcomes. However, both past and present DOHaD Society presidents highlight that DOHaD's translation to policy has been hindered by the kinds of evidence

that DOHaD science has produced, citing the ‘much needed transition from observational to interventional studies’ [1, p. 265] alongside developing knowledge of the pathways to policymaking.

While interventions during pregnancy were an obvious first step, outcomes of behavioural interventions demonstrated limited evidence of efficacy in what is a very narrow time period. The LIMIT trial demonstrated that antenatal lifestyle interventions did not decrease the risk of infants born large for gestational age or impact maternal outcomes, but did reduce the risk of birthweight exceeding 4kg [7]. The UPBEAT trial similarly showed that antenatal lifestyle interventions for obesity in pregnancy are insufficient to affect rates of large-for gestational-age births and gestational diabetes [8]. A narrative systematic review of 27 studies of the effects of weight management via dietary counselling and dietary interventions in overweight or obese pregnant women showed little effect of these on childhood obesity outcomes [9].

There is thus a significant swing to assess interventions *before conception* to shape intergenerational health. Preconception care is an explicit focus of the World Health Organization’s (WHO) 2017 report of the Commission on Ending Childhood Obesity and the subject of a 2018 *Lancet* Series [10]. A systematic review and meta-analysis of the association between pre-pregnancy body mass index and child obesity confirmed the significantly increased odds of child obesity with increased maternal BMI, to the order of 264 per cent [11], with those authors recommending preconception interventions as a logical course of action in the light of these findings.

Testing the preconception intervention hypothesis requires large-scale trials of complex public health interventions that commence before pregnancy and track individuals and their potential offspring for long periods to assess intergenerational health impacts. In partnership with WHO, HeLTI is the first consortium of randomised controlled trials of this kind in China, Canada, India, and South Africa. HeLTI aims to evaluate the efficacy of interventions initiated prior to conception and for those that become pregnant, continued during pregnancy, infancy, and early childhood to address offspring obesity and development. As the test case for starting interventions in the preconception period, HeLTI is thus of huge significance to DOHaD science. Building on long-standing efforts towards interdisciplinary collaboration in trial contexts, HeLTI is also an important test case for what this volume terms ‘biosocial collaboration’. Biosocial collaboration here refers both to methodologically innovative ways of working and conceptual collaborations between disciplines (see Béhague et al., 2008 [12]), which should work in tandem to produce new models of understanding health and disease.

Lifecourse approaches encounter significant challenges around the best research practices and techniques in studies that include both long-term observational and interventional components [13]. Public health research thus increasingly works to understand not only whether a particular intervention will improve health or not but also how that intervention works to do so [14]. To achieve this, trial design, especially for behavioural and other complex public health interventions, increasingly employs ‘complex’, ‘pragmatic’, or ‘realist’ frameworks. As aims have shifted to encompass not only ‘what’ works (or not) but also ‘how’ it works (or not), trial design and process evaluation have incorporated interdisciplinary collaboration between epidemiologists, implementation scientists, evaluation specialists, and qualitative health researchers [15]. There is an expanding literature on the integration of qualitative methods into randomised controlled trials, especially of complex public health interventions [5]. Historically there

have been epistemological limitations placed on the kinds of qualitative methods deemed applicable in the biomedical framework of trials, which has constrained the use of approaches from disciplines such as anthropology, sociology, or psychology [16]. However, the ‘turn to the complex’ in public health research acknowledges a broader set of social factors that influence health [14] and obliges pragmatic and adaptive trial designs that encompass more innovative and iterative qualitative methods.

### 21.3 Bukhali: The HeLTI–SA Trial

For HeLTI–South Africa, the *Bukhali* individual randomised controlled two-arm trial has recruited between 6000 and 7000 women aged 18–28 in Soweto for a complex public health intervention, which statistically should lead to a pregnancy and birth cohort of about 1530 mother–child pairs. All women aged 18–28 years are eligible except for those with a prior diagnosis of type 1 diabetes mellitus or epilepsy and those who are unable to provide informed consent. The primary trial outcome is to assess the effect of a four-phase intervention (preconception, pregnancy, infancy, and early childhood) on the index child’s adiposity at five years of age (fat mass index [fat mass/height]<sup>2</sup> derived from dual-energy X-ray absorptiometry). The trial also assesses a range of secondary child outcomes (anthropometric, metabolic, developmental, and behavioural); secondary maternal outcomes (anthropometric, nutritional, physical health, mental health, and behavioural); and phase-specific outcomes in the 4-phase trial [17]. The intervention is community healthcare worker-driven and comprises a programme of nutritional and health screening and support interventions, including micronutrient supplements, health information booklets, and monthly informational interventions in-person or by telephone that use healthy conversation skills, a motivational interviewing technique that focuses on empowering participants to explore opportunities for and obstacles to behaviour change [18]. These sessions cover themes, including diet, exercise, sleep, contraception, safe sex, and emotional well-being, as well as health checks and measurements at in-person visits. The control group receives ‘standard of care plus’, comprising access to standard community primary healthcare provisions, as well as additional services provided by the control team at the trial site, including free HIV and pregnancy tests, and general non-health-related advice, for example finances, insurance, and accessing child support. Women in the intervention arm who become pregnant receive additional interventions including an ultrasound scan and health promotion materials on diet and physical activity in pregnancy, child developmental milestones, and accessing state child support. In the postnatal period, interventions will focus on current messaging about breastfeeding, nutrition, care, and developmental stimulation outlined in the South African ‘Road to Health’ booklet received by each birthing parent at the child’s birth, and women will be encouraged to return to preconception healthy behaviours. For the full trial protocol, see Norris et al. 2022 [17].

### 21.4 A Pragmatic DOHaD Trial

HeLTI–SA exemplifies the ‘pragmatic’ trial model. There is an explicit framework of trial as a process, where ongoing learning and adaptation to new knowledge as it arises are expected and desirable, such that the trial becomes a dynamic platform that does not just test the primary hypothesis – that preconception interventions might improve childhood metabolic and developmental outcomes – but also undertakes process evaluation

analyses, as well as generating new hypotheses as situations arise, that can then also be tested in the course of the trial.

From the outset, the HeLTI team have needed to adapt the framework to a complex context of urban poverty. Pilot trial implementation of Bukhali led to significant changes to both the trial design and implementation approaches [19]. While the trial was initially conceptualised as a cluster randomised trial with 30 random geographical units in Soweto, the pilot demonstrated significant cluster contamination due to participants' movement between households and parts of Soweto as part of a strategy of resource-sharing between different households [19]. This accords with the 'domestic fluidity' that anthropologists have noted as common for southern African households [20, 21]. HeLTI-SA was consequently converted to an individual randomised model. Pilot qualitative work was also able to capture the key priorities and key challenges for women in Soweto. Women are focused on obtaining further education and securing employment, while navigating difficult socio-economic circumstances [19]. As a result of the pilot, other key changes to Bukhali design and implementation included modifications to the intervention delivery, from group to individual sessions and to mostly telephonic rather than in-person delivery (a requirement further amplified by the onset of the COVID-19 pandemic and lockdowns in South Africa); the inclusion of additional incentives that respond to some of the priorities women discussed (such as making provision for the printing of their CVs at the research unit); and the implementation of a system for the delivery of supplements to participants' homes.

The focused approach to adapt to the contextual complexities of the trial goes beyond the pilot. The pragmatic trial model means that the research team is highly responsive to new challenges or concerns as they arise [18]. The pilot findings that women preferred telephonic engagements meant a switch to delivering interventions telephonically. South Africa ranks third in Africa with regard to mobile phone penetration and therefore provides a robust platform for mHealth prospects [22]. The widespread availability of mobile phones has enhanced healthcare communication [23] as they are cost-effective and facilitate health professionals in clinical trials to stay in contact with participants and, where possible, deliver intervention components telephonically [23, 24]. Crucially, this adaptation preceded the COVID-19 pandemic and meant that the trial continued even during periods of lockdown in South Africa.

However, for the duration of the trial thus far, this has also meant a reliance on mobile coverage and continuity of mobile phone numbers for participants, raising concerns over participant accessibility in clinical trials that have been previously recognised within telemedicine and medical informatics [25]. Although a large proportion of individuals who are enrolled in the HeLTI trial own mobile phones, lower retention rates were observed among some participants who were hard to reach by mobile phone. The lack of accessibility and reachability of these participants was largely attributed to changes in their mobile phone numbers. Losing contact with some participants prompted further qualitative work to assess the reasons behind frequent changing of mobile numbers by trial participants and to identify other factors contributing to the challenges of contacting participants. Although a mixed-methods approach was employed to understand this outcome, the quantitative data produced contradictory results that did not confirm the qualitative findings as the majority of the participants had not changed their mobile phone numbers, contrary to what was observed in the qualitative data. Twenty in-depth interviews were conducted with the HeLTI cohort who

were hard to reach by mobile phone. Their narrative accounts revealed that the participants predominantly changed their numbers due to mobile phone technical issues, such as poor battery life, faulty charging systems and mobile phones, and application crashes. Other challenges with contacting participants included network coverage issues, not personally owning a mobile phone, and phone (and thus sim card) theft. Participants also often left their phones at home to mitigate against theft. The significance of the daily risk of crime becomes a key data point for understanding participants' 'unreachability' and why proposed interventions may or may not work in this context.

During the implementation of HeLTI–SA, questions also arose over terminations of pregnancy among HeLTI participants, observed to occur in about 5.2 per cent of pregnancies enrolled prior to 20 weeks gestational age. This has led to a qualitative inquiry into participants' reasons for terminating their pregnancy. Using 10 in-depth interviews, the team used a socio-ecological model [26, 27] to explore how contextual and social complexities at micro- and macro-levels, including the COVID-19 pandemic, impacted participants' decision to terminate their pregnancy [28, 29]. The main reasons for termination included intra-personal factors, such as financial instability and dependency; not being emotionally prepared for pregnancy; and the impact of pregnancy on future employment and education opportunities. Reported interpersonal reasons included a lack of partner support and stability and the threat of an adverse impact on family dynamics, including abusive behaviour. In addition, participants' experiences reflected the impact of family and community beliefs around termination, accessibility, and attitudes of termination services, and the participants' sense of agency in choosing to terminate. Interestingly, the COVID-19 pandemic seemed to play a secondary and indirect role in participants' choice to terminate their pregnancy, mainly as a potential contributor to socio-economic insecurity. Exploring these factors across socio-ecological domains provides an understanding of unintended pregnancies in this setting and can help align termination services more effectively with women's needs. By extension, it also sheds light on the social and contextual elements impacting (1) the practical implementation of HeLTI in terms of pregnancy loss and (the team's understanding of) the number of participants retained in the trial through pregnancy and (2) participant experiences of (unintended) pregnancy, which can contribute to an informed interpretation of participant engagement with the intervention in its various phases. In the preconception phase, for example, a deeper understanding of participants' circumstances and priorities can help explain the degree to which intervention components resonate with young women without (current) pregnancy intent. In the pregnancy phase, insight into the experiences and challenges faced in the context of unintended pregnancy can, for instance, highlight the need for additional support among participants.

Utilising a dynamic approach means that emerging obstacles also present opportunities to address novel research questions. Attending to new questions through qualitative work with trial participants not only allows for practical adjustments to trial protocols to ensure participant retention but also illuminates social factors that might later account for or help trialists to make sense of trial outcomes. Equal investment in the gathering of biological samples and qualitative data means that integrated biosocial analyses are possible. In a nutshell then, intervention trials that adopt biosocial models are not only more likely to ensure that the trial reaches completion, but they are also more likely to offer meaningful conclusions that contextualise findings in ways that matter for learning and policy recommendation.

## 21.5 Discussion

The novelty of DOHaD intervention studies raises important theoretical and methodological questions that cannot be parsed without a biosocial lens. This is especially crucial for DOHaD research that employs complex public health interventions, given that these present their own unique methodological and epistemological issues [14, 30, 31]. The manner in which social context is understood and accounted for in trials has the potential to amplify or diminish attention to the social drivers of health inequities. Collaborations that encompass anthropological and science studies perspectives are more likely to account for the structural and processual factors that might offer ‘real-world’ explanations of trial outcomes [16]. Pragmatic and adaptive designs in DOHaD intervention trials allow for both the robust methodology and contextual relevance that are required when testing complex public health interventions [14]. Ensuring that this balance is struck is essential given that it will have a direct bearing on how recommendations are framed at the end of the trial. In sum then, a biosocial collaboration that affords ‘the social’ equal weight as an aspect of the trial to be studied, incorporated, and analysed means that trial outcomes are better explained and that recommendations are more suitable to local context [32].

As Béhague and colleagues described some time ago, focusing on methodological innovation without an equally rigorous approach to conceptual collaboration risks reinventing old dichotomies (deductive or inductive; specific or generalisable) that do not hold in reality, where ill-designed qualitative methods can be equally reductionist [12]. A commitment to the development of shared conceptual models that are theoretically innovative and critically informed alongside appropriate methods is thus a better hallmark of meaningful biosocial collaboration. Examples include the development of the syndemics framework (see Chapter 15 in this volume); bioethnography (Chapter 15 in this volume); and foundational work that has developed novel methods to integrate ethnography and statistics [33].

On ‘doing’ biosocial collaboration in practice, it is useful to borrow Anthony Stavrianakis’s concept of collaboration: ‘a worthwhile collaboration is one in which two kinds of participants, in their engagement, are able to name a problem or do a practice that in their position as participants (prior to engagement) they would not have been able to do . . . Collaborative participation presupposes an endeavour of transformation’ [34]. This is very rarely straightforward, given the necessary work required to delineate the boundaries of collaboration and to navigate pre-existing organisational and disciplinary hierarchies and the range of ethical and social demands that collaboration as a practice may introduce ([34], see also Niewöhner in this volume). However, it is critical for both the constitution of evidence in DOHaD research and the framing and communication of the DOHaD message. As outlined in the introduction, DOHaD requires an expansion of its evidence base, and in a fashion that is likely to have a policy impact. As DOHaD scientists themselves begin to take on the language of seeking evidence for ‘politically palatable’ solutions, it is crucial that social scientists seize the opportunity at hand – the openness of DOHaD to transdisciplinary evidence synthesis as a more productive way to find scalable solutions to the question of fostering intergenerational health. This transdisciplinary approach in HeLTI will in itself serve as a case study and will be documented so we may further learn how to better integrate these ideas in future DOHaD-inspired RCT research.

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