Technical appendix

1. Excess HIV infections attributable to injectable hormonal contraception use (IHC), X

We assume that the current estimated HIV incidence, $\overline{I_j}$, among women in country j is a weighted mean of HIV incidence among IHC users, θI_j, and the underlying HIV incidence among non-IHC users, I_j, where the incidence rate ratio (IRR) associated with IHC use is denoted by θ and the proportion of adult women who use IHC is denoted by h_j:

$$\overline{I_j} = \theta h_j I_j + (1 - h_j) I_j \qquad (1)$$

Rearranging (1) gives the underlying HIV incidence among non-IHC users:

$$I_j = \frac{\overline{I_j}}{\theta h_j + (1 - h_j)} \qquad (2)$$

Subtracting (2) from $\overline{I_j}$ gives the excess HIV incidence due to IHC use; this is multiplied by the number of uninfected adult women in the country, $(1 - p_j)N_j$, to give an estimate of the number of HIV infections per year currently attributable to IHC use, X_j:

$$X_j = (1 - p_j) N_j \overline{I_j} \left[1 - \frac{1}{\theta h_j + (1 - h_j)}\right] \qquad (3)$$

Here,

p_j= HIV prevalence in country j [1-5];

N_j = adult (age 15-49) female population of country j [6].

$\overline{I_j}$ is estimated by assuming equilibrium prevalence and a mean survival time with HIV infection of ten years $\left(\overline{I_j} = \frac{p_j}{10}\right)$.

2. HIV-related deaths attributable to IHC use per year

The excess HIV infections attributable to IHC X_j are converted into future HIV-related deaths by discounting these women's estimated survival time based on current ART coverage for the relevant country, T_j. With discount rate r and estimated survival time s_t for women on ART or s_u for untreated women, the excess number of HIV-related deaths attributable to a possible IHC-HIV interaction, D_j, is given by:

$$D_j = X_j\left[T_j e^{-rs_t} + (1 - T_j) e^{-rs_u}\right] \qquad (4)$$

An excess infection is only counted as an HIV-related death if the expected survival time, including the effects of ART, is shorter than that estimated using the mean age of infection $\bar{a}$ and the country-specific life expectancy L_j [7]:

$$s_t = \begin{cases} 20 & L_j - \bar{a} \geq 20 \\ \infty & otherwise \end{cases}$$

(5)

$$s_u = \begin{cases} 10 & L_j - \bar{a} \geq 10 \\ \infty & otherwise \end{cases}$$

We use a discount rate r of five per cent per year for survival post-infection and assume a mean age of infection $\bar{a}$ of 25 years for all countries. Women with HIV are assumed to have a survival time of 10 years if untreated [8] or 20 years if treated [9, 10].

3. Excess live births on cessation of IHC

The total number of live births per year for country j, B_j, can be calculated as

$$B_j = b_j N_j \quad (6)$$

where b_j is the per-woman per-year live birth rate in country j and N_j is the adult female population as defined above.

The birth rate b_j is dependent on the prevalence and method mix of contraceptive types used by women in the country in question and their respective failure rates. Initially, we assume that women in the population use a mixture of IHC, h_j, non-IHC contraceptives, k_j, and no contraception, x_j (Table T1). Then, for proportion A of IHC users, IHC is replaced by an alternative replacement contraceptive; the remainder $(1 - A)$ are assumed to stop using contraception.

Contraceptive type	Current contraceptive prevalence in country *j* [11]	Contraceptive prevalence in country *j* after IHC replacement	Failure rate per year [12]
IHC	h_j	0	σ_h
Non-IHC contraceptive	k_j	k_j	σ_k
No contraceptive	x_j	$x_j + (1 - A)h_j$	σ_x
Specific replacement contraceptive	0	Ah_j	σ_a
Total	**1**	**1**	**-**

Table T1. Notation for contraceptive failure rates and prevalence.

The current birth rate can therefore be estimated as:

$$b_j = h_j\sigma_h + k_j\sigma_k + x_j\sigma_x \quad (7)$$

Once IHC has been replaced, the new birth rate is estimated as:

$$\widehat{b_j} = k_j\sigma_k + \big(x_j + (1-A)h_j\big)\sigma_x + Ah_j\sigma_a \qquad (8)$$

The difference in per-woman per-year birth rates after replacing IHC, Δb_j, is therefore estimated by subtracting (7) from (8):

$$\Delta b_j = h_j[A\sigma_a + (1-A)\sigma_x - \sigma_h] \qquad (9)$$

Thus the change in the total number of live births, ΔB_j, is given by substituting (9) into (6).

$$\Delta B_j = N_j h_j[A\sigma_a + (1-A)\sigma_x - \sigma_h] \qquad (10)$$

Rearranging (6) and inputting the reported live births [13] and estimated current birth rate (7) gives:

$$N_j = \frac{B_j}{h_j\sigma_h + k_j\sigma_k + x_j\sigma_x} \qquad (11)$$

which is substituted into (10) to give the change in the total number of live births:

$$\Delta B_j = B_j h_j \frac{A\sigma_a + (1-A)\sigma_x - \sigma_h}{h_j\sigma_h + k_j\sigma_k + x_j\sigma_x} \qquad (12)$$

Our baseline assumption is that the replacement contraceptive has the same failure rate as the background non-IHC contraceptives already in use in the country, and that the proportion transitioning to this hypothetical mix is the same as the proportion of non-IHC users in the country who use some non-IHC form of contraception:

$$\sigma_a = \sigma_k;\ A = \frac{k_j}{1-h_j}$$

$$\Delta B_j = B_j h_j \frac{k_j\sigma_k + x_j\sigma_x - \big(1-h_j\big)\sigma_h}{\big(1-h_j\big)\big(h_j\sigma_h + k_j\sigma_k + x_j\sigma_x\big)} \qquad (13)$$

We then conduct sensitivity analyses by varying the failure rates of the background and replacement contraceptives, and setting *A* to 0.2 and 0.8 for each country to represent low and high levels of IHC replacement, respectively.

4. Maternal deaths due to cessation of IHC

The change in live births on cessation of IHC use ΔB_j is converted into change in maternal deaths ΔM_j using the per-country maternal mortality ratio per 100 000 live births, m_j [14]:

$$\Delta M_j = \Delta B_j m_j \times 10^{-5} \qquad (14)$$

5. Change in overall deaths

The net change in HIV-related deaths and maternal deaths ΔU_j is estimated by subtracting the HIV-related deaths (4) from the maternal deaths (14):

$$\Delta U_j = \Delta M_j - \Delta D_j \quad (15)$$

6. Offsetting HIV risk in women using IHC

HIV incidence among IHC users is then reduced by fraction Q to simulate increased prevention efforts in this group, for example increasing condom use. With decreased incidence among IHC users, the overall incidence, $\overline{I_{Q,J}}$ becomes:

$$\overline{I_{Q,J}} = (1 - Q)\theta h_j I_j + (1 - h_j)I_j \quad (16)$$

Thus the change in incidence, $\overline{I_{Q,J}} - \overline{I_J}$, produces a change in total infections of:

$$X_{Q,j} = -\left(1 - p_j\right)N_j\overline{I_J}\frac{Q\theta h_j}{\theta h_j + (1 - h_j)} \quad (17)$$

The excess infections attributable to IHC use are offset by reductions in incidence when $X_j = X_{Q,j}$, hence:

$$1 - \frac{1}{\theta h_j + (1 - h_j)} = \frac{Q\theta h_j}{\theta h_j + (1 - h_j)} \quad (18)$$

which simplifies to:

$$Q = 1 - {}^{1}/_{\theta} \quad (19)$$

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