

Strategie di Prevenzione Vaccinale

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Nessun Conflitto di Interesse



Centro di Riferimento Oncologico
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

27 • 28 ottobre, Verona
**CONVEGNO
NAZIONALE
GISCI 2022**

La mia presentazione comprenderà:

- Aggiornamento sulla **diffusione globale** della vaccinazione HPV (principalmente nelle ragazze)
- Evidenza **sull'efficacia di una sola dose** vaccinale da clinical trials (*M. Zappa ieri: Migliorare l'Efficacia nell'Intera Popolazione*)
- Ultime Raccomandazioni dal WHO Strategic Group of Experts on Immunization (**SAGE, 2022**).

2022, 97, 261–276

No 24



World Health
Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

17 JUNE 2022, 97th YEAR / 17 JUIN 2022, 97^e ANNÉE

No 24, 2022, 97, 261–276

<http://www.who.int/wer>

Contents

261 Meeting of the Strategic
Advisory Group of Experts
on Immunization, April 2022:
conclusions and
recommendations

Sommaire

**Meeting of the Strategic
Advisory Group of Experts
on Immunization, April
2022: conclusions and
recommendations**

**Réunion du Groupe
stratégique consultatif
d'experts sur la vaccination,
avril 2022: conclusions et
recommandations**

Global strategy to accelerate the elimination of cervical cancer

VISION: A world without cervical cancer

THRESHOLD: All countries to reach < 4 cases 100,000 women years

2030 CONTROL TARGETS

HPV vaccination
estimated to avert
> 45M deaths over
next 100 years

90%

of girls fully vaccinated
with HPV vaccine by 15
years of age

70%

of women screened with
a high precision test at
35 and 45 years of age

90%

of women identified
with cervical disease
receive treatment and
care

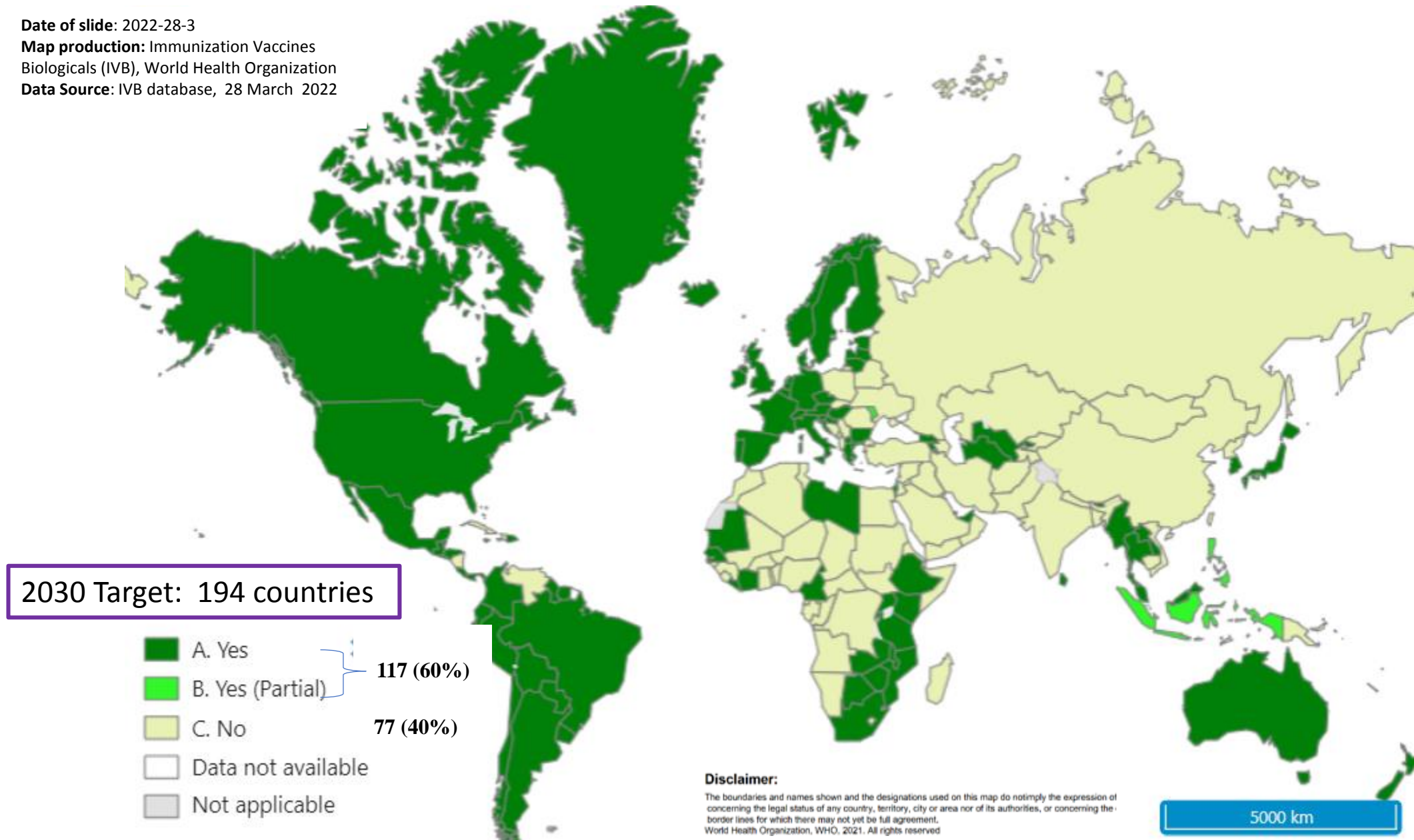
SDG 2030: Target 3.4 – 30% reduction in mortality from cervical cancer

Countries with HPV vaccine in the national immunization programme

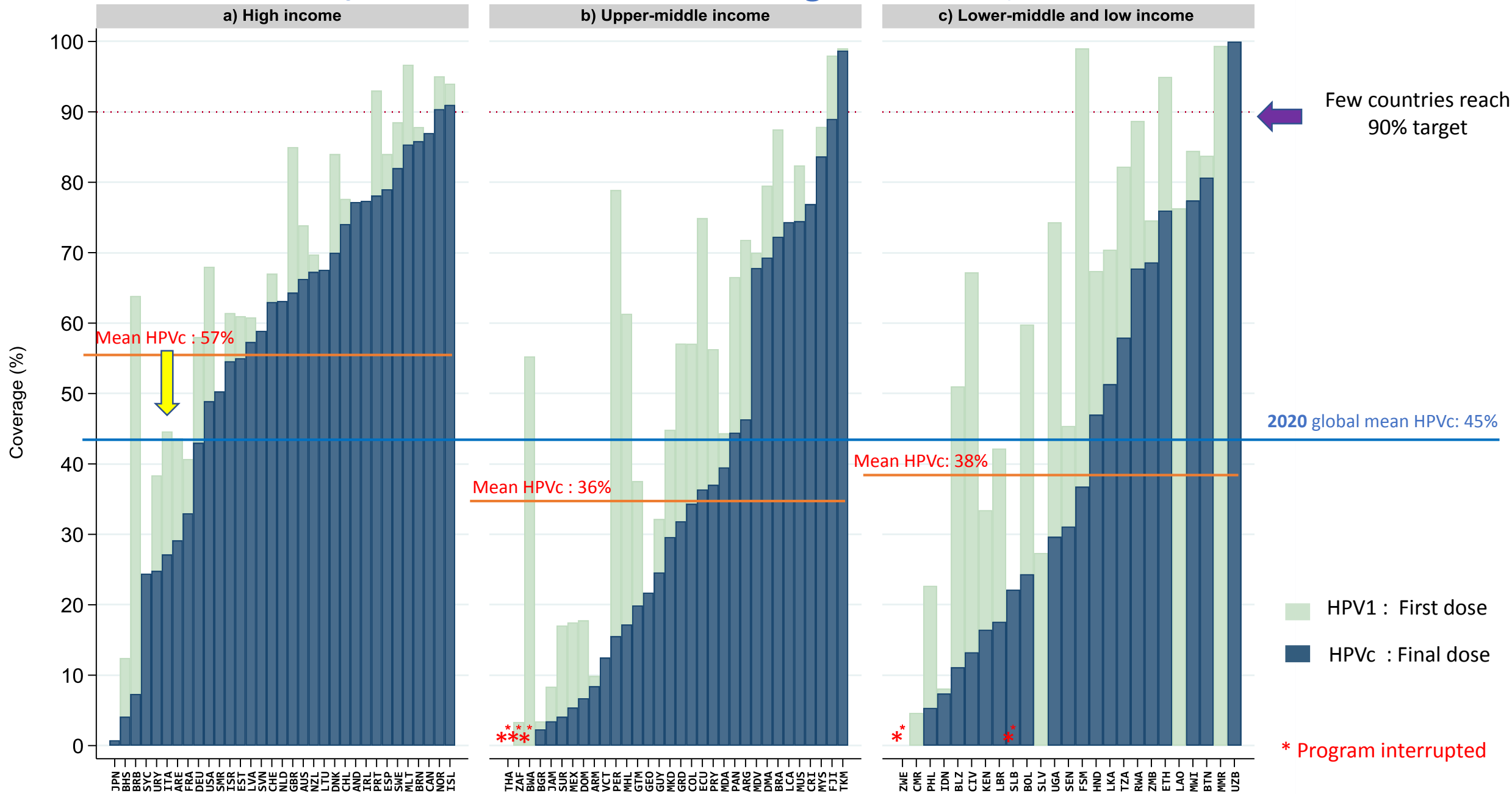
Date of slide: 2022-28-3

Map production: Immunization Vaccines
Biologicals (IVB), World Health Organization

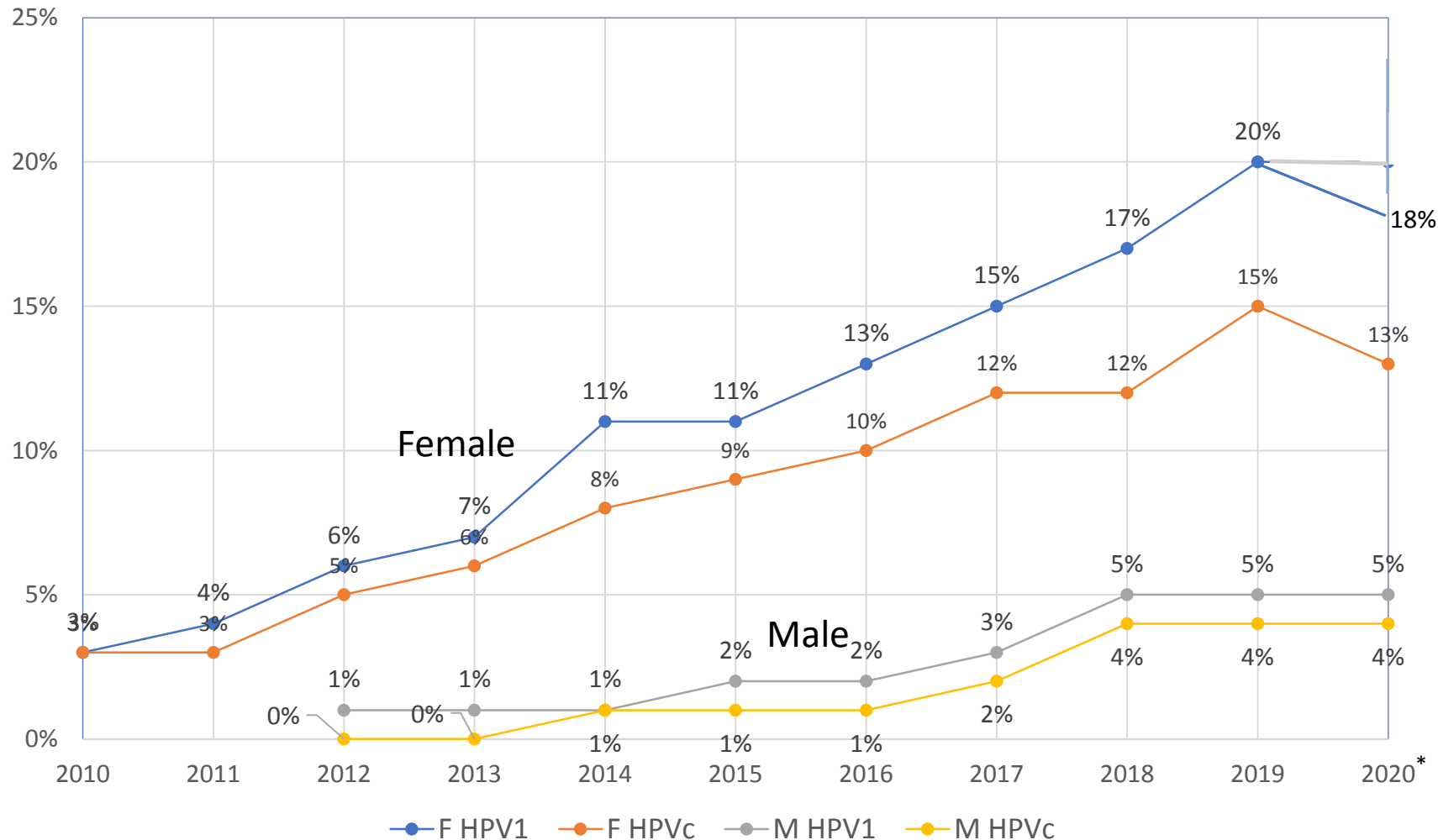
Data Source: IVB database, 28 March 2022



WHO/UNICEF HPV vaccine coverage estimates, 2020



Global HPV vaccine coverage decreased - for the first time - in 2020



*2020 non reporting countries imputed using extrapolation from 2019 level with mean change by WHO region (15 July 2021)

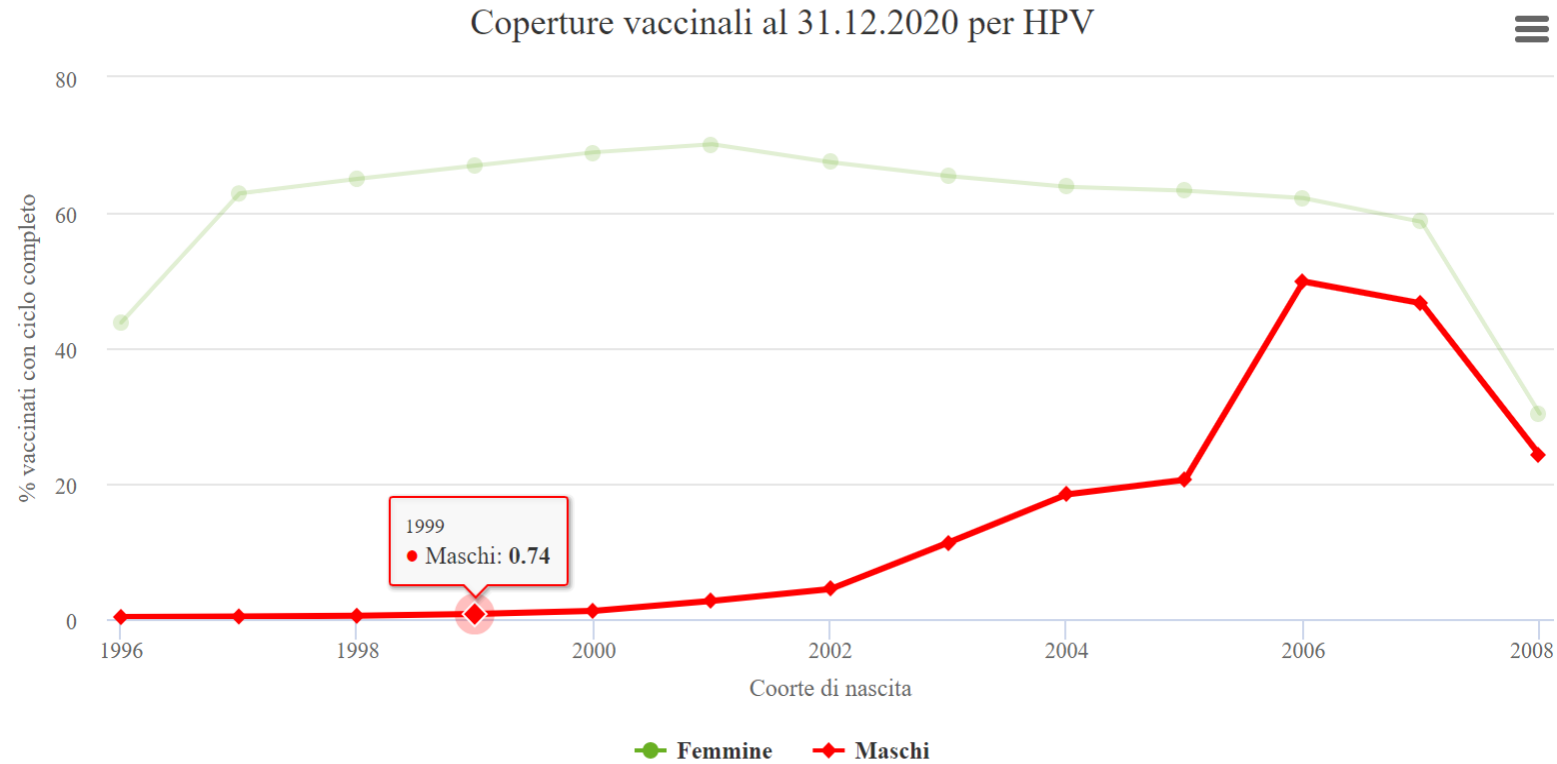
HPV vaccine coverage was affected by COVID-19 pandemic and only 13% of girls are fully protected.

Currently less than third of the world's population of girls 9-14 years of age live in countries that provide the HPV vaccine.

More countries now provide Male vaccination. Over a third of all HPV programmes provide the vaccine to males.

Copertura vaccinale in Italia

Papillomavirus umano (HPV) ☰



% vaccinate con ciclo completo

Target primario della vaccinazione: offerta attiva e gratuita nel 12° anno di vita

*tutti i dati sono aggiornati al 31/12/2020 - fonte ministero della Salute

By Courtesy of Prof Paolo Bonanni

Evidence on single-dose HPV since 2019

From Sage* meeting, April 2022, see Weekly epidemiological record, No 24, 2022, 97, 261–276, <http://www.who.int/wer>

- Since the SAGE meeting in 2019, evidence on single-dose HPV vaccine has been accumulating
- 2021: Publication of data from several studies implemented to definitively assess the potential for single-dose HPV vaccine as a routinely recommended schedule
- April 2021: Therefore, the SAGE HPV WG was reconvened **to reassess the evidence on single-dose HPV vaccination** strategy and to identify the remaining research needs

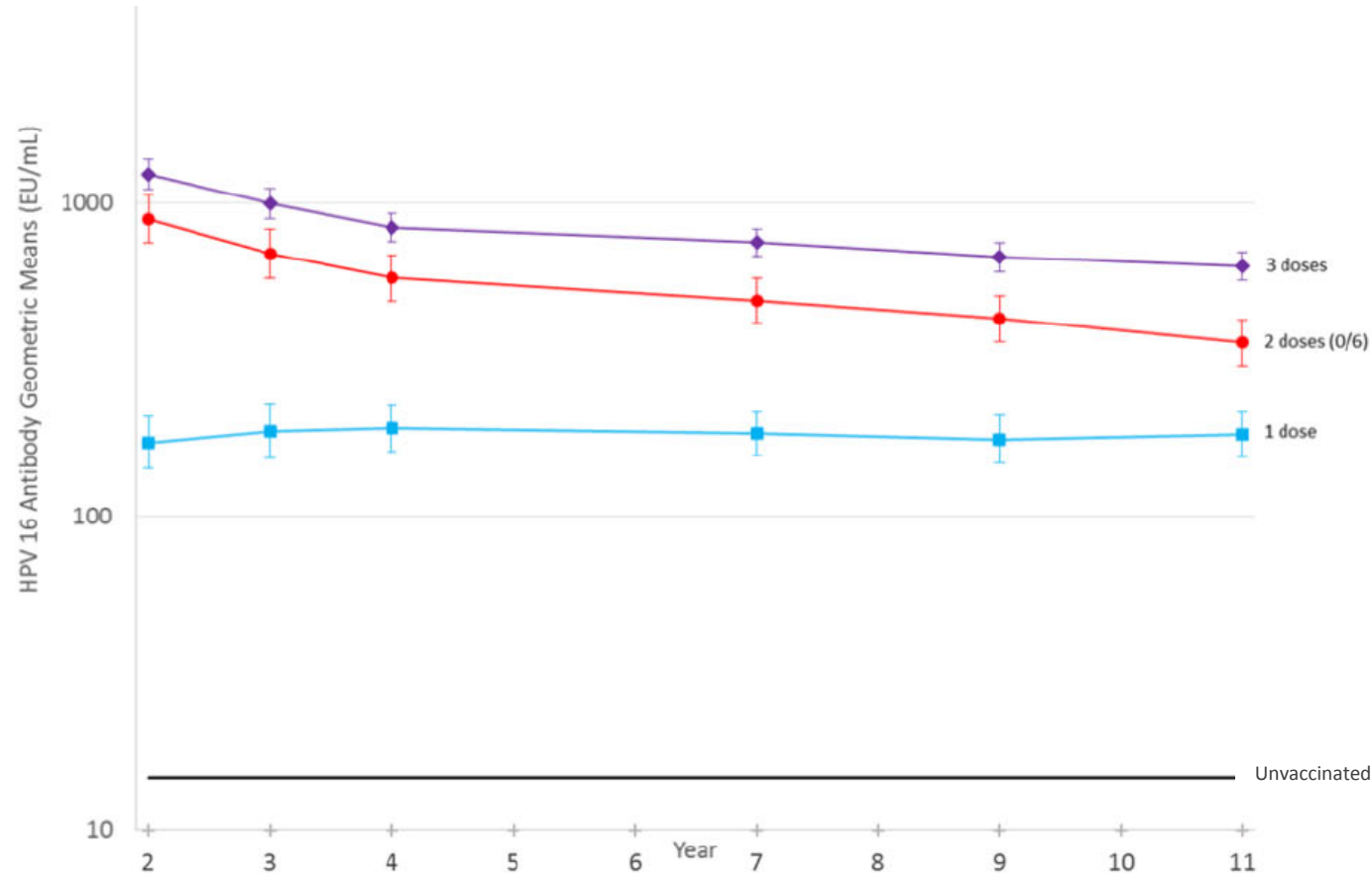
**Strategic Advisory Group of Experts on Immunization (SAGE): advice WHO and GAVI about priority vaccination in the poorest World Countries*

Protection after 1, 2 or 3 doses of 2vHPV through 11 years, Costa Rica Vaccine Trial

Post-hoc analysis of RCT: women vaccinated at age 18–25 years randomized to receive 3 doses of 2vHPV or control, but not all completed series

Doses	Number	Prevalent 16/18 HPV % (95% CI)	Vaccine efficacy % (95% CI)
3 doses	1365	2.0 (1.3–2.8)	80.0% (70.7–87.0)
2 doses	62	1.6 (0.1–7.7)	83.8% (19.5–99.2)
1 dose	112	1.8 (0.3–5.8)	82.1% (40.2–97.0)
Control	1783	10.0 (8.7–11.4)	Reference

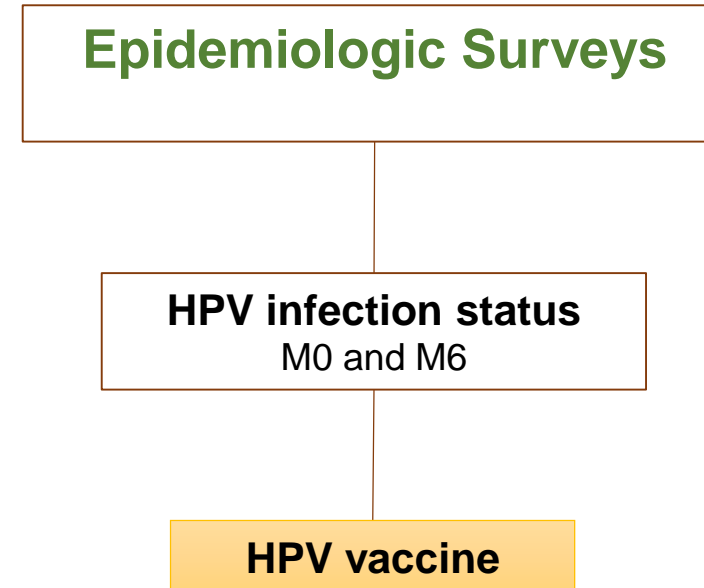
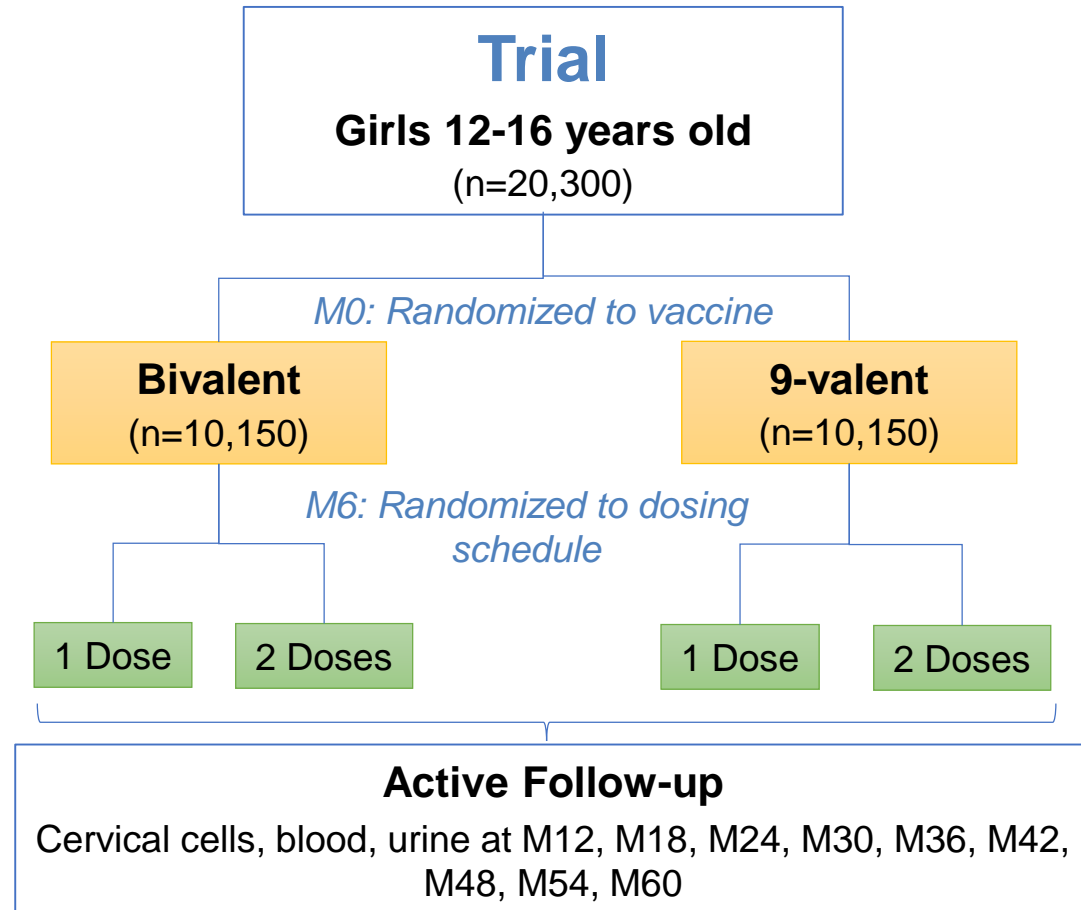
HPV 16 antibody after 1, 2 or 3 doses of 2vHPV through 11 years, Costa Rica Vaccine Trial (similar data from India, Basu, et al. Lancet Oncology Oct 2021)



Stable HPV 16 and 18 antibody levels (by ELISA) through 11 years post vaccination with different dosing schedules, at least 10-fold above levels in unvaccinated

ESCUDDO, Costa Rica

- RCT to evaluate non-inferiority of one versus two doses of 2vHPV and 9vHPV for prevention of new cervical HPV16/18 infections that persist 6+ months
- Evaluate one dose compared to zero doses



KEN-SHE

- Randomized trial of **1 dose of 9vHPV or 2vHPV or meningococcal vaccine**
 - 2250 Kenyan women aged 15–20 years; 1-5 lifetime partners; HIV negative
- 1458 girls evaluated for efficacy at month 18 in mITT HPV 16/18 cohort

Study arm	Number	Incident persistent HPV 16/18	Incidence/100 PY	VE % (95% CI)
9vHPV	496	1	0.17	97.5% (81.7–99.7)
2vHPV	489	1	0.17	97.5% (81.6–99.7)
MCV	473	36	6.83	Reference

Enrollment between December 2018 and June 2021

mITT, modified intention to treat: HPV 16/18 HPV DNA negative (external genital and cervical swabs) at enrollment and month 3 (self-collected vaginal swab) and HPV antibody negative at enrollment

Barnabas, et al. DOI 10.21203/rs.3.rs-1090565/v1; accepted for publication at NEJM Evidence

Overview of key evidence on 1-dose HPV vaccination

Outcome		Results	Key study	GRADE
Immunogenicity	Seroconversion	One, two and three doses similar (> 97%)	DORIS (RCT)	High
	Antibody titers	Lower GMT with 1 dose (vs. 2 or 3 doses)	DORIS (RCT)	High
	Persistence of antibody	GMTs stable up to 11 years, and comparable for 1, 2 and 3 doses (HPV2/4)	CVT, IARC (Post-RCT) DORIS (RCT)	Moderate High
Protection in trials (vaccine efficacy)	Protective efficacy against <ul style="list-style-type: none"> Persistent infection (HPV 16/18) Persistent infection (HPV 16/18/31/33/45/52/58) Persistent infections (HPV 16/18) Prevalent infections (HPV 16/18) 	VE for one-dose vs. 0 dose		
		• 97.5% (HPV2/9)	Kenshe (RCT)	High
		• 88.9% (HPV9)	Kenshe (RCT)	
		• 94.2% (Similar to 2 & 3 doses) (HPV4)	IARC (Post-RCT)	Low
	• 82.1% (Similar to 2 & 3 doses) (HPV2)	CVT (Post-RCT)	Low	
Duration of protection	Up to 10 years against HPV16/18 (HPV4) Up to 11 years against HPV16/18 (HPV2)	IARC (Post-RCT) CVT (Post-RCT)	High	
Population level effectiveness	Against prevalent infections (HPV 16/18)	VE 1 dose <u>83.3%</u> (vs 0 dose) (HPV2) VE 2 dose <u>93.6%</u> (vs 0 dose) (HPV2)	Thailand impact	<i>Not graded</i>

Brief summary: Comparison with the current WHO position:

		Current WHO position	Draft Recommendations
Primary target group		Girls aged 9-14 years old	Girls aged 9-14 years old
Vaccination Schedule	9-14 years old	2-dose schedule	Either a 2-dose or a 1-dose vaccination schedule can be used
	15-20 years old	3-dose schedule	Either a 2-dose or a 1-dose vaccination schedule can be used
	≥21 years old	3-dose schedule	2-dose schedule can be used
	Immuno-compromised (any age)	3-dose schedule	Should be prioritized and should receive at least 2 doses but ideally 3 doses, if programmatically feasible. <i>Further research on immunocompromised persons to be prioritized.</i>
Vaccination prioritization	MAC	<i>Temporarily postpone</i>	SAGE recommends countries, where feasible and affordable, to prioritize catching-up missed girls through multi-age cohort (MAC) vaccination
	Boys	<i>Temporarily postpone</i>	Introducing the vaccination of boys and older females should be postponed until the global supply situation is fully unconstrained. <i>Further research on schedule optimization in boys & older cohorts</i>
	Older age cohorts	<i>Temporarily postpone</i>	

Criticità della vaccinazione HPV

Il vaccino HPV è sicuro e straordinariamente efficace tanto che da tre si è passati a due dosi e il WHO ne raccomanda ora **anche una sola dose a 9-20 anni d'età** (off-label, SAGE, 2022). **Già recepita in Gran Bretagna e Olanda**

Bisogna capire perché la **vaccinazione HPV** fa così tanta fatica a diffondersi. Tra le spiegazioni possibili:

- **Scarsa comunicazione**
- **Altre priorità** vaccinali, mancanza di secondo richiamo per chi non si presenta
- Fascia d'**età** difficile da raggiungere: adolescenti e giovani donne
- Scarsa «previdenza» in giovani, famiglie e medici (**rimandare si può...**)
- Stigma inconfessato per la trasmissione **sessuale** dell'HPV

Grazie, dal Centro di Riferimento Oncologico, IRCCS
di Aviano (PN)

