

# **Vaccines and vaccination against Yellow Fever**

WHO Position Paper – June 2013

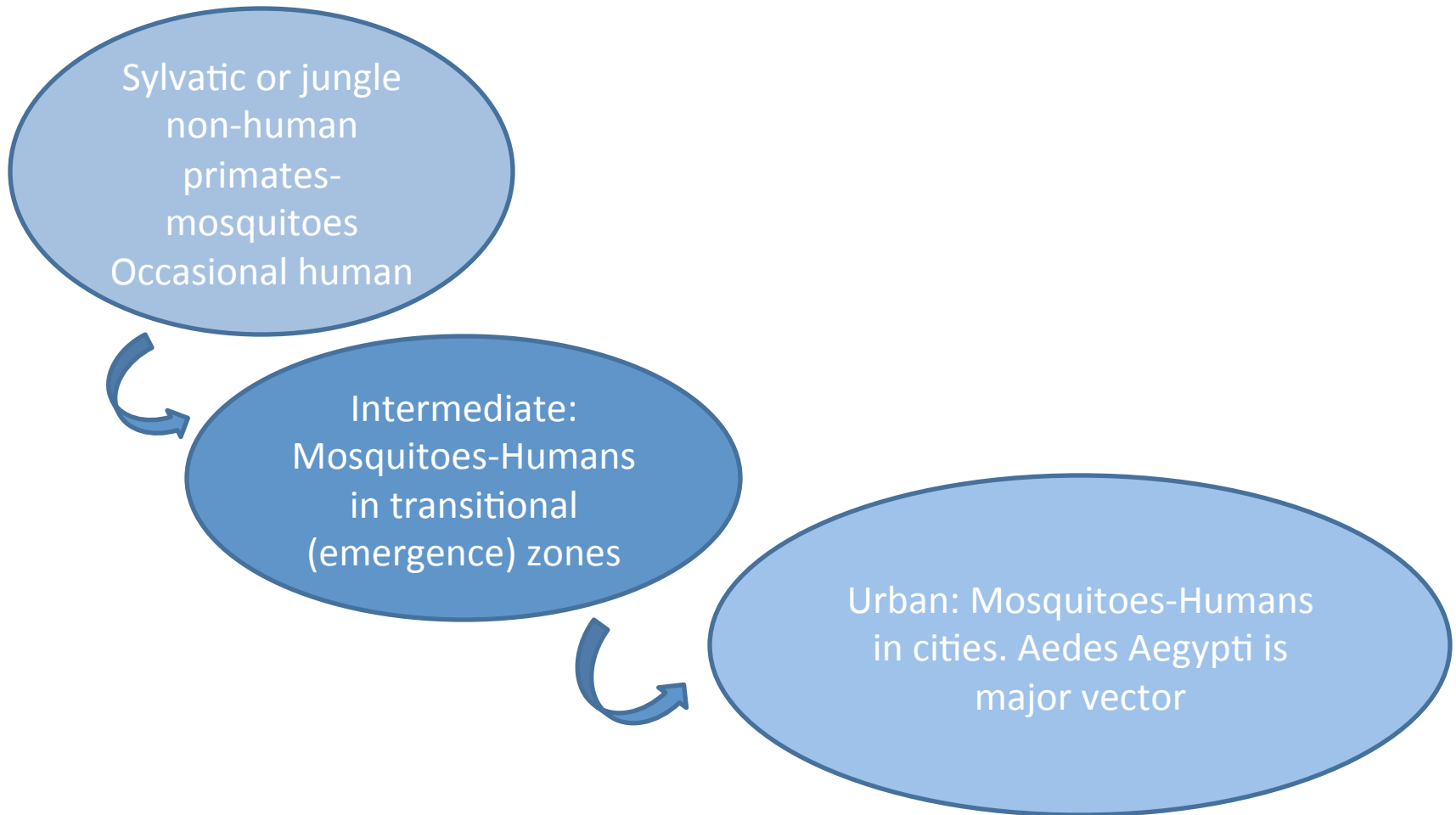


World Health  
Organization

# Yellow fever epidemiology

- A mosquito-borne viral disease of humans and other primates.
- Endemic in 44 countries (2013) in Africa and South America.
- 200 000 cases of YF, with 30 000 deaths, are expected globally each year.
- The majority of cases and deaths occur in sub-Saharan Africa.

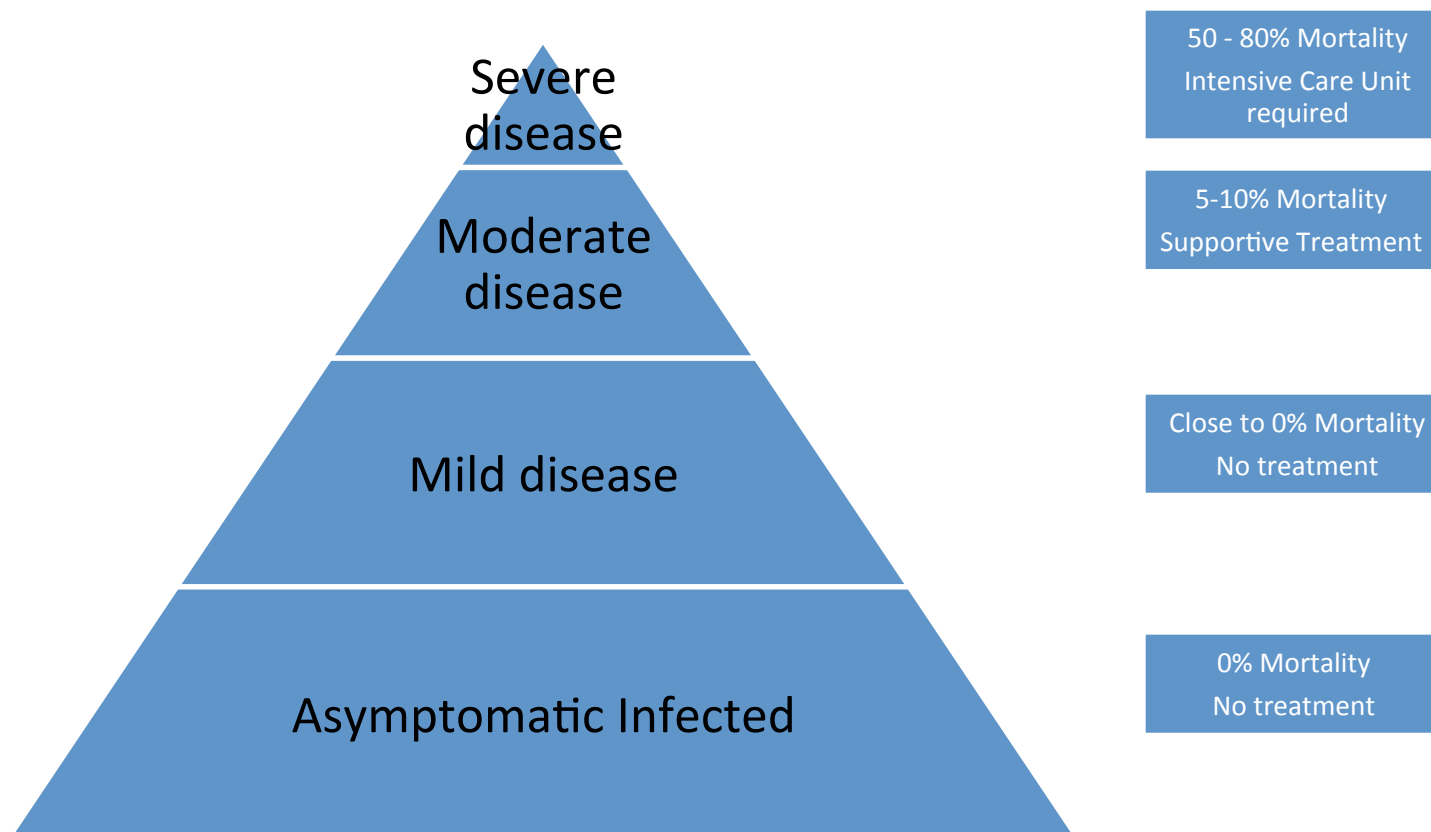
# Yellow fever transmission patterns



# Yellow fever disease

- YF virus infection causes a wide spectrum of disease-from nil or mild symptoms to severe illness with bleeding, jaundice and, ultimately, death.
- Symptoms appear 3–6 days after a mosquito bite, typically sudden onset fever, muscle pain, backache, headache, shivering, anorexia, nausea, vomiting.
- There is no specific curative treatment for YF; Treatment is supportive.

## Proportion with different clinical presentations, associated mortality and treatment required



Source: Up-date on Yellow Fever Management and Treatment (Background paper) Eduardo Gotuzzo, Maria Alejandra Mena

# Yellow fever vaccines

- All current YF vaccines are live attenuated viral vaccines from the 17D lineage
- Single dose (0.5 ml) only
- Injected either subcutaneously or intramuscularly
- May be administered simultaneously with other vaccines
- Protection appears to last for life

## Impact of vaccination

Large scale YF vaccination has been very effective. However, where coverage has not been sustained, the disease has recurred.

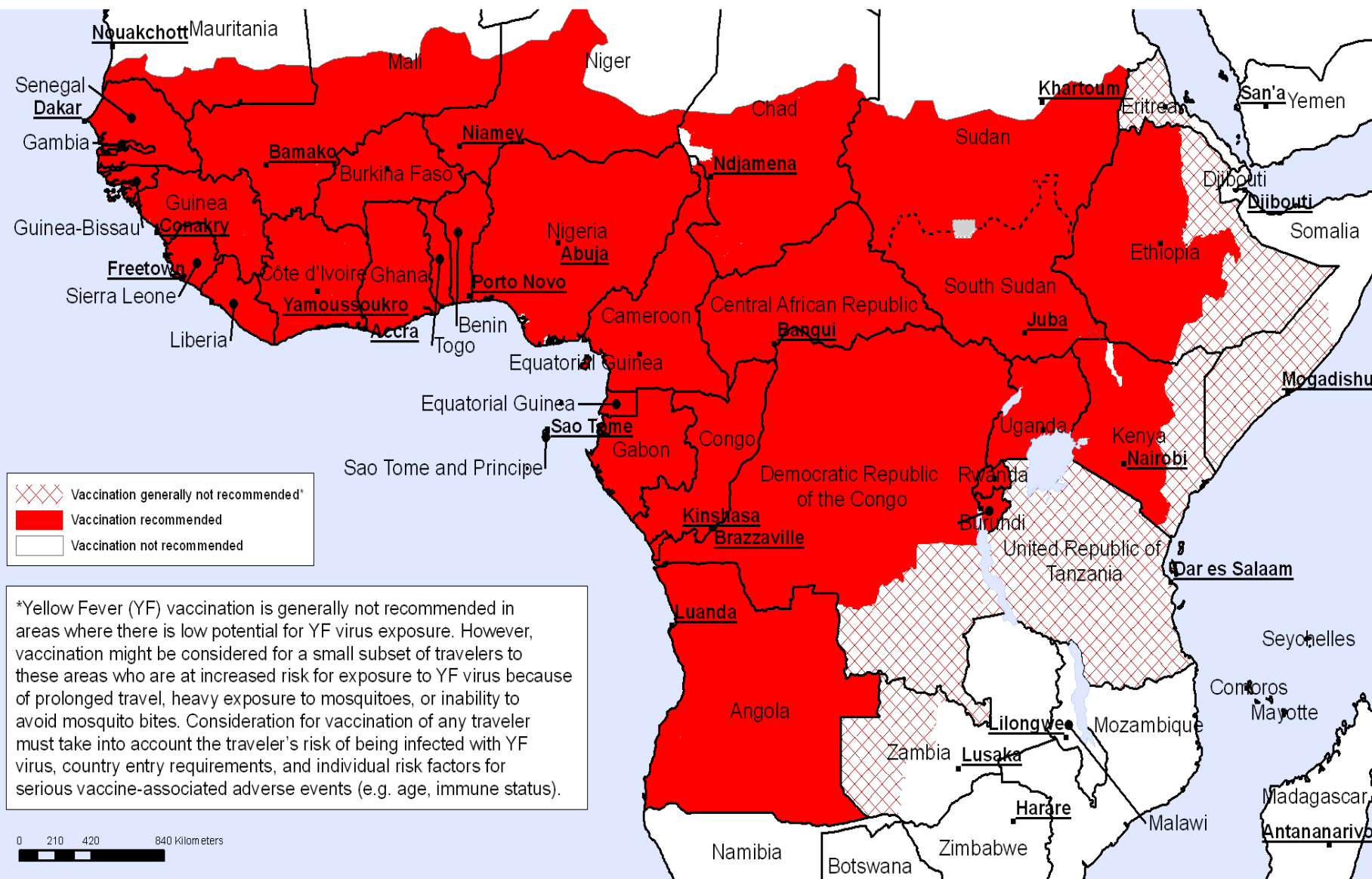
Table shows estimated numbers in thousands, (95% confidence intervals) of yellow fever infections, cases and deaths in 32 African countries. Numbers of infections, cases and deaths predicted to be averted in 2013 by mass vaccination programme are also shown.

Year	Infections	Cases*	Deaths
1995	1600 (1100 - 2100)	160 (110 - 210)	54 (38 - 72)
2005	1800 (1200 - 2400)	180 (120 - 240)	62 (43 - 83)
2013	1300 (840 - 1700)	130 (84 - 170)	44 (29 - 60)
Predicted numbers averted in 2013 by GAVI mass vaccination programme			
	460 (350 - 560)	46 (35 - 56)	16 (12 - 20)

\*Cases = matches YF case definition based on jaundice

Source: Garske et al 2013 [http://www.who.int/csr/disease/yellowfev/YellowFeverBurdenEstimation\\_Summary2013.pdf](http://www.who.int/csr/disease/yellowfev/YellowFeverBurdenEstimation_Summary2013.pdf)

# Yellow Fever Vaccination Recommendations in Africa, 2011



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization  
Map Production: Public Health Information and Geographic Information Systems (GIS)  
World Health Organization



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# Adverse events following immunization (AEFI)

## AEFI with YF vaccine fall into 3 categories

Immediate severe hypersensitivity or anaphylactic reactions.

YF vaccine-associated neurologic disease (YEL-AND).

YF vaccine-associated viscerotropic disease (YEL-AVD).

# YEL-AND and YEL-AVD

- All reported cases of YEL-AND and YEL-AVD have been in primary vaccinees
- Reported rate for YEL-AND:  
0.25–0.8 per 100 000 vaccine doses
- Reported rate for YEL-AVD:  
0.25 to 0.4 per 100 000 vaccine doses.

# WHO position

- Yellow Fever vaccination is performed to :
  - I. protect populations living in areas subject to endemic and epidemic disease;
  - II. protect travellers visiting these areas;
  - III. prevent international spread by viraemic travellers.
- A single dose of YF vaccine is sufficient to confer sustained life-long protective immunity against YF disease.
- A booster dose is not necessary.

# WHO position

## Vaccination strategies- endemic countries

- All endemic countries should introduce YF vaccine into their routine immunization programmes, giving it to children at age 9–12 months at the same time as the measles vaccine.
- Preventive mass vaccination campaigns are recommended where there is low vaccination coverage.
- Vaccination should be provided to everyone aged  $\geq 9$  months in any area with reported cases.
- Countries with areas at-risk of YF disease should plan to introduce YF vaccine into their immunization programmes.

# WHO position

## Vaccination strategies-travellers

- YF vaccine should be offered to all unvaccinated travellers aged > 9 months, travelling to and from at-risk areas, unless they belong to a group of individuals for whom YF vaccination is contraindicated

# WHO Position

## Contraindications

- YF vaccine is contraindicated in children aged **<6 months**. It is not recommended for those aged **6–8 months**, *except* during epidemics.
- severe hypersensitivity to egg antigens
- severe immunodeficiency e.g. primary immunodeficiencies, thymus disorder, symptomatic HIV infection or CD4 T-cell values  $<200$  per  $\text{mm}^3$ , malignant neoplasm treated with chemotherapy, recent haematopoietic stem cell transplantation, immunosuppressive drugs (e.g. high dose systemic corticosteroids, alkylating drugs, antimetabolites, TNF- $\alpha$  inhibitors, IL-1 blocking agent), and current or recent radiation therapies.

# WHO position

## Precaution-age over 60 years

- The overall risk of adverse effects is higher in primary vaccinees  $\geq 60$  years of age, but remains low. A risk benefit assessment should be performed, taking into consideration the following:
- the risk of acquiring YF disease (e.g. location, season, duration of exposure, occupational and recreational activities, and local rate of virus transmission in the potential area of exposure)
- the risk of a potential adverse event following immunization (e.g. age, underlying medical conditions, medications being taken).

# WHO position

## Individuals infected with HIV

- YF vaccine may be offered to asymptomatic HIV-infected persons with CD4 T-cell counts  $\geq 200$  cells/mm<sup>3</sup>.
- YF vaccine may be administered to all clinically well children: HIV testing is not a pre-requisite for vaccination.



# WHO position

## Pregnant and lactating women

A risk-benefit assessment should be undertaken for all pregnant and lactating women noting that:

- In YF endemic areas the benefits of YF vaccination outweigh the risk of potential transmission of vaccine virus to the fetus or infant.
- Pregnant women and nursing mothers should be counselled on the potential benefits and risks of vaccination; lactating women should be advised that the benefits of breastfeeding far outweigh alternatives.
- Vaccination is recommended, if indicated, for pregnant or breastfeeding women travelling to endemic areas when such travel cannot be avoided or postponed.

# WHO position

## Co-administration

- YF vaccine may be administered simultaneously with other vaccines.
- As a general rule, any live vaccine may be given either simultaneously or at an interval of 4 weeks.
- Oral polio vaccine may be given at any time in relation to YF vaccination.

# WHO position

## Surveillance

- YF control strategies should include sound epidemiologic surveillance, supported by appropriate diagnostic facilities, for both YF disease and adverse events following immunization.
- Surveillance and clinical studies should be used to identify specific risk groups (such as infants or HIV-infected patients) that may benefit from a second or booster dose.
- Additional data is needed on YF vaccine safety and immunogenicity including persistence of immunity in HIV-positive adults and children.
- Well-designed and adequately-powered studies are needed to assess co-administration of YF vaccine with other live vaccines, including MMR, and to assess the safety and immunogenicity of YF vaccine in pregnant women and in people aged  $\geq 60$  years.
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# WHO position

## Research priorities

- YF vaccination and HIV: Safety and immunogenicity, including persistence of immunity in HIV-positive adults and children.
- Co-administration of YF vaccine with other live vaccines, including MMR
- Safety and immunogenicity of YF vaccine in pregnant women and people aged  $\geq 60$  years.

# Further information

- YF vaccine position paper:

<http://www.who.int/wer/2013/wer8827.pdf>

- Background information presented to the Strategic Advisory Group of Experts on Immunisation (SAGE) April 2013:

[http://www.who.int/immunization/sage/meetings/2013/april/presentations\\_background\\_docs/en/index.html](http://www.who.int/immunization/sage/meetings/2013/april/presentations_background_docs/en/index.html)