One way that researchers have devised to get around this Heisenbergian challenge is to design studies that continue past the duration of most efficacy trials (ie, beyond 4–6 years) (3). Women remain randomly assigned to condition, but they no longer receive regular testing as part of the trial. Instead, the researchers follow the women over the next decades by linking their identities to national cancer registries. The ethical justification is that routine screening and medical treatment outside the trial are the standard of care. In contrast, HPV vaccine provision to older women is not the standard of care, and the majority of HPV infections will have already occurred during the ages in which women were enrolled in the trial.

The other alternative to get around this Heisenbergian challenge is to evaluate HPV vaccine impact at the population level by use of one of the many alternatives that we have previously reviewed elsewhere (4). These evaluations have to rely on prospective cohort studies and other nonexperimental study designs that yield weaker evidence than randomized controlled trials. One such study (5) recently reported decreases in the incidence of genital warts after implementation of a national HPV vaccination program in Australia. It is highly likely that additional studies, many of which are under way, will provide similar correlational evidence for the population-level impact of HPV vaccine on cervical cancer. While we wait for further evidence to accumulate, it is important to remember that most randomized controlled trials cannot and will not tell us whether HPV vaccines prevent cervical cancer.

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References