Gender Integration Impact in Clinical Trials: The KEN-SHE Trial

This brief was prepared for the Gender Integration Team with the purpose of: (1) Reporting on performance and impact of gender integration in PST investments for GE leadership and (2) Ongoing learning for the GI Team and GenderTech on effective GI approaches across PST sectors. The brief summarizes findings from the KEN-SHE trial publication[1] and a focus group discussion with the Principal Investigator and study team.

Project Background and Approach to Gender Integration

The KEN-SHE trial aimed to address a macro-level barrier to access to the human papillomavirus (HPV) vaccine through addressing gaps in the global supply, as well as reducing barriers to access posed by multi-dose administration. It was a clinical trial comparing single-dose administration of two types of HPV vaccines (bivalent and nonavalent) with meningococcal vaccination among 15-to-20-year-old Kenyan adolescent girls and young women. Eligibility for potential participants included screening by healthcare providers of detailed medical history, HPV screening, and cervical cancer screening. Providers saw participants 3 months and 6 months after enrollment, and then every 6 months until 18 months after enrollment. Clinical questionnaires were conducted at each of these visits, and cervical or vaginal swabs were collected.

The investment was gender intentional, with a thoughtful approach to the design and implementation of the trial to address gender gaps and barriers and promote agency of participants where possible, while also supporting opportunities for advancing women in science—and particularly women of color among project staff. Throughout the design and implementation, the study was conducted in ways that adhered to clinical trial standards and good practices, while also identifying and adopting less-conventional approaches based in scientific rigor to center the strategic needs of adolescent girls and young women while recognizing them as agents throughout the process.

- **The trial was designed to reach a population that was excluded from HPV vaccination efforts in Kenya** (adolescents age 15 and older). HPV vaccination coverage in Kenya is low, and due to supply constraints, the vaccine has been provided only to 10-year-old girls, despite plans to provide the vaccine to girls ages 9-14 as part of the national immunization plan. There were no plans for catch-up vaccination for older adolescents. Therefore, the target group would not have access to the vaccine outside of the context of the study.
- **Measures were taken to address barriers to participation that catered to the needs of the adolescent girl participants.** For example, participants were provided with childcare during visits, and transportation costs were covered. Additionally, communication was designed so that participants could state their needs and, where possible, staff could be responsive to those needs. For example, there were cases where some participants did not feel comfortable taking public transportation (e.g., due to COVID-19 or safety concerns). In these cases, program staff arranged private transportation to take them to and from appointments. **Retention of participants over the 18-month trial period was 98 percent, which is extraordinarily high and most likely partly due to the gender intentional approach to implementation**.
- **The trial offered access to resources beyond the HPV vaccine**, including sexual and reproductive health services (contraception, sexually transmitted infection diagnosis and treatment, and HIV preexposure prophylaxis) upon enrollment at all subsequent visits. Participants were also offered job training.
- **The study was designed to provide benefits to all participants, regardless of whether they were in the treatment or control group.** In a departure from how clinical trials are typically designed, the study team chose to use the meningococcal vaccine as control, as opposed to a saline placebo, which would provide no clinical benefits to the control group participants. Meningococcal vaccines are used during outbreaks in Kenya, so they are not readily available on a regular basis. While it is uncommon to use another vaccination as a control in clinical trials, the researchers chose the meningococcal vaccine because it provides clinical benefits and there is no evidence that it affects HPV outcomes. At the conclusion of the trial (36 months after enrollment), participants in the control groups will receive HPV vaccinations and those in the treatment groups will receive meningococcal vaccines.

- **Although advancing agency was not explicitly included as a primary outcome for the investment, the study team actively looked for ways to recognize and promote agency of the adolescent girl participants, as well as among staff at all levels–particularly women of color.** For example:
  - » **Participants were provided with the option to self-administer vaginal swabs rather than have cervical swabs collected by providers.** Although not having identical collection methods could be considered a weakness in the study, given the robust evidence of the high correlation between self-collected vaginal swabs and provider-collected cervical swabs, the study team determined that the benefit of providing participants with the choice outweighed the small risk. Sensitivity analysis confirmed that this approach did not compromise the study results, as there was no difference in the results when results from self-collected swabs were excluded from analysis.
  - » **The study team reworked the approach to informed consent to a shorter, more participatory process that promoted true understanding by participants.** They started with a more traditional approach to informed consent, which provides lots of information in formats that are not always easily understood and usually takes quite a bit of time. However, they quickly realized that these traditional approaches are designed primarily to protect researchers and not to promote true understanding. Therefore, they changed the format to a shorter, more interactive approach, with parts of it completed in groups to allow community reflection and interaction among participants, and opportunities throughout to reflect and ask questions.
  - » **The study team's leadership made it a priority to recruit and retain good talent, while providing opportunities for professional growth and development for the next generation of workers joining the public health sector, particularly for women of color.** They intentionally created a culture that championed and empowered all roles and created joint ownership over the work. They ensured staff were comfortable bringing ideas, feedback and questions to leadership, and provided opportunities for career growth at different levels within the project.
- **A strong community advisory board was convened to identify and address risks and unintended consequences.** The study team was in frequent communication with the advisory board throughout the trial period.

Highlights of Impact Achieved

- **The clinical trial demonstrated vaccine efficacy of 98 percent for single-dose administration of vaccines against two types of high-risk HPV** (types 16/18, which cause 70 percent of cancers) for two HPV vaccines–bivalent, which targets types 16/18, and nonavalent, which also targets low-risk HPV types that cause genital warts and five additional high-risk HPV types.[2] Nonavalent vaccine efficacy for these types of HPV was 89 percent for single-dose administration.
- **The KEN-SHE trial made significant contributions to the growing body of evidence on the efficacy of single-dose administration of HPV vaccination, which has great potential to increase global supply and access to HPV vaccines in lower- and middle-income countries (LMICs).** Single-dose administration of the vaccine could reduce the cost by up to half, simplify logistics of delivery, and reduce barriers to access on the demand side.
- **In response to this growing body of evidence, the WHO has changed its guidelines to recommend one or two doses for girls and women ages 9-20, and 24 countries have now switched to single-dose administration.** As adoption of single-dose administration grows, there is huge potential to reduce incidences of cervical cancer and avert deaths from the disease in LMICs, including in sub-Saharan Africa, where cervical cancer is the second-most-common cancer among women and the leading cause of cancer deaths.

References and notes

1. Barnabas, R.V., et al. (2022). Efficacy of Single-Dose Human Papillomavirus Vaccination among Young African Women. The New England Journal of Medicine, 1(5), https://doi.org/10.1056/EVIDoa2100056
2. HPV 16/18/31/33/45/52/58/6/11.

Acknowledgements

This brief was commissioned by the Bill & Melinda Gates Foundation's Gender Integration Team and researched and written by a team from the Global Center for Gender Equality (GCfGE), with valuable inputs and review from foundation staff and partner staff. The GCfGE Team included Amy Belle Pennington and Shelby Bourgault, technical review by Angela Hartley, Abigail Donner and Lucero Quiroga, and project management support by Whitney Walton. The brief benefited from interviews and review by members of the project team from Massachusetts General Hospital and the International Clinical Research Center Ruanne Barnabas and Hannah Leignang, and review by Ruane Barnabas and Hannah Leignang and review from foundation staff Peter Dull, Carolyn Wendell, Graham Snead and Keiko Valente. The brief was copyedited by Kathy Schienle and designed by RRD Design.