science Research-based evidence

The Tswaka Study

A journey into an innovative public–private–private research partnership

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Key messages

- This is a report on the learnings gathered by a partnership established to perform a complex study: the Tswaka Nutrition Intervention study.
- The study was a community-based randomized controlled trial carried out in North West province, South Africa, on the efficacy of two small-quantity lipid-based complementary food supplements provided to children aged 6–12 months.
- The Tswaka study was completed in 2015 and its results have been recently published.[1]

> This report summarizes the key lessons learned and discusses what it takes to make such partnerships work. The key lessons appear on pp. 28–29.

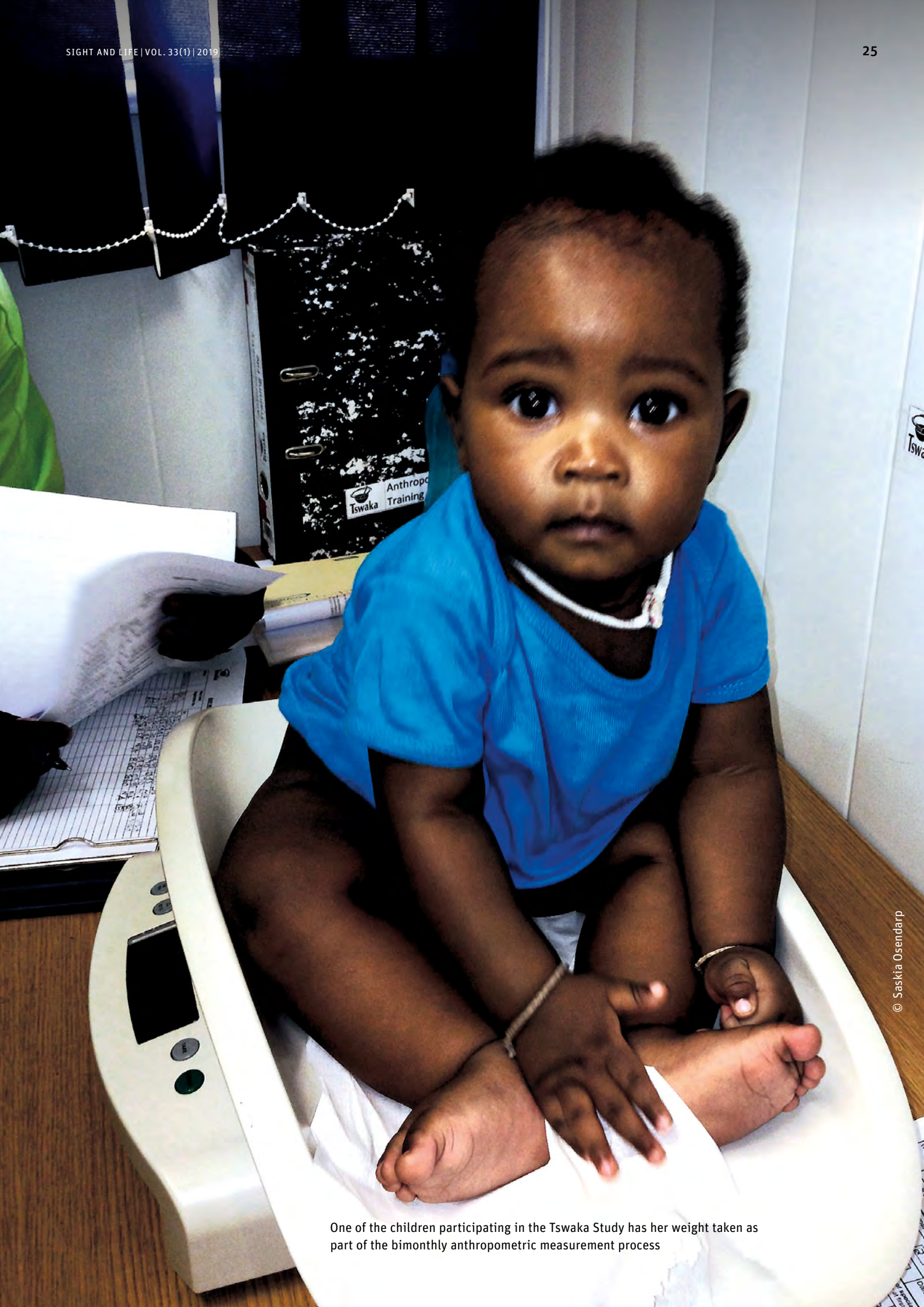
This is a report on the learnings gathered by a unique partnership, consisting of two private-sector partners, one NGO and an academic partner, established to perform a complex study: the Tswaka Nutrition Intervention study.

The study was a community-based randomized controlled trial carried out in North West province, South Africa, on the efficacy of two small-quantity lipid-based complementary food supplements provided to children aged 6–12 months. The Tswaka study – which means 'mixing' in the local Setswana language, referring to the fact that the supplement should be mixed into home-cooked food – was completed in 2015, and its results have recently been published.[1]

The journey embarked on in 2010 presented many challenges before it was successfully completed following eight years of effort. This report summarizes the key lessons learned and discusses what it takes to make such partnerships work. We hope that our experiences and insights will be of value to others entering into partnerships in the nutrition space. In the end, our joint success came down to the three Ps: Personal relationships and trust, Perseverance and determination, and the Passion to make this project a success.

Inception: aligning motivations to create a single concept

In 2010, an NGO (GAIN) and a private-sector partner (Unilever) joined forces as a Funding Consortium to facilitate a research project investigating a novel fortified complementary food supplement. For the detailed design and execution of the intervention study, it was decided that an Academic Research Partner would be selected via a call for proposals.



One of the children participating in the Tswaka Study has her weight taken as part of the bimonthly anthropometric measurement process

The motivation for the study was different for each of the partners in the Funding Consortium. While GAIN was interested in working with private-sector partners on product formulation and demonstration of the feasibility of a market-based approach, Unilever was interested in testing the efficacy of such a product before considering an innovation project on the feasibility of a market-based approach.

Unilever wanted to collaborate with GAIN on this research because GAIN was considered a trusted intermediary between Unilever and the Academic Research Partner. Initial discussions between Unilever and GAIN, however, identified a potential conflict of interest if GAIN were to work on a study assessing the efficacy of a product from just one private-sector partner.

To address this issue, a second private partner, DSM, was invited to join the partnership. DSM wished to demonstrate efficacy for a similar product formulation that contained certain extra ingredients with additional benefits for growth and development. Despite their different motivations, the three partners recognized the benefits of sharing their complementary expertise as well as sharing the research costs within the framework of an NGO/private-partner Funding Consortium.

To align the different motivations into one achievable goal acceptable to all three partners took some time. There were discussions about the requisite levels of transparency and openness and about the dynamics driving the choices and decisions required for a successful partnership. To avoid potential complications and to keep the study to a manageable size and acceptable cost levels, it was designed in such a way that the sample size would not allow direct comparison between the two products.

> "The more organizations you have to involve, the more important it is to have regular, open communication"[2]

While these initial discussions were still ongoing, and prior to DSM joining the partnership, GAIN and Unilever had already developed a call for proposals based on an initial concept note, and an independent expert committee was formed to select the Academic Research Partner to perform the study.

North-West University, South Africa, won the bid in partnership with the South African Medical Research Council ('the research team') and started to work on a full proposal, which had to be adapted into a three-arm design when the second private partner, DSM, joined the Funding Consortium.

Simultaneously, contract negotiations had started. The idea was that GAIN would act as the official study sponsor, and also as an intermediary between the private-sector sponsors and the research team. Therefore, two contracts had to be aligned and agreed upon: one bilateral grant agreement between GAIN and the research team, and one trilateral agreement between GAIN and the two private-sector partners (the Funding Consortium), who each contributed one-third of the research costs.

Issues concerning intellectual property (IP) rights for data and for products, as well as publication and dissemination clearance procedures, had to be discussed at senior management level in all the partner organizations. The entire contract negotiations took more than a year and were eventually concluded in 2011.

Preparation phase: managing risks and building trust

The preparation phase turned out to be the most delicate phase of the entire process. There were no products ready yet, and negotiations started between the two private-sector partners with the aim of creating a single joint development process for the study products. A joint development process was thought to be beneficial because this would allow for blinding of the two intervention arms by having two products comparable in taste and appearance, albeit with different compositions. As product development and product ingredient formulations are among a company's most valued IP, it took some time for the two private partners to agree on a joint development agreement (JDA). When an issue occurred during the actual production of one of the study products, however, the private-sector partners decided to terminate the JDA and to continue further scale-up and production independently of one another.

In March 2013, the acceptability study among mothers and children with the first product samples started in South Africa. The acceptability study yielded positive results but also revealed some mild side effects, assessed as being unrelated to the intervention products as such.[3] Meanwhile, however, within the private-sector partners, changes in leadership and company strategies had taken place, leading to a revised assessment of the potential reputational risk for all partners involved in this community-based trial among very young and vulnerable children in a disadvantaged population.

To better manage and control these risks, it was initially decided to hire an independent monitor to remotely review the quality of the study execution. In addition, a Safety Monitoring Board (SMB) was established to monitor adverse effects and identify any potential causal relationships to study participation or test product. In addition, an independent study physician was hired to train and support the research team as and when needed. The study monitoring was further upscaled by hiring an independent Contract Research Organization (CRO) to ensure the quality and safety of the study by monitoring the implementation of the study on site and for data management on site.

There was a clear need to balance the risk exposure of all parties involved. Whereas the private partners wished to implement processes such as monitoring, a centralized database and extensive medical supervision and reporting, the research team wished to make sure that its credibility as an independent academic team would not be jeopardized.

Having an intermediate party in the form of GAIN turned out to be critical, ensuring effective communication between the research team and the private-sector partners and coordinating negotiations about the changing needs of both the research team and the Funding Consortium.

In addition, a site visit by the Funding Consortium helped to provide a more realistic view of the circumstances at the study site and to improve understanding of the practical dilemmas the research team faced in day-to-day management of a community-driven study of this size in this setting. It also further strengthened trust between the responsible individuals within each of the partner organizations. Due to these personal relationships and a shared commitment to succeed, it was possible to commence data collection in the fall of 2013.

Data collection: trust and transparency

While scaling-up of the production of the study product and negotiations on the involvement of the CRO were still ongoing, research staff had already been hired, and mobilization in the community for recruitment had already taken place. By the time the research team was in a position to start enrolling infants into the study, the children of mothers initially mobilized had aged over the 6 months (+ 2 weeks) enrollment criterion, with the result that they had to be excluded from participation. This caused distrust within the community, and the research team had to step up its efforts to restore confidence in the study. At the same time, the CRO, which was familiar with Phase III pharma studies, had to get used to the complexity, uncertainty and changing conditions in which community-based nutrition interventions are carried out.

Anyone experienced in conducting trials with vulnerable populations in disadvantaged communities knows that unexpected challenges are the rule rather than the exception. Continuous communication with the community members is necessary to engage all individuals involved in the partnership. The Tswaka research team had to deal with rumors and distrust within the community, while at the same time trying to explain all this to the representatives of the funding partners, some of whom had limited experience of working in these difficult settings and with this age group. GAIN played a central role in channeling initial bilateral discussions toward more central discussions throughout the project, which helped to build trust at every level.

The study site visit by the sponsors was crucial in improving understanding between the partners. Investments were made in keeping the momentum from the site visit with the community and the field workers. To keep the onsite research team motivated, extra training opportunities were offered by the funding partners.

> "The fact that there was a signed obligation between the partners meant we had to move forward and could not withdraw"

The renewed confidence within the partnership allowed for more open discussions on the issues of sponsor involvement and authorship. The dilemma was whether the growing involvement of the study sponsors in the various stages of study implementation needed to be made transparent in the publication of the study results at the level of coauthorship. For the research team, sponsor authorship was considered to reduce the independence of the individual scientists involved, and there was a realistic fear that it would also affect the credibility of the study results.[4,5]

There did not seem to be a perfect solution. When industry sponsors are not included as coauthors, this can be construed as an attempt to disguise their involvement. When they are included as authors, however, this may raise questions as to their influence on the interpretation of findings. In recent years, there has been increased recognition that stricter rules may help safeguard the independence and credibility of public–private research partnerships.[5] In the current partnership, this issue was addressed by all partners agreeing on a joint author and sponsor contribution statement, according to the international criteria for authorship. It was explicitly agreed that, while results would be discussed with all partners, the Academic Principal Investigator had full responsibility to decide on the final interpretation and dissemination of the study's results.

Data collection for the Tswaka study was completed in July 2015. Once the final statistical plan had been agreed and all descriptive statistics had been completed, a blind-review meeting was organized at the study site in November 2015. In this meeting, with all funding partners and the CRO present, data was presented and agreed prior to locking the database and de-blinding the study.

Post-data collection phase

Data management of a large study such as the Tswaka study is complex and also prone to delays for various reasons. In this case, one reason was the decision to outsource data management to a CRO with rigorous quality standards.

The rigorous and extensive data quality and data transfer steps for the collection of data on adverse events and morbidity required by the CRO's data management system slowed the research team's speed of response. To overcome this, the research team had ended up keeping its own records. In consequence, two independent databases on morbidity were kept. Given the size of the study, within a vulnerable age group, many mild adverse events occurred, making discrepancies in morbidity data almost inevitable. Having two datasets on morbidity provided the opportunity to address and counter-check some of these discrepancies. However, this caused additional delays, as data analysis could only start after the two databases had been checked for inconsistencies and combined into a single, locked database. These delays put pressure on the availability of allocated statistical support staff.

In May 2016, almost a year after completion of data collection, the databases were locked, and study codes were unblinded. The de-blinded dataset was only accessible to the research team and not to the funding partners throughout data analyses and the reporting process, to further ensure the integrity of scientific interpretation by the Academic Principal Investigator. The preliminary results of the Tswaka study were presented at the Micronutrient Forum global conference in Cancún, Mexico, in October 2016. The discussions about the interpretation of the study findings – probably the most sensitive part of any industry-sponsored research – took place following the predefined disclosure statements. The Academic Principal Investigator's final interpretation and wording of the conclusion were fully endorsed.

> "Things change often within a business environment – what is a challenge and an interest today may be different tomorrow. Priorities and people change."

All discussions, mostly academic in nature, were documented for full transparency, while the final manuscript was shared with the industry partners for clearance without further editing rights.

With the Tswaka study project and funding coming to an official end, the remainder of the work to be done (final statistical analyses, final report writing and manuscript preparation) became dependent on the personal time and commitment of the Funding Consortium team involved. This was not a problem, as the team was determined to bring this project to a successful completion. And so it happened.

Issues to be managed

Setting up a new type of public–private nutrition research partnership can be challenging, as many issues need to be managed along the way.

Real and perceived risks in areas such as safety, conflict of interests, project management, reputation and scientific independence need to be identified from the start of a partnership and managed carefully – something that requires commitment and flexibility from all partners. On the other hand, such partnerships offer unique opportunities for the different partners that cannot be realized individually. The private-sector partners, for example, had the opportunity to carry out studies on a shared costs basis and to enjoy access to scientific expertise, study teams, study environments and key experts with in-depth knowledge of the local context. The research team benefited from access to quality study product development, as well as tolling capabilities, access to quality monitoring services, and scientific nutrient knowledge, besides receiving appropriate funding. For both parties, learning from each other's expertise and developing awareness of each other's strengths and weaknesses increased mutual understanding and will be a benefit in the case of future collaborations. Last but not least, private–public partnerships can contribute to the education of a new generation of scientists with experience in dealing with these types of partnerships. In this particular project, for instance, three PhD students were involved.

Conclusions

The influence of industry funding on the perceived credibility of nutrition research is currently under debate,[4] and some guiding principles for how to manage industry funding of food and nutrition research have been proposed.[5] The Tswaka study research partnership showed that these public–private research partnerships can be successful if managed carefully and transparently. Personal commitment, trust, perseverance, passion and patience were among the key success factors. Some of the main learnings from this partnership, which may inform future research partnerships, are summarized below.

Lessons learned

1. Establishing alignment between multiple partners involves managing tensions between objectives and agendas. It takes time, it should be transparent and it should clearly identify how the respective partners' priorities will be managed.
2. Having a clearly defined, achievable and shared public health goal is important for a successful public–private partnership.[5]

3. When a consortium is being established, it is essential to have all required knowledge and expertise represented in the team and all roles and responsibilities clearly defined before commencing the study.

4. Full transparency is required from the start regarding the status of negotiations between funding partners, as well as regarding product development, to allow realistic deadline setting by the research team.

5. For research projects that involve a high reputational risk for the sponsor and/or the research team, having an independent third partner (a 'coordinator') can be helpful. The coordinator can align the academic and private sector, and can communicate regularly and directly with all consortium partners, in an effort to make best use of industry involvement (e.g., optimizing study and product quality) and to minimize direct industry involvement in the execution of the study and direct interactions with researchers.

6. Accepting industry funding involves dealing with different priorities and comes at a cost for researchers: perceived and real conflict of interests, and perceived and real reputational risks, will need to be managed; lines of communication will need to be kept open; and all roles and responsibilities will need to be clarified and agreed upon up front in well-documented author and sponsorship involvement statements, preferably before contracts are signed. Throughout the project, excellent communication is required between all partners, facilitated by the coordinator.

7. Within organizations, strategies and leadership change all the time, making it difficult to rely on continuous leadership and project ownership for a multiple-year research project. Champions within the various organizations are essential to push the project forward and bridge the different internal needs with academic needs.

8. Unexpected issues will arise and cause delays and additional expenses, as in every complex project – something all partners need to deal with. Having an independent coordinator is again helpful for aligning partners and managing expectations.

9. Building personal relationships early in the project (e.g., by visits to the study sites and face-to-face meetings between partners) is important for creating trust, mutual understanding and commitment.

Six voices say what they are most proud of having achieved through the Tswaka Study Research Partnership

VOICE 1

"We developed a very difficult product specially designed for older infants, and we achieved it with so many partners."

VOICE 2

"We completed an extraordinarily complex process to implement what we thought was a straightforward idea. We have done great research and established the groundwork for a more systematic approach for organizations to work together."

VOICE 3

"We have learned a great deal for our organizations regarding partnerships, and also for ourselves personally. We can do things better in future, but we achieved our goal in the end."

VOICE 4

"I estimate that I spent more than 9 weeks in conversations to keep this study going – but we have done it, and many from the community and research team have had opportunities as a result of it."

VOICE 5

"We have shown that these products are beneficial – that is important for children."

VOICE 6

"We managed to complete a unique PPP, and we overcame enormous hurdles through everyone's commitment and without jeopardizing our relationships."

Disclosure statement

Authors' roles

Saskia JM Osendarp: Consultant, Young Child Nutrition and Partnership at GAIN

Cornelius M Smuts: Academic Principal Investigator of the study

Klaus Kraemer: Managing Director of *Sight and Life* Foundation, a Swiss foundation funded partially by DSM

Maaike J Bruins: Study Coordinator and Senior Scientist Nutrition at DSM

Leon GJ Frenken: Project Leader at Unilever

Dominic Schofield: President of GAIN

Jane Badham: Managing Director at JB Consultancy, consultant in end-of-project evaluation

Cornelius M Smuts received traveling support from Unilever, DSM and *Sight and Life*.

Saskia JM Osendarp is a consultant to GAIN and was working on this partnership for Unilever R&D from 2010 to 2011 before starting as a consultant with GAIN.

GAIN was the sponsor of the study and is a non-profit organization working in micronutrient nutrition.

Maaike J Bruins is employed by DSM Nutritional Products, a supplier of vitamins, carotenoids, and omega-3 and -6 nutritional lipids.

Leon GJ Frenken is employed by Unilever R&D, Vlaardingen, the Netherlands.

DSM and **Unilever** were co-funders of the study and provided the test products free of charge. None of the other researchers has any conflict of interest.

This research was supported by GAIN, DSM and Unilever. Interpretation of data was jointly discussed among the Principal Investigator of the study (Cornelius M Smuts), sponsor (Saskia JM Osendarp) and co-funders (Maaike J Bruins and Leon GJ Frenken); however, final decisions on interpretation and dissemination of results rested with the Academic Principal Investigator of the study (Cornelius M Smuts).

The responsibilities of the sponsor and co-funders in this project are as follows:

1) During preparation

GAIN and Unilever developed the initial study idea and followed this with a Request for Proposals.

GAIN, DSM and Unilever reviewed, commented and approved the study proposal.

DSM and Unilever developed, produced, shipped and ensured the quality of the study products.

2) During data collection

The Academic Principal Investigator (API) was responsible for data collection. GAIN, DSM and Unilever monitored the quality of data collection throughout the study via an independent study-monitoring agency and via regular phone and face-to-face meetings throughout the data collection process.

3) During data analysis and interpretation of results

The API was responsible for data analysis.

The final interpretation of data was jointly discussed among API, sponsor and co-funders. However, final decisions on the interpretation and dissemination of results rested with the API.

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