Assessing the impact of HPV vaccination programs in countries - ways to measure the real-word impact in Low- and Middle-Income Settings.

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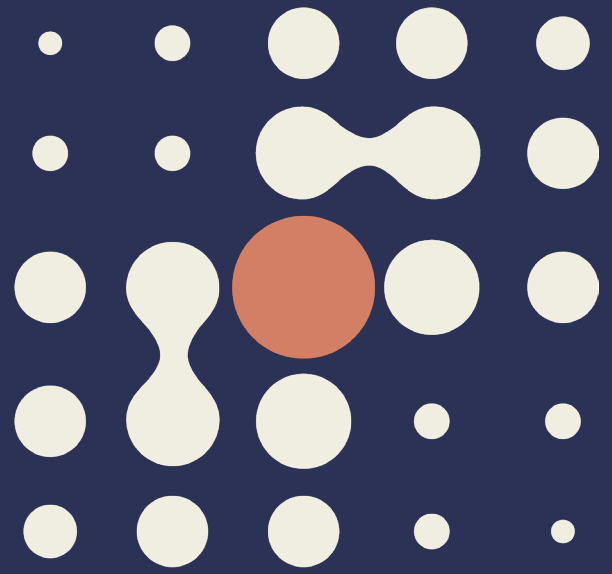
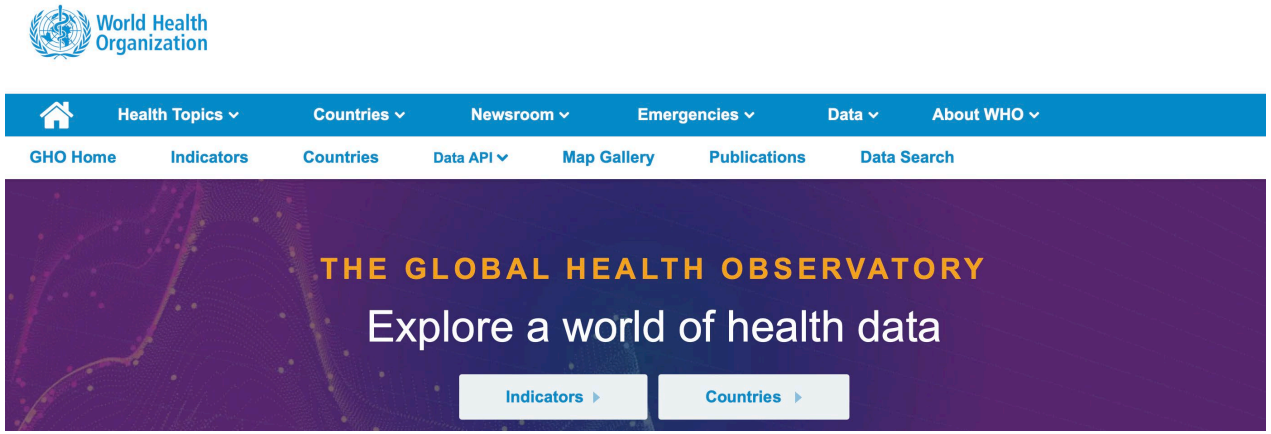
International Agency
for Research on Cancer

World Health
Organization




No conflict of interest to disclose.
HPV
Human papilloma Virus

Monitoring Global Health Data



The main purpose of the GHO is to provide updated information by country for a wide range of specific health indicators to assess the current (and trends) of health status of a specific population

https://www.who.int/data/gho

Examples of indicators

- Tuberculosis
  - Drug resistant TB
  - Co-epidemics of TB and HIV
  - Treatment success
  - Tuberculosis cases and deaths
- Vaccine-preventable communicable diseases
  - Vaccine-preventable communicable diseases
    - Diphtheria - number of reported cases
    - Rubella - number of reported cases
    - Total tetanus - number of reported cases
    - Neonatal tetanus - number of reported cases
    - Yellow fever - number of reported cases
    - Japanese encephalitis - number of reported cases
    - Congenital Rubella Syndrome - number of reported cases
    - Poliomyelitis - number of reported cases
    - Mumps - number of reported cases
    - Measles - number of reported cases
    - HPV (-related cancers)?

Data sources - Global tuberculosis report 2022

Notification systems & Prevalence Surveys

Currently, all countries have **national systems for notification** (i.e. reporting) of TB cases and most report national notification data to the WHO on an annual basis.

However, in many countries (including most high TB burden countries) the number of notified cases each year is not a good proxy for the actual number of people who develop TB disease, for two reasons: **underreporting** and **underdiagnosis**.

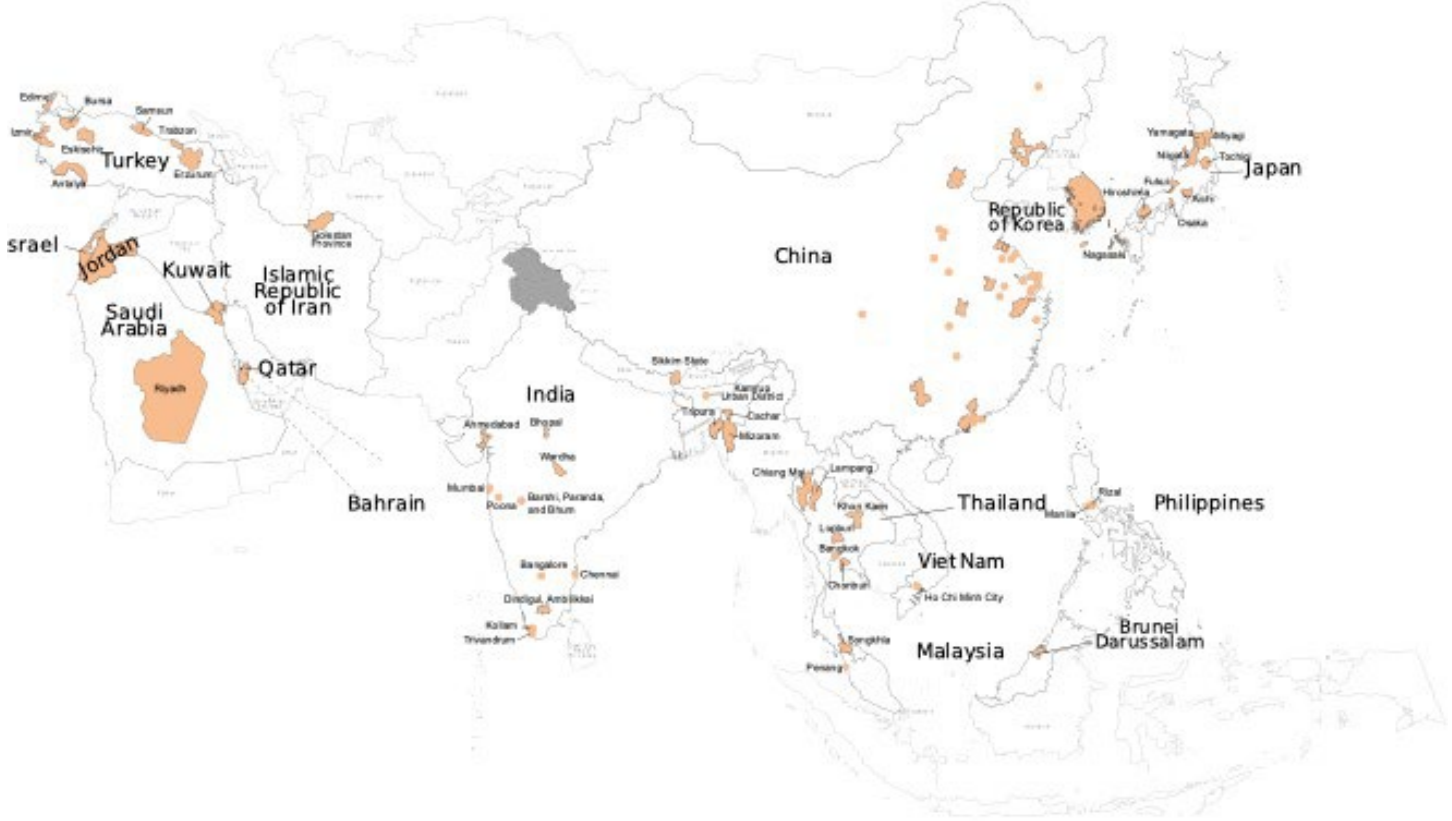
National TB **prevalence surveys** are the best way to **directly measure** the burden of TB disease in the population

National surveys of the prevalence of TB disease, actual (2000–21) and planned (2022–23).

2000	China				
2001					
2002	Cambodia				
2003	Malaysia				
2004	Indonesia[a]				
2005	Eritrea[b]				
2006	Thailand				
2007	Philippines	Viet Nam			
2008	Bangladesh[b]				
2009	Myanmar				
2010	China				
2011	Cambodia	Ethiopia	Lao People's Democratic Republic	Pakistan	
2012	Gambia	Nigeria	Rwanda	United Republic of Tanzania	Thailand
2013	Malawi	Ghana	Sudan		
2014	Indonesia	Zambia	Zimbabwe		
2015	Bangladesh	Kenya	Mongolia	Uganda	
2016	Democratic People's Republic of Korea	Philippines			
2017	Mozambique	Myanmar	Namibia	South Africa	Viet Nam
2018	Eswatini	Nepal			
2019	Lesotho				
2020	India				
2021					
2022/3	Cambodia	Pakistan	Timor-Leste		

https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

Cancer registries: coverage of Asia & Africa



Population-based cancer registries are resource-demanding, case definition and ascertainment is complex (as compared to other IDs) and time-lag between HPV vaccination and expected impact on cervical cancer is long (decades).

Bray F et al, 2021. Cancer Incidence in Five Continents, Vol. XI. IARC Scientific Publication. https://publications.iarc.fr/597

From HPV prevalence estimates to cervical cancer projections

HPV – prevalence surveys.

Empirical **age- and type-specific HPV prevalence estimates** can be used to assess the cohort-specific risk of cervical cancer.

Variations in HPV prevalence attributable to vaccination **occur earlier** than variations in cervical cancer incidence and are **easier to monitor**.

*example from Pakistan, using published HPV prevalence data using **advanced modelling techniques** it is possible to **predict the expected** cervical cancer incidence in a specific population.

Age-specific prevalence of HR-HPV types in Pakistan.

Age-group	High-risk HPV prevalence %	Target age-group	Exp. Incidence/ 10^5 w-y*	90% PI
	South Karachi (Sindh)			
20-24	1.2	25-29	0.4	0.2-0.9
25-34	2.1	30-39	2.8	1.6-5.0
35-44	0.8	40-49	3.6	2.1-6.4
45-54	1.7	50-59	13.7	6.3-29.5
	Punjab			
20-24	1.8	25-29	0.3	0.1-0.8
25-34	2.2	30-39	2.7	1.5-4.8
35-44	2.3	40-49	9.5	5.8-15.3
45-54	2.1	50-59	13.8	8.4-23.0

Adhikari I. et al. In preparation

Raza et al, 2010 & Aziz et al, 2018

HPV prevalence surveys and HPV vaccination effectiveness

HPV vaccination effectiveness studies (by IARC)

A series of **repeat surveys** have been or are being performed in Africa and Asia to assess the **population-level impact** of HPV vaccination.

Study procedures are getting **standardized** and **exportable** to a wide range of settings.

Other institutions have conducted similar initiatives in LMICs (e.g. HOPE study in South-Africa).

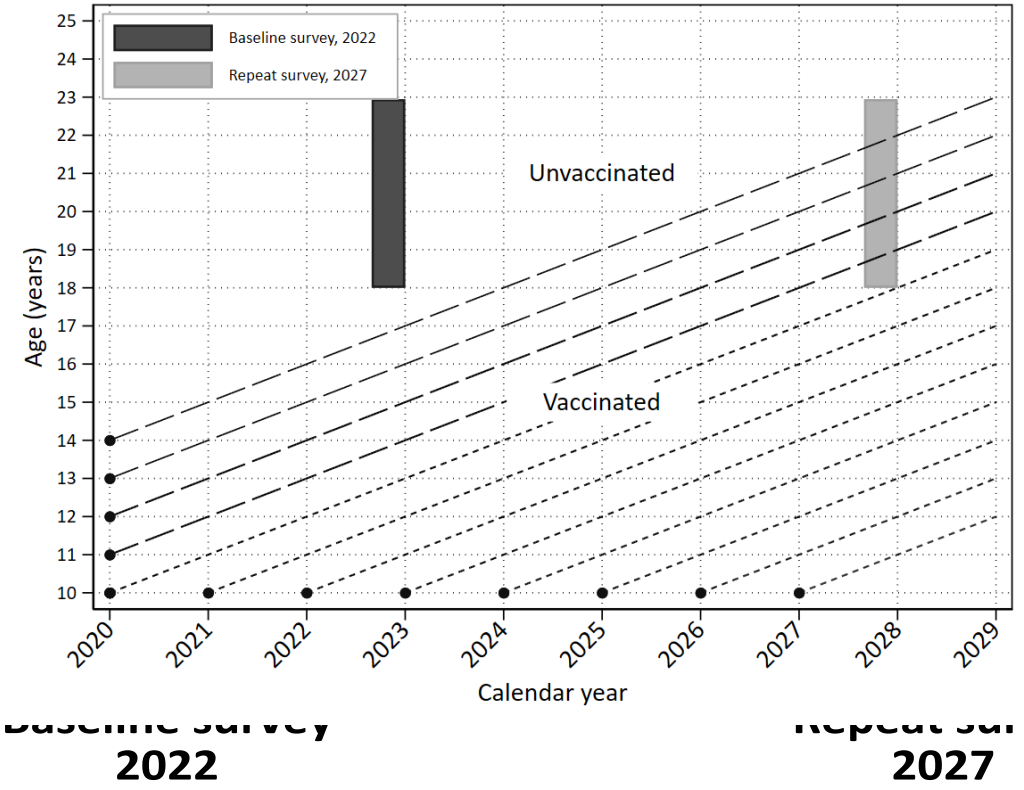
IARC's effectiveness studies, by country & status of completion

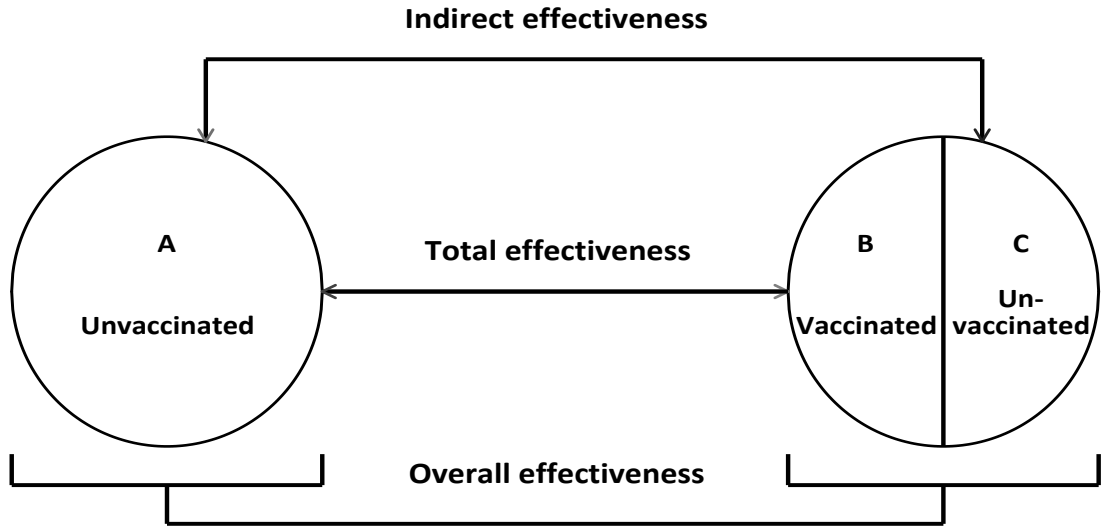
Country	Local partner	Baseline survey (pre-vaccination)	Repeat survey (post-vaccination)
Bhutan	Ministry of Health	Completed	Completed
Rwanda	Ministry of Health	Completed	Completed
Armenia	FIDEC	Completed	To be defined
Uganda	LSHTM	Ongoing (end 2023)	To be defined
The Gambia	LSHTM	Ongoing	To be defined
Laos	Ministry of Health	Completed	Due in 2027
Zimbabwe	Harare Health Research Consortium	Completed	Due in 2027

Standardized methods

Basic components of vaccination effectiveness monitoring

- **Baseline** and one or more **repeat** HPV prevalence surveys.
- **Context-responsive timescales** (age and period) to minimize sample size and time interval between surveys.
- Standardized **statistical protocols** to assess Overall effectiveness, Herd Effect (indirect effectiveness), and Total effectiveness.
- Of note, the assessment of **overall effectiveness**, does not need **ascertainment of vaccination status** of participants.





Baussano et al, Vaccine 2018

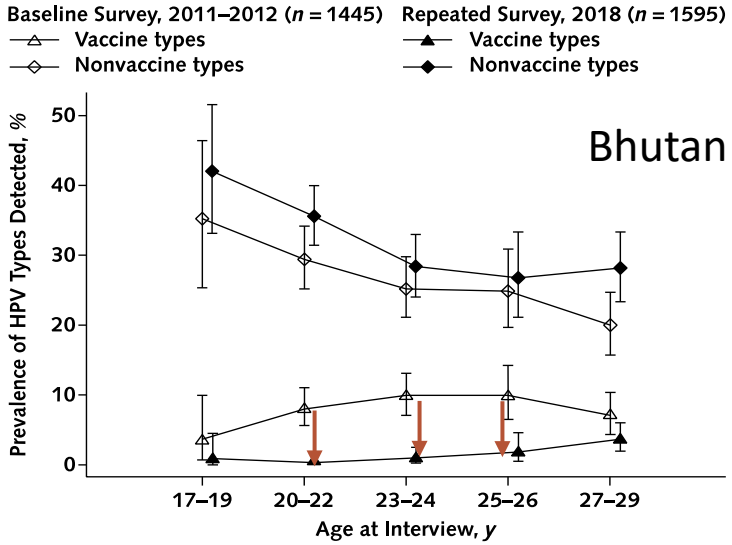
Standardized outputs

Vaccination effectiveness by age (crude and adjusted)

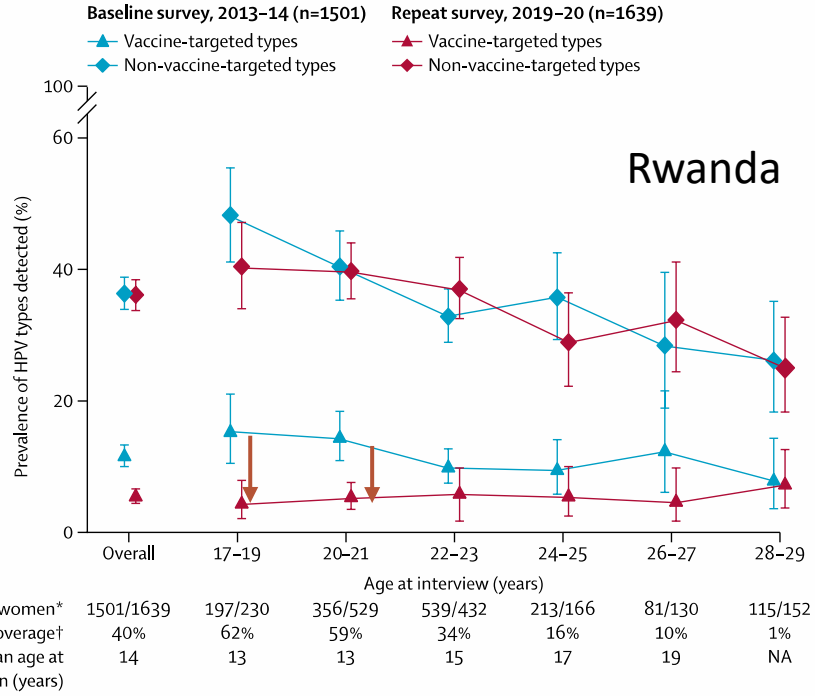
- Using modelling techniques, effectiveness estimates can be **translated into expected impact** on future cervical cancer incidence (see below).
- Effectiveness estimates can **inform health-economic assessments**.
- Effectiveness estimates can **inform design of screening programmes** (e.g. Bhutan's Flagship program).

	Vaccine effectiveness (95% CI)			Lifetime risk (95% UI)*		Annual age-standardised incidence rate (95% UI)*	
	Overall	Total	Indirect	Without vaccination	With vaccination	Without vaccination	With vaccination
HPV16 and 18	48% (27 to 64)	66% (42 to 81)	32% (−1 to 54)	..	..	..	..
HPV31, 33, and 45	40% (15 to 58)	37% (1 to 60)	41% (8 to 62)	..	..	..	..
Cervical cancer	..	..	..	2663 (1989–3462)	1660 (1239–2161)	28·0 (20·9–36·4)	17·5 (13·0–22·7)

Age-standardised incidence rates were standardised on the world population. HPV=human papillomavirus. UI=uncertainty interval. *Cases per 100 000 women, estimated among women in both the baseline survey (without vaccination) and repeat survey (with vaccination).



GP5+/6+, excluding 4 vaccine types. Error bars represent 95% CIs. HPV = human papillomavirus.



https://www.pmo.gov.bt/?stm_service=flagship-programs

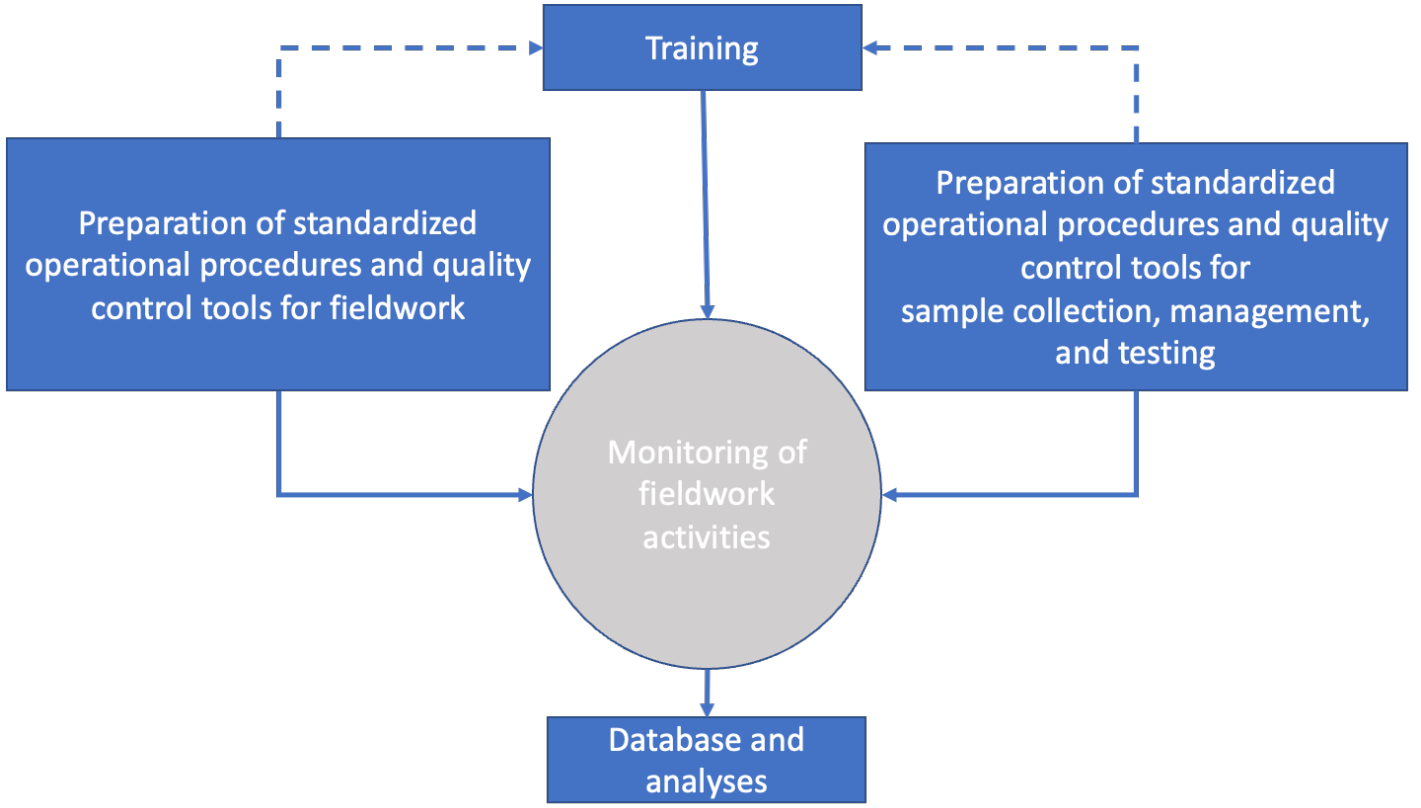
Baussano et al, Annals Int Med 2020, Sayinzoga et al, Lancet Glob Health 2023

Next steps: knowledge and skill transfer to local actors

Standardized procedures for key steps

1) Study staff selection, recruitment, and training,
2) Completion of legal, ethical, and administrative procedures underlying study approval and execution,
3) Purchase and shipment of study material,
4) Preparation of the settings in which the survey will be actually performed,
5) Definition and identification of the source population,
6) Design of recruitment and enrolment procedures,
7) Sample collection from and interviewing of survey's participants,
8) Sample and data transfer and storage,
9) Sample testing and data analyses,
10) Consolidation of findings and reporting.

Coordination of HPV vaccination effectiveness surveys, worldwide



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