



ELIMINATING HPV-RELATED CERVICAL CANCER: THE ROLE OF PREVENTIVE VACCINE R&D

Human papillomavirus (HPV) is the most common viral infection of the reproductive tract, affecting more than one in ten women and one in five men worldwide. In sub-Saharan Africa, almost a quarter of women and more than three-quarters of men are infected.¹ While most infections are asymptomatic and resolve spontaneously, infection with key HPV strains can result in pre-cancer and cancer.

HPV infection is the causal agent in almost all cases of cervical cancer, which is the fourth most frequent cancer worldwide and a leading cause of cancer death in women.² There were over 604,000 new cases of and 342,000 deaths from cervical cancer in 2020, with the vast majority of these occurring in low- and middle-income countries (LMICs).³ While effective HPV preventive vaccines, diagnostics and pre-cancer and cancer treatment options exist, mortality from cervical cancer persists. This is specifically true for women in LMICs – where access to biomedical products is either limited, and/or those products are not suited to an LMIC context.

Elimination through prevention – a vaccine story

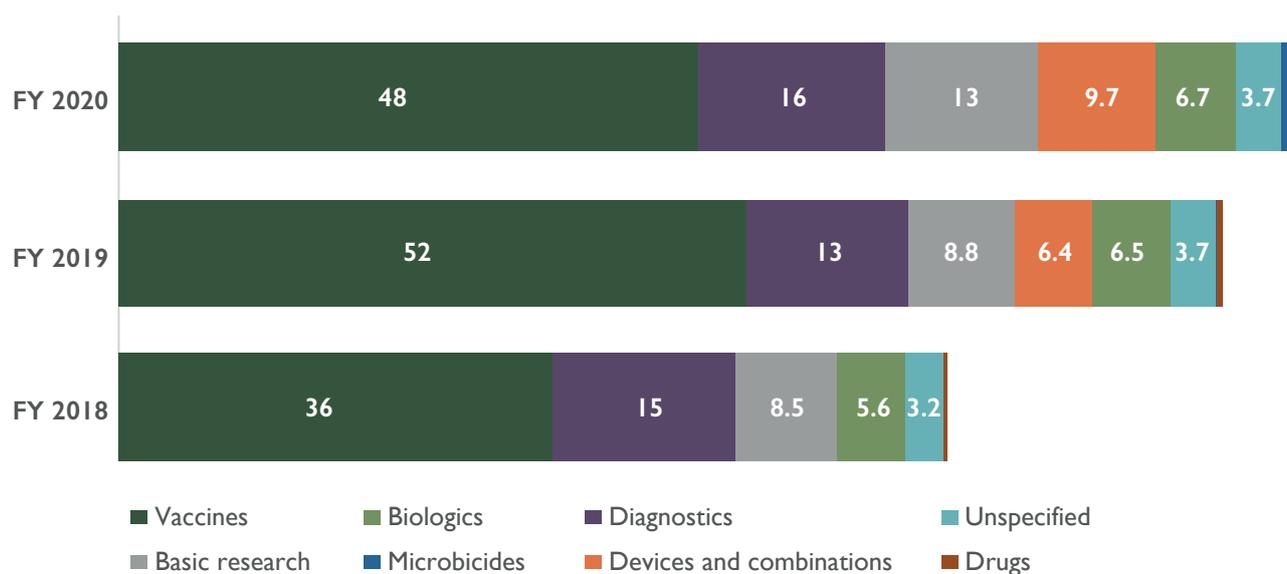
In 2020, the World Health Organization (WHO) launched the first Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem.⁴ At its core, it recognises that primary prevention through HPV vaccination is the most effective intervention for reducing the risk of cervical cancer, and that elimination is feasible with the currently available (WHO pre-qualified) virus-like particle-based HPV vaccines – MSD's Gardasil and Gardasil 9, GSK's Cervarix, and Inovax's newly pre-qualified Cecolin – with studies suggesting that effective implementation of HPV vaccine programmes could prevent up to 90% of HPV-positive cancers of the cervix.⁵ Indeed recent data from the United Kingdom demonstrates that the UK's national HPV immunisation program, which was introduced in 2008, has effectively eliminated cervical cancer from women born since September 1995.⁶

To date, Gavi, the Vaccine Alliance has played a leading role in facilitating low-cost access to existing vaccines in at least 30 countries.⁷ However, these vaccines follow a two-dose or three-dose schedule – which can pose logistical and cost barriers in LMICs – and do not protect against all high-risk HPV strains. While the global elimination strategy focuses on the scale up of existing interventions, it also acknowledges that 'more ground-breaking technology' will be needed to reduce the incidence of cervical cancer further, beyond elimination thresholds.⁸ Current HPV vaccine research and development (R&D) therefore includes both dose reduction and longer interval studies for existing HPV vaccines, as well as development of novel preventive vaccines, including those with different or broader strain specificity.

Funding trends for HPV vaccine R&D (2018 to 2020)

Since 2018, as part of the G-FINDER Sexual and Reproductive Health project, Policy Cures Research has been tracking global investment in HPV R&D for a range of biomedical products, including preventive vaccines.ⁱ In 2020, funding for HPV preventive vaccine R&D totalled USD \$48m. This was a small dip in investment compared with \$52m in 2019 (down \$4.1m, a decrease of 7.8%), but nonetheless, it remained well above 2018 funding levels (\$36m). Preventive vaccines have in fact persisted as the biomedical product with greatest R&D investment, remaining at the top for the past three years and averaging \$45m (53% of total) across 2018, 2019 and 2020. See Figure 1.

FIGURE 1. HPV and HPV-related cervical cancer R&D funding by product type 2018 - 2020 (USD millions)



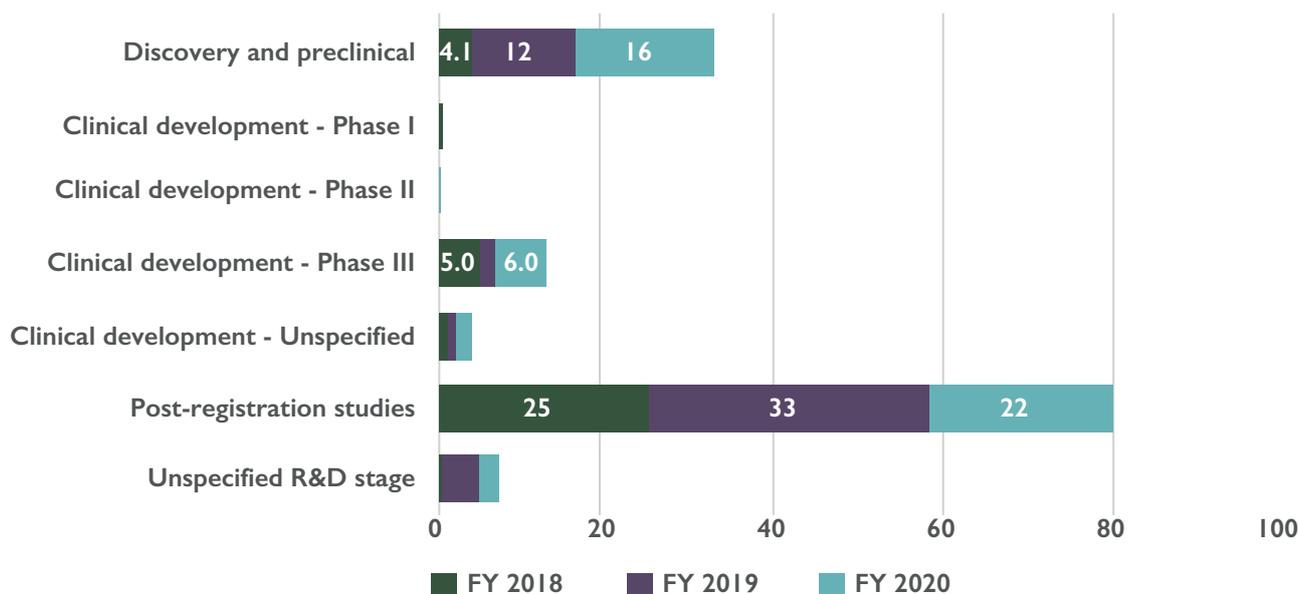
The steady dominance of vaccine funding in HPV R&D is consistent with the concerted global effort towards the elimination of HPV-related cervical cancer through prevention, with an R&D landscape pivoted towards dose reduction studies of existing vaccines to optimise their use, particularly in LMICs. In fact, post-registration studies have in total averaged over half of all vaccine R&D funding across all three years of the survey (\$26m, 59%). Both the US NIH and the Bill and Melinda Gates Foundation have remained the two top funders of vaccine post-registration R&D since the start of the survey, together making up 93% in 2018, 95% in 2019 and 94% in 2020 of total post-registration vaccine R&D funding. At least half of this – most of the Gates Foundation funding – was for dose-optimisation of existing HPV vaccines, with LMIC markets in mind.

That said, studies on newer vaccines are also underway. This includes funding in 2020 from the German Federal Ministry of Education and Research (BMBF) and the Gates Foundation to PATH to undertake a head-to-head comparative study on the effectiveness of the now newly pre-qualified vaccine Cocolin against Gardasil, in a large trial known as CHOISE (Comparing HPV Vaccine Options: Immunogenicity and Safety Evaluation) taking place in Bangladesh and Ghana. The study commenced recruiting at the end of 2020.⁹ Prior to this, vaccine clinical development has been driven by industry investment, which peaked at \$3.6m in 2018 (54% of vaccine clinical development funding), dropping to \$1.6m in 2019 (but still representing 54% of vaccine clinical development funding in that year), and shifting to \$2.0m in 2020, but representing just 26% of vaccine clinical development R&D funding.

ⁱ G-FINDER's scope only includes R&D for preventive vaccines that represent an improvement over existing products (e.g., single dose, expanded oncogenic HPV strain protection, LMIC-focused, etc). Funding for HPV therapeutic vaccines is captured and reported under the 'biologics' category.

Concurrently, discovery and preclinical research for completely novel vaccines – including those with different or broader specificity – represents a solid chunk of the R&D funding landscape. [See Figure 2](#). In 2020, funding to early-stage vaccine R&D was \$16m (34% of all vaccine funding), the second highest investment in vaccine research by R&D stage after post-registration studies. This was a \$4.3m increase (up 36%) compared with 2019, which itself represented a near trebling of investment compared with 2018 (up \$7.9m, an increase of 190%). The year-on-year increases in funding to vaccine discovery and preclinical R&D have largely been driven by sizeable investments from industry, whose early-stage research into novel HPV preventive vaccines quintupled between 2018 (\$1.2m) and 2019 (\$6.0m), only to double again between 2019 and 2020 to peak at over \$12m.

FIGURE 2. HPV preventive vaccine funding by R&D stage 2018 - 2020 (USD millions)



Overall, aggregate industry, the US NIH and the Gates Foundation have remained consistently within the top three funders of HPV preventive vaccine R&D across 2018, 2019 and 2020 – albeit in different orders. In 2020, industry dominated vaccine investment at \$15m, just shy of a third of the total (32%), and following two years of consecutive growth including a doubling of investment between 2019 (\$7.6m) and 2020. While the US NIH fell marginally (down \$2.8m, a decrease of 16%) between 2019 and 2020, funding from the Gates Foundation saw a large drop within the same years, down a quarter (a decrease of \$9.3m), largely due to a near halving of funding to post-registration studies (down \$8.3m) across a range of projects and recipients. Apart from new funding from German BMBF in 2020, most other funders have contributed less than \$1m each across the years of the survey. [See Table 1](#).

TABLE I. **Funders of HPV preventive vaccine R&D 2018 - 2020 (USD millions)**

FUNDERS	FY 2018	FY 2019	FY 2020
Aggregate industry	5.8	7.6	15
US NIH	11	17	14
Gates Foundation	17	22	13
German BMBF			4.4
UK MRC	0.8	0.8	0.6
UK NHS	0.0	0.3	0.3
Wellcome	0.2	0.2	0.2
Australian NHMRC	<0.1	0.2	0.2
Brazilian FACEPE			0.1
Carlos III Health Institute			<0.1
Canadian CIHR	<0.1		
Indian BIRAC	1.5		
Indian DBT		4.1	
TOTAL	36	52	48

A promising future

Global investment in HPV vaccine R&D continues – not in spite of, but because of the incredible effectiveness of existing HPV vaccines. With continued support to R&D aimed at improving accessibility, suitability and cost-effectiveness of preventive HPV vaccines in LMIC settings – whether via improvements to existing or development of entirely new vaccines to better serve LMIC needs – the future looks bright for similar national success stories like the one in the UK to emerge across other countries and regions, demonstrating and celebrating the effective elimination of HPV-related cervical cancer in women and girls.

Endnotes

- 1 “WHO | Human Papillomavirus (HPV),” accessed April 15, 2020, <https://www.who.int/immunization/diseases/hpv/en/>.
- 2 Ibid.
- 3 Hyuna Sung et al., “Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries,” *CA: A Cancer Journal for Clinicians* 71, no. 3 (2021): 209–49, <https://doi.org/10.3322/caac.21660>.
- 4 “Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem,” accessed November 12, 2021, <https://www.who.int/publications-detail-redirect/9789240014107>.
- 5 Silvia de Sanjosé et al., “Burden of Human Papillomavirus (HPV)-Related Cancers Attributable to HPVs 6/11/16/18/31/33/45/52 and 58,” *JNCI Cancer Spectrum* 2, no. 4 (October 2018): pky045, <https://doi.org/10.1093/jncics/pky045>.
- 6 Milena Falcaro et al., “The Effects of the National HPV Vaccination Programme in England, UK, on Cervical Cancer and Grade 3 Cervical Intraepithelial Neoplasia Incidence: A Register-Based Observational Study,” *Lancet* (London, England), (November 3, 2021), [https://doi.org/10.1016/S0140-6736\(21\)02178-4](https://doi.org/10.1016/S0140-6736(21)02178-4).
- 7 “HPV Vaccine Manufacturers Commit to Provide Enough Supply to Immunise at Least 84 Million Girls in Gavi Countries,” accessed July 6, 2020, <https://www.gavi.org/news/media-room/hpv-vaccine-manufacturers-commit-provide-enough-supply-immunise-least-84-million>.
- 8 “Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem,” accessed November 12, 2021, <https://www.who.int/publications-detail-redirect/9789240014107>.
- 9 “Expanding Access to HPV Vaccines,” accessed November 12, 2021, <https://www.path.org/media-center/expanding-access-hpv-vaccines-path-evaluate-safety-and-immunogenicity-new-hpv-vaccine/>.