Liver cancer prevention: HBV vaccination and aflatoxin control

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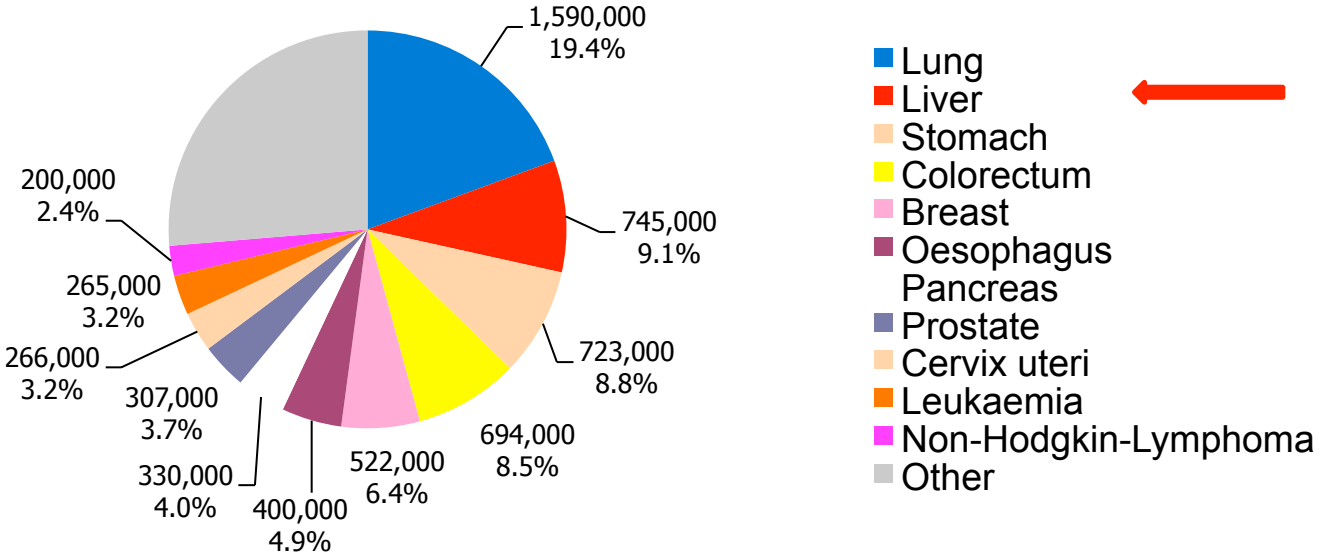
Global Burden of Cancer (2012)

Mortality: 8.2 million deaths worldwide (both sexes)

(2.9 in more developed regions, 5.3 in less developed regions)



Source: GLOBOCAN 2012
http://globocan.iarc.fr

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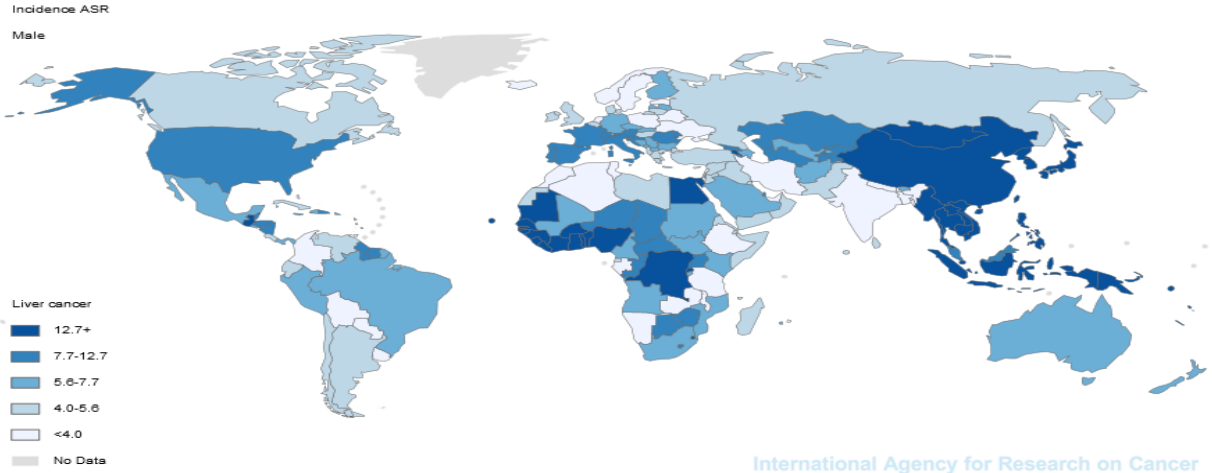
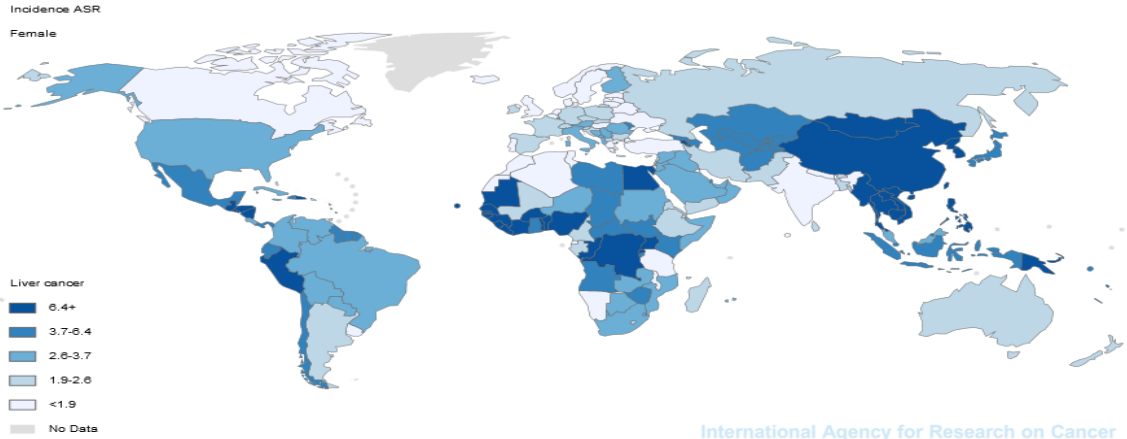


Source: GLOBOCAN 2012 (IARC)



Source: GLOBOCAN 2012 (IARC)

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Incidence of HCC worldwide

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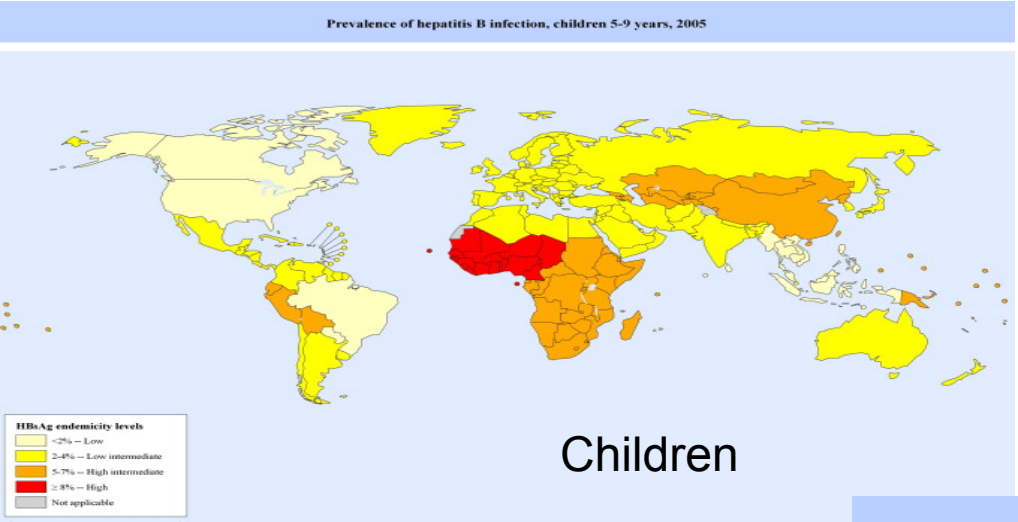
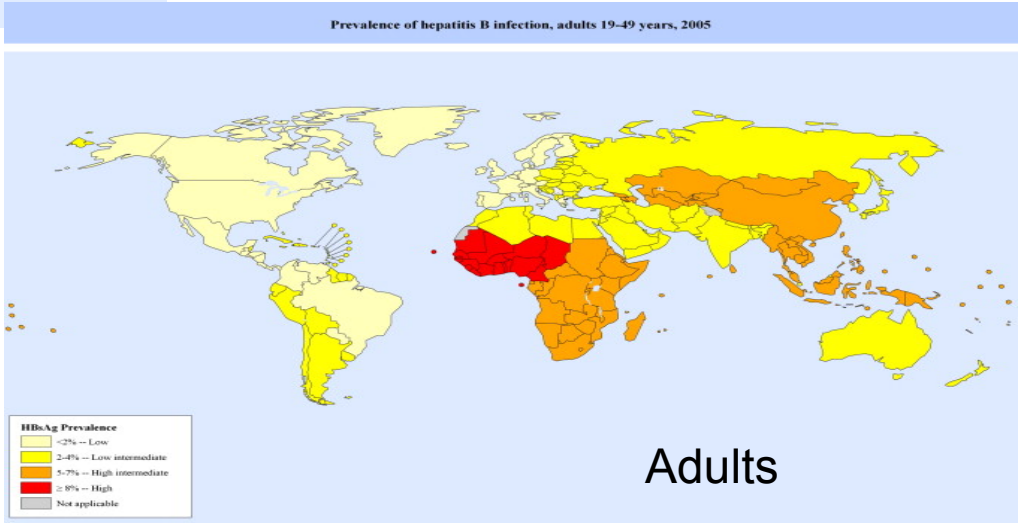
Prevalence of HBV infection worldwide



Children



Adults

J.J. Ott , G.A. Stevens , J. Groeger , S.T. Wiersma (2012) Vaccine, 30: 2212 - 2219

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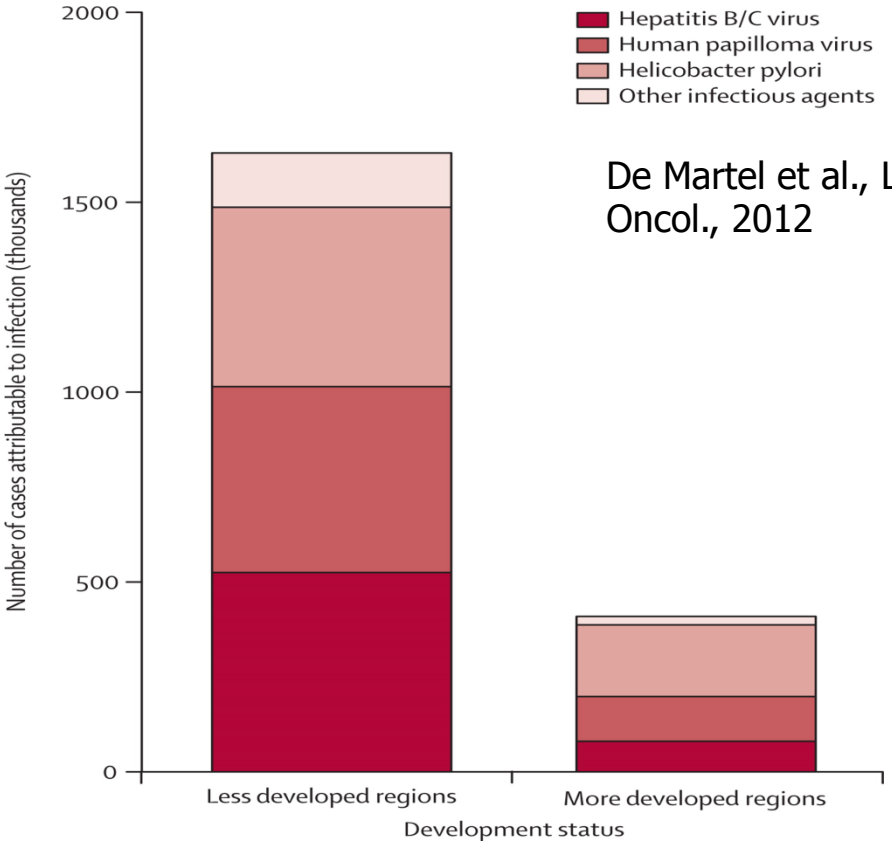
Cancers attributable to infections (2008)

570,000 liver cancer cases linked to HBV and HCV



De Martel et al., Lancet Oncol., 2012

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Decreased incidence of HCC following HBV vaccination

Birth Cohort	Person-yrs	No. HCC	RR*
Non-vaccinated	78 496 404	444	1.00
Vaccinated	37 709 340	64	0.31 (0.24 – 0.41)

* Age and sex-adjusted relative risk

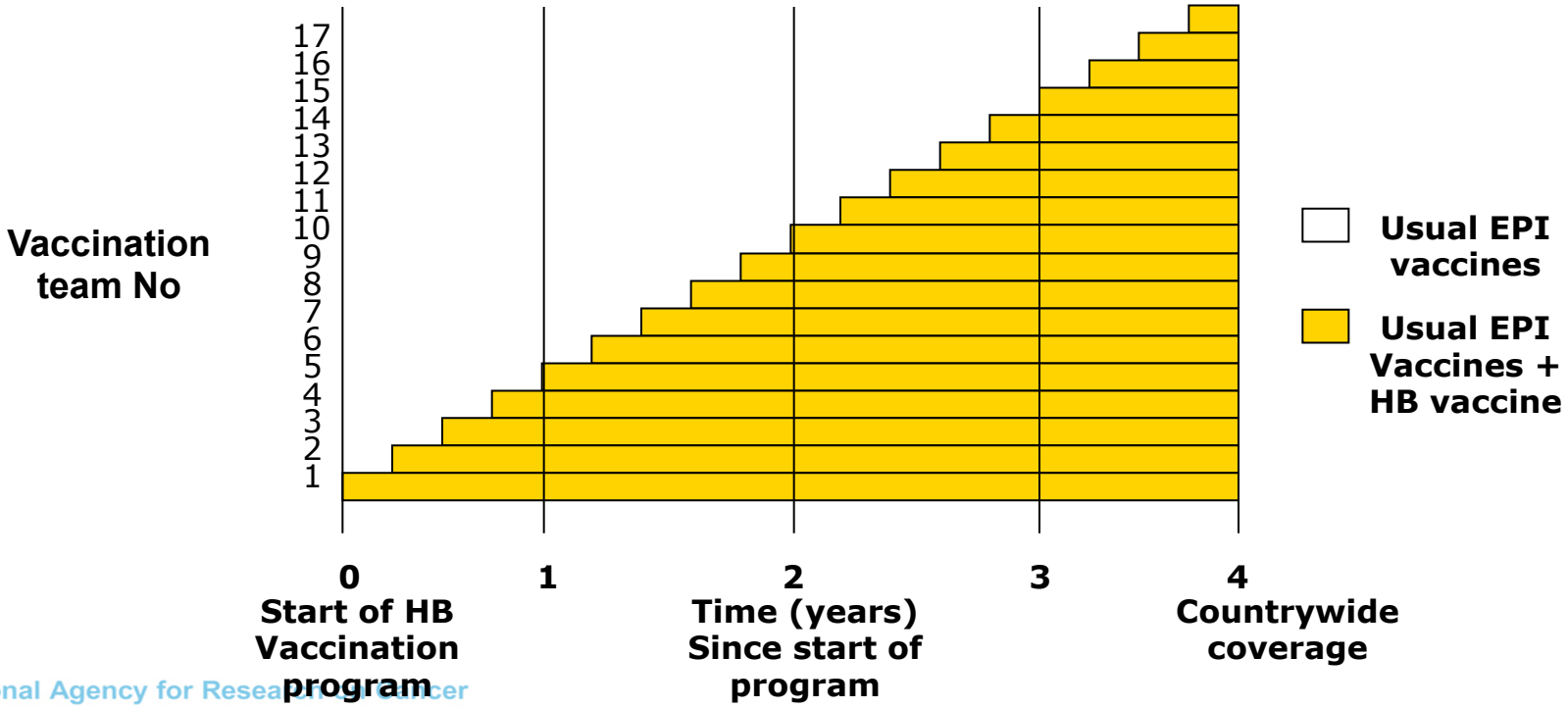
- Universal HBV vaccination introduced in Taiwan in 1984
- Vaccine coverage rate >90%
- Identified children aged 6-19 years diagnosed with HCC
- Compared HCC in vaccinated versus unvaccinated birth cohorts

Gambia Hepatitis Intervention Study – randomized trial of HBV vaccine

- Evaluation of the HBV vaccine to prevent liver disease and liver cancer
- Begun in mid-1980s including ~120,000 children – expected results in next 5-10 years
- Identification of cases through the Gambian National Cancer Registry

•Collaboration between IARC, MRC UK and The Gambian Government

Stepped wedge design for introducing HBV vaccine in the EPI



Impact of routine EPI on chronic HBV infection in The Gambia

Age	HBsAg-	HBsAg+	Percentage	Total
1.0-4.9	1,918	3	0.2	1,921
5.0-9.9	1,585	6	0.4	1,591
10.0-14.9	815	10	1.2	825
15.0-18.5	271	5	1.8	276
Total	4,589	24	0.5	4,613

Peto TJ, Mendy M., Lowe Y., Webb EL., Whittle HC and Hall AJ (2014) BMC Infectious Diseases 14: 7

Aflatoxins and human health

Widespread exposure through contamination of staple foods (cereals and nuts):

- Aflatoxicosis
- Liver cancer
- Growth impairment
- Immune modulation?

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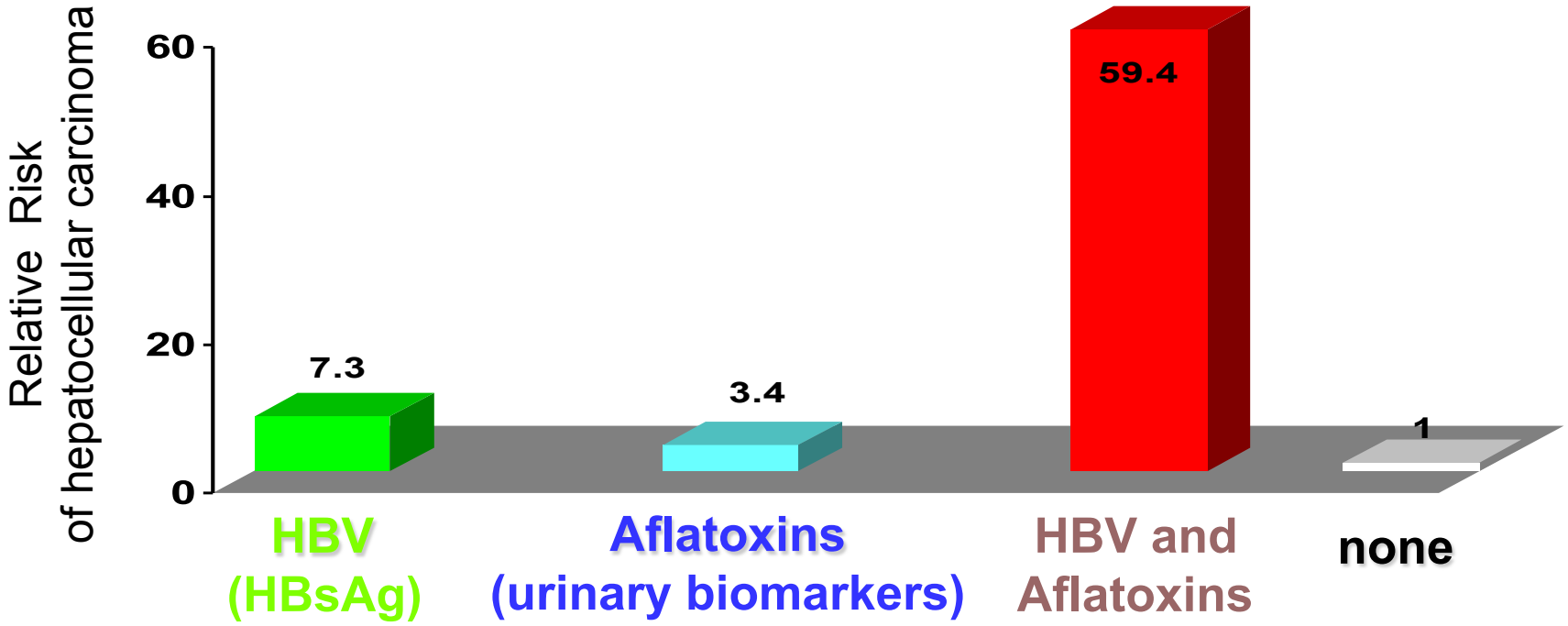
See Wild and Gong, Carcinogenesis 31, 71-82, 2010

Interaction between HBV infection and aflatoxins in HCC



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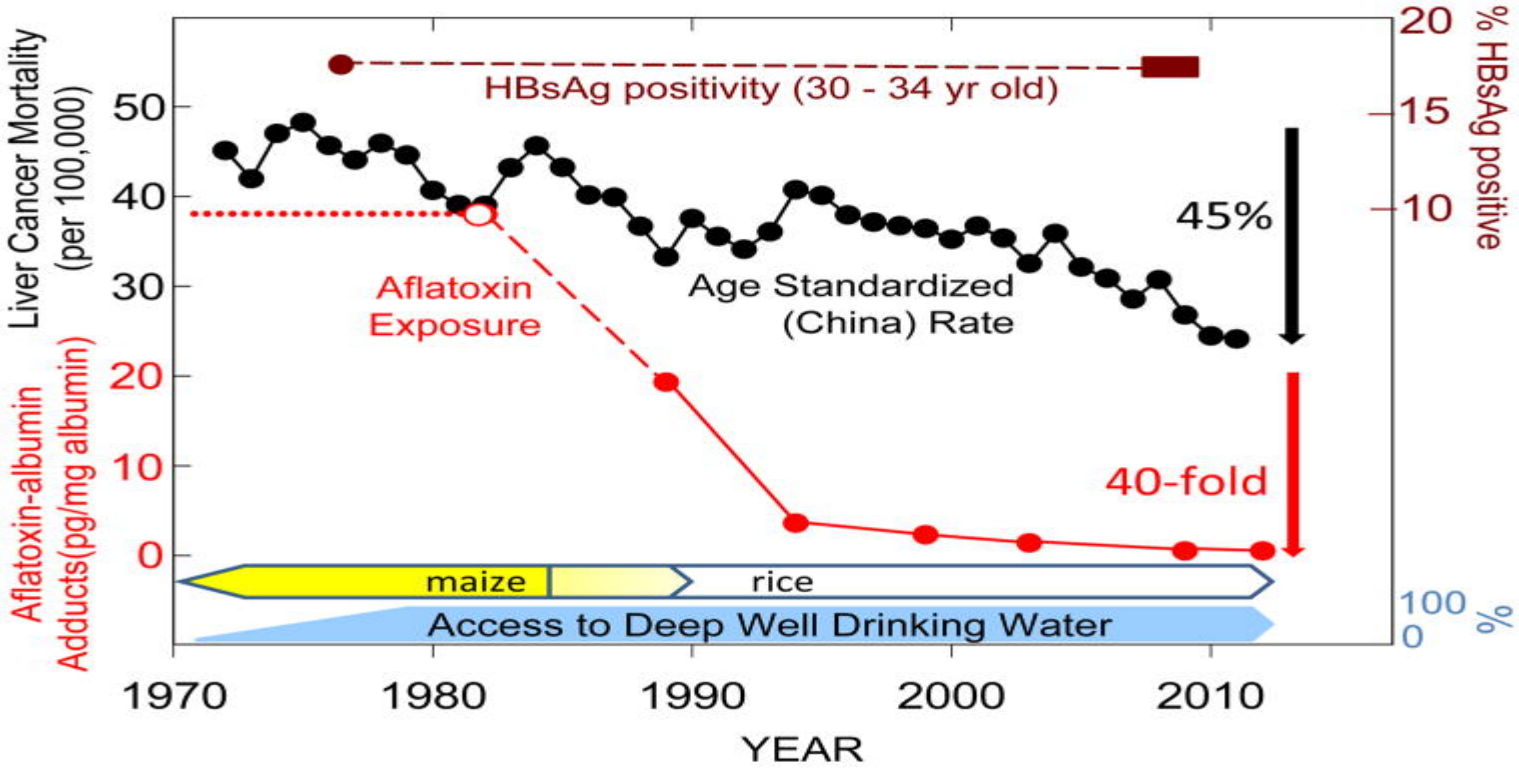
adapted from Qian et al, CEBP 1994, following Ross et al., Lancet 1992

Reduced aflatoxin exposure and falling liver cancer rates in China



IARC – scientific evidence review for aflatoxin control

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- Summary of evidence:
  - occurrence,
  - adverse effects and
  - available interventions

Optimum strategies for aflatoxin control and reducing liver cancer incidence

Aflatoxin Intervention

Individual Level

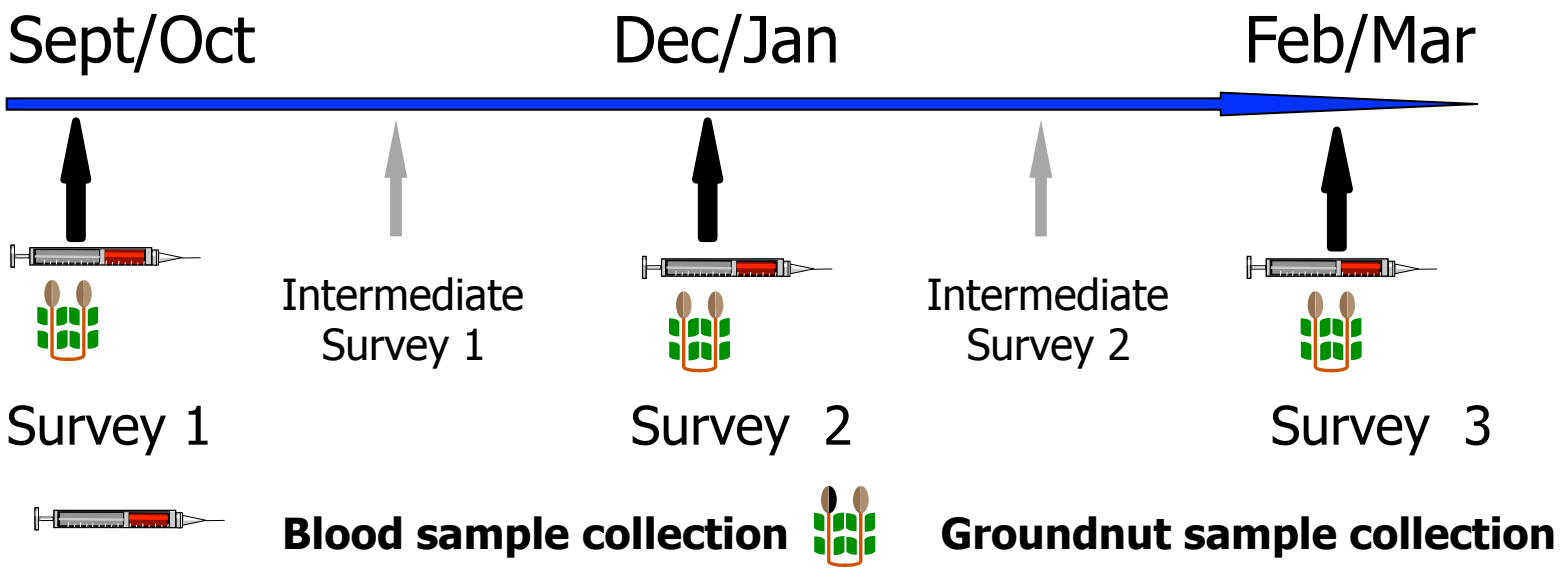
- **Dietary Change**
- **Chemoprevention**
  (e.g. modified metabolism, absorptive clays)

Community Level

- **Pre-harvest**
  Genetic resistance in crops- natural/GM
  Biocontrol e.g. atoxigenic strains
  Agricultural practices (reduce crop stress- irrigation, insecticides, fungicides)
- **Post-harvest**
  improved drying, sorting and storage

Biomarkers and intervention studies – aflatoxin in subsistence farms in Guinea

20 Villages (10 intervention, 10 control), 30 subjects per village

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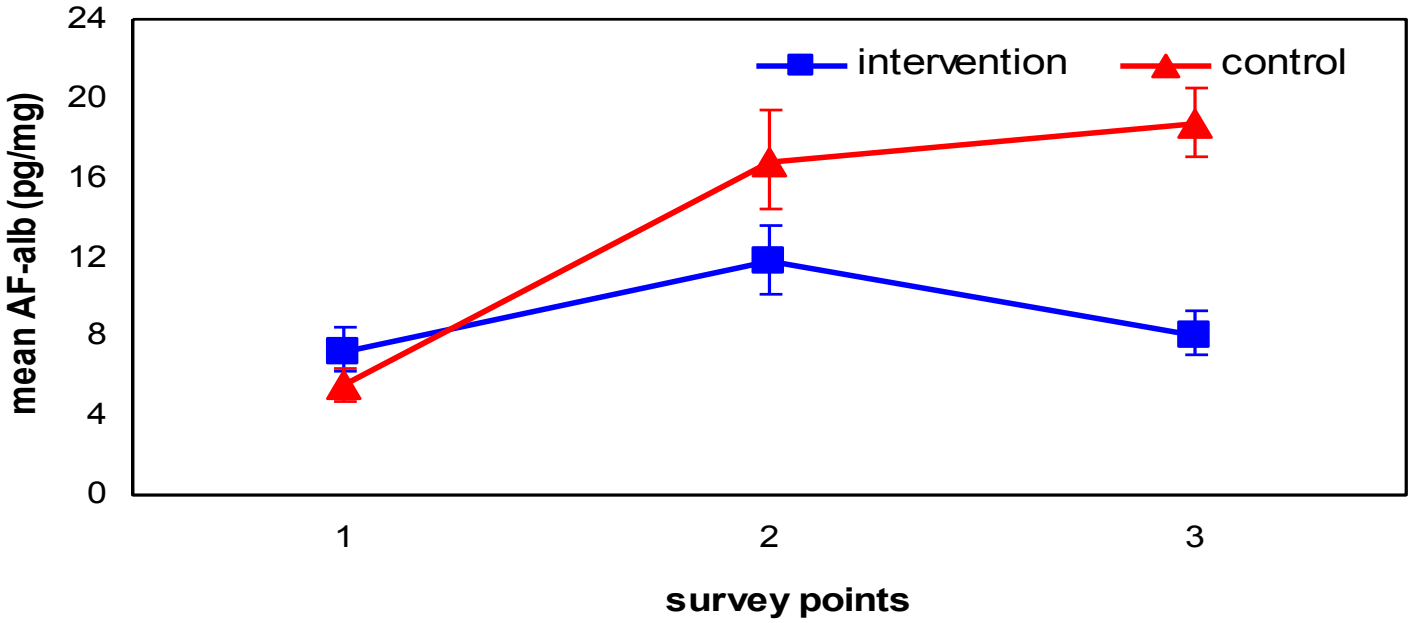
Mean blood levels of aflatoxin are reduced in individuals following intervention



Turner et al., (2005) The Lancet, 365, 1950-1956

IARC Working Group: evaluation of interventions against aflatoxins (June 2014)

1. Sufficient evidence for implementation
2. Needs more field evaluation
3. Needs formative research
4. No evidence/ineffective

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Approach	Grade	Comments
Storage, sorting and agronomic techniques	1	Ready to implement; requires use of package of measures developed with end-users
Sorting	1	Acceptable but requires formal training; concern over rejected food use
Nixtamalization	1	Requires water for washing; not adapted from Latin America to Africa or Asia
Biocontrol *(non-aflatoxigenic strains)*	2	Requires evidence of consistency of effect across geography and users; concern over genetic recombination
Chemoprevention *(broccoli, dithiolethiones, green tea)*	2	Locally acceptable products needed; possible use in toxic outbreaks
Adsorbents *(clays, chlorophyll)*	2	Delivery strategies; possible use in toxic outbreaks; effects on infants, children, pregnant women?
Genetic resistance	3/4	Large environmental effects on phenotype; resistance is polygenic