5. Research gaps and further considerations

Selection of one strategy over another (PICOs 1 and 2)[8]

Regarding the screening tests, it would be useful to have data on using different genotypes of HPV in both the general population of women and women living with HIV to see if specificity could be improved without losing too much sensitivity. Additionally, the GDG noted that more data are needed about the specificity and sensitivity of tests among women living with HIV, including those taking ART.

Another special population needing research is transgender men, non-binary and intersex individuals who have a cervix, to determine the prevalence of cervical pre-cancer and the appropriate screening frequency and approach. Special implementation considerations and successful interventions for overcoming barriers to screening are also needed for these groups of people. Whether there is an upper age cut-off for self-sampling for screening was another area noted for more research.

Different duration of follow-up with the same or a different screening test (PICO 3–7)

The GDG would like to expand studies that evaluate the best follow-up interval after treatment. The group noted that a comparison of two negative screens (at either 12 or 24 months follow-up) versus one negative screen (at 12 months) before returning to regular screening would be important, as the evidence is currently based on modelled data. This would be potentially more important in women living with HIV due to the high recurrence rate. The GDG would like better longitudinal data on the recurrence of HPV after treatment. Given the debate about progression in women living with HIV compared with that in women in the general population, and about progression by age, more research is needed in these groups to quantify the differences in progression, over 3, 6 and 12 months, of CIN2/3 to invasive cancer.

Age at first screening, and minimum number of lifetime screenings (PICO 8i and 8ii)

We have suggested to start screening at the age of 25 years for women living with HIV. The GDG would like data that could identify whether there are subgroups of women who could be screened later (e.g. those on ART with well controlled disease) or earlier (e.g. those with perinatally acquired HIV). The GDG would also like better data on histologically confirmed cervical pre-cancer and cancer occurring before 25 years of age in women living with HIV, as the evidence from empirical studies and programmes in this age group is sparse.

[8] All the PICO questions are listed in *Table 2.1, in Chapter 2*.

Timing of treatment after positive screening or diagnosis (PICO 9 and 10)

The GDG noted that in women living with HIV, more research is needed about the efficacy of CKC and LLETZ in the treatment of AIS. Evidence is needed for the costs and cost-effectiveness of CKC versus LLETZ for AIS in both the general population of women and in women living with HIV.

For the future implementation recommendations (Phase 3; see *section 1.4*), the GDG also discussed some research gaps to be addressed. One would be the integration of screening to prevent cervical cancer into HIV treatment programmes: will the screening be overlooked, or will this integrated approach lead to increased uptake of screening? The GDG mentioned that more research would be important into why women who screen positive are subsequently lost to follow up and do not get treatment. For initiating or transitioning to HPV DNA screening, it would be beneficial to have research on the training and retraining costs (e.g. transitioning from VIA to HPV DNA screening).