20 years into the Gambia Hepatitis Intervention Study

Assessment of initial hypotheses and prospects for evaluation of protective effectiveness against liver cancer

Hilton Whittle


0 25 50 km
0 25 50 mi
SENEGAL
North Atlantic Ocean
BANJUL
Serekunda
Brikama
Gambia
Keneba
Farafenni
Mansa Konko
Sukuta
Georgetown
Gambia
Basse
Santa Su
SENEGAL
Casamance
GUINEA-BISSAU

Background 1980's

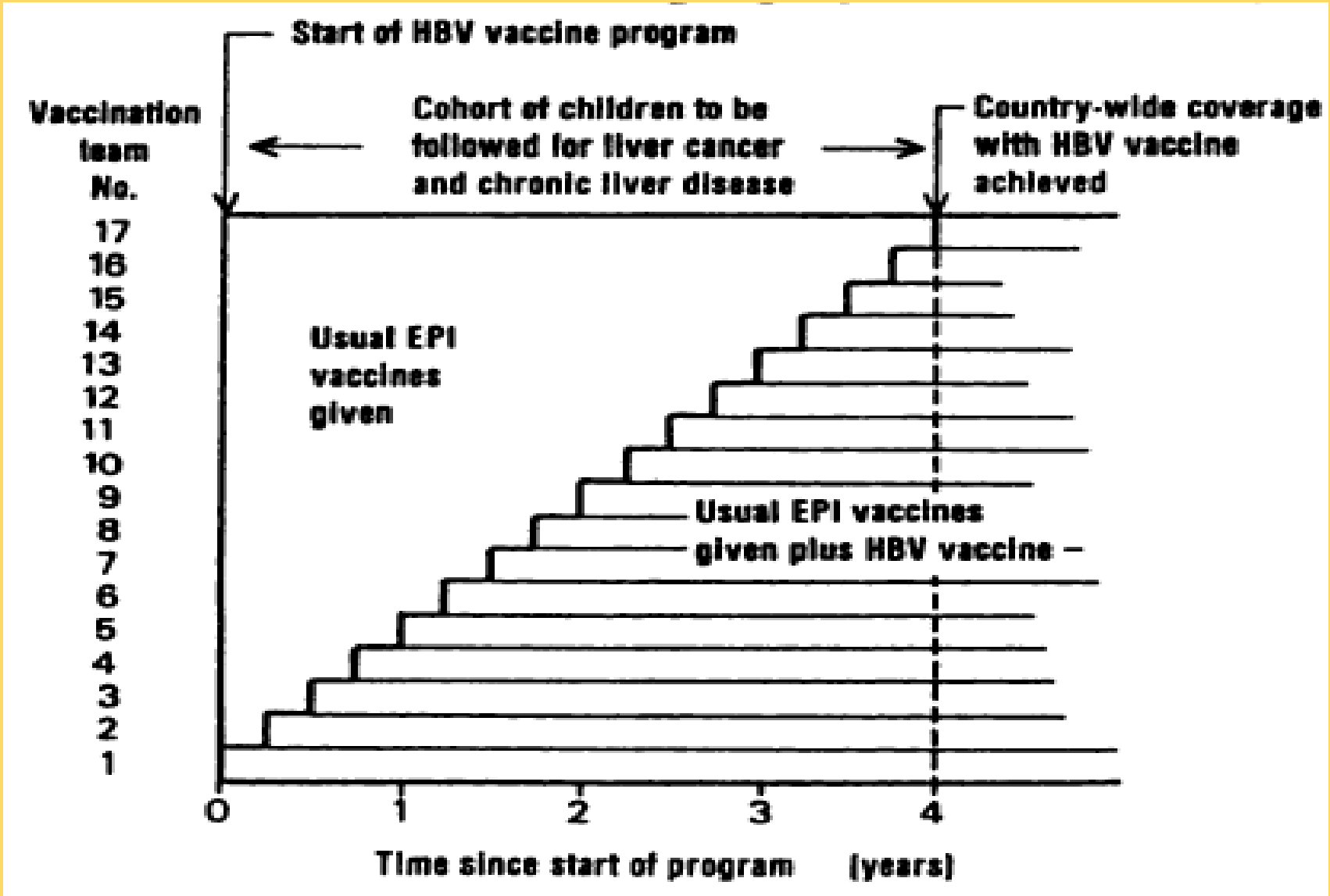
- Population 1 million.
- HBsAg carriage: children 10%, adults15%.
- Transmission horizontal.
- Aflatoxin exposure very high.
- HCC rates: males 23 per 100,000/year.

Gambia Hepatitis Intervention Scheme

A partnership between International Agency for Research on Cancer, MRC and The Gambian Government

1986-1990:	**Phase 1**	**Phased introduction of hepatitis B vaccination**
1990-2010:	**Phase 2**	**Establishment of National Cancer Registry;Vaccine efficacy studies**
2010-2035:	**Phase 3**	**Intensive surveillance for Hepatocellular cancer. 35 cases needed.**

Phased introduction of Hepatitis B vaccination in The Gambia. GHIS (1987)



GHIS: additional information

- Vaccine: plasma derived, 4 doses.
- Identification: demographic, hand and foot prints, site of BCG vaccination.
- Nation-wide Cancer Registry started.
- Liver cancer and cirrhosis defined by clinical, ultrasound and biochemical means.

Original Assumptions

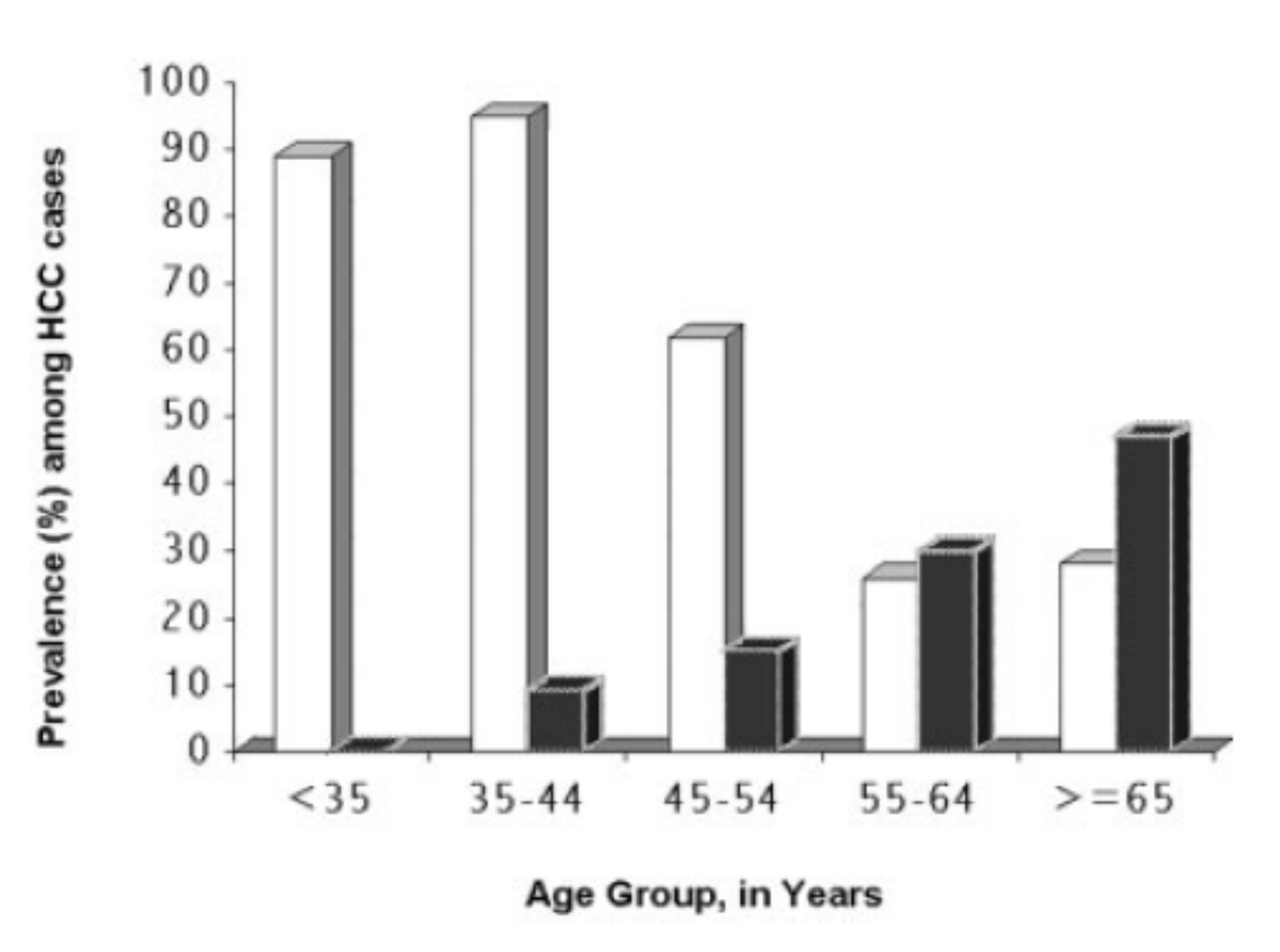
- Vaccine coverage: 85% one, 80% two, 75% three injections.
- Vaccine efficacy: depends on dose, 95% have a durable response after 3 doses.
- Perinatal acquisition :10%, half prevented.
- Attributable risk: 80% HCC under 50 due toHBV.
- Attrition: 50% due to death or migration.

Coverage of HBV vaccine in The Gambia 1990-2008

year	1 dose %	3 doses %
2008	92	92
2007	90	90
2006	95	95
2005	90	88
2004	95	90
2003	99	90
2002	99	90
2001	99	84
2000	89	91
1999	-	90
1998	-	93
1997	-	93
1996	-	-
1995	-	-
1994	-	84
1993	-	45
1992	-	62
1991	-	-
1990	-	**93**

WHO 2008

HBV or HBC markers in HCC patients by age group



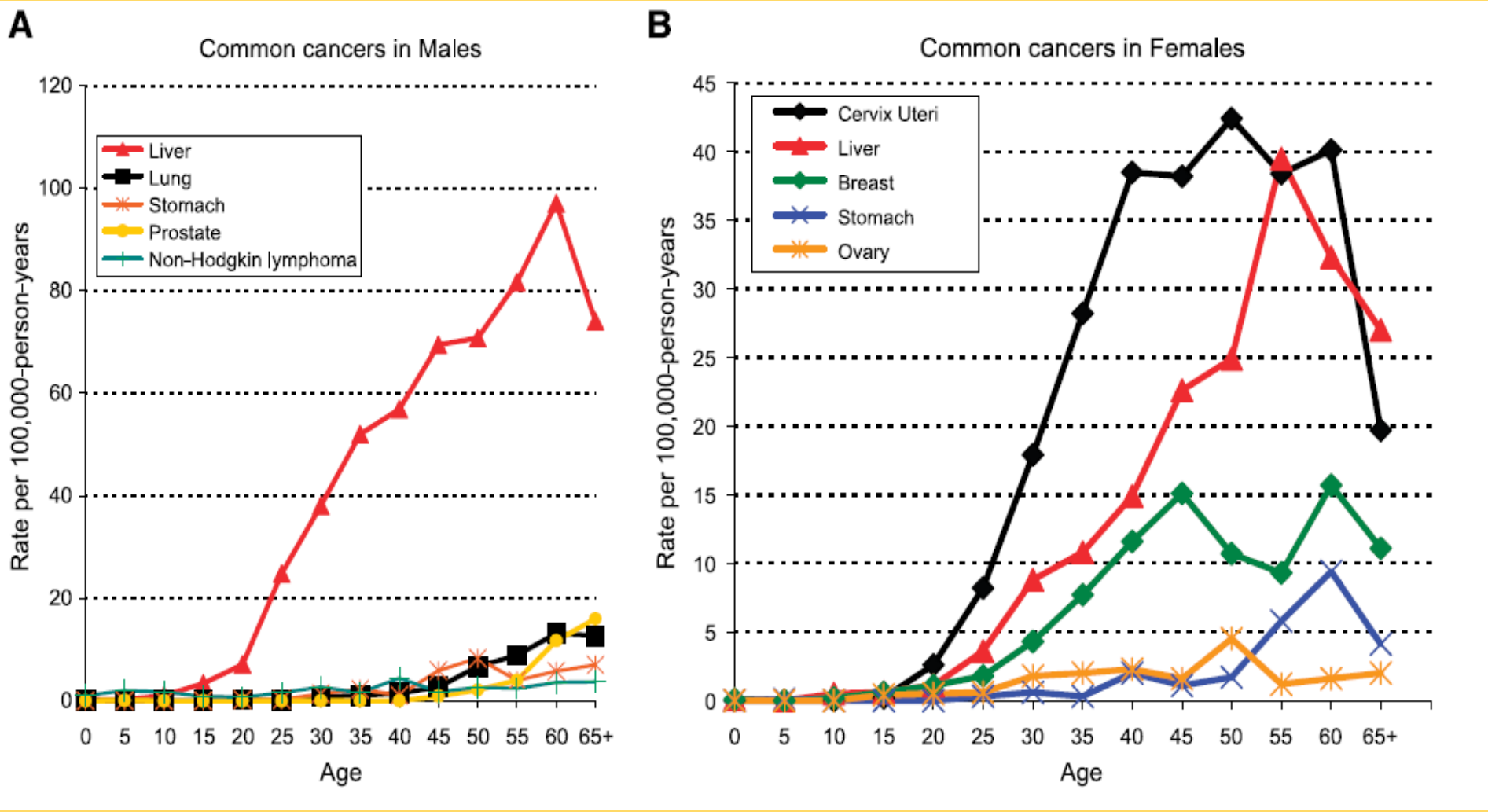
Kirk et al. Hepatology 2004

Table 3. Number of hepatocellular carcinoma cases required in the unvaccinated and vaccinated cohorts to be 95% sure of detecting a difference if the vaccine is truly effective

Protective efficacy	Expected number of cases required*	
	Unvaccinated cohort	Vaccinated cohort
95	13	1
90	15	2
80	21	4
70	29	9
60	42	17
50	65	33
40	109	65
30	205	143
20	487	390
10	2,057	1,851
5	8,443	8,021

GHIS Cancer Research 1987.

Age-specific incidence rates of common cancers in The Gambia: 1987-2002



Viviani et al. 2008.

Table 4. Expected cumulative number of hepatocellular carcinoma cases in GHIS unvaccinated subjects under the hypothesis of 50% attrition, 70% attributable risk (that is, 68% vaccine efficacy against hepatocellular carcinoma)

Age group	M		F		Total (M+F)
	Incidence rates*	Cumulative number of cases	Incidence rates*	Cumulative number of cases	
0-4	0.3	0	0.1	0	0
5-9	0.1	0	0.0	0	0
10-14	0.7	1	0.4	0	1
15-19	3.4	3	0.5	1	4
20-24	5.2	7	0.9	1	8
25-29	16.3	20	3.3	4	24
30-34	25.7	39	7.9	10	49
35-39	39.9	69	8.8	16	85
40-44	46.8	104	13.0	26	130
45-49	72.0	158	17.2	39	197

Abbreviations: M, males; F, females.

*Age-specific incidence rates for HCC in The Gambia, 1987-2002.

Viviani et al. Cancer Epidemiol Biomarkers Prev 2008.

Additional factors that may affect outcome

- Attrition and difficult linkage: 75% identified at 1 year, 58% probably and 38% certainly identified at year 15. Internal migration 30%.
- Inadequate cancer registration and case definition.
- Increase in HIV or HCV incidence?
- Increase in aflatoxin exposure?
- Escape mutants?
- Ineffective HBV vaccination through EPI?

Conclusions

- **GHIS on track to conclude by 2017-2020.**
- **Routine HBV vaccination very successful.**
- **Linkage, cancer registration and clinical identification needs strengthening.**

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- Staff of EPI.
- People of The Gambia.