



World Health Organization

WHO Centre for Health Development (Kobe)

Advancing the Agenda:

Vaccines for Older Adults

Knowledge, adaptation, implementation

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Director

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- **WHO Ageing and Life Course Department**
- **WHO Regional Office colleagues, and....**
- **WHO Kobe Centre**

Outline

- The need
- Adaptation
- Implementation – Actions to move forward

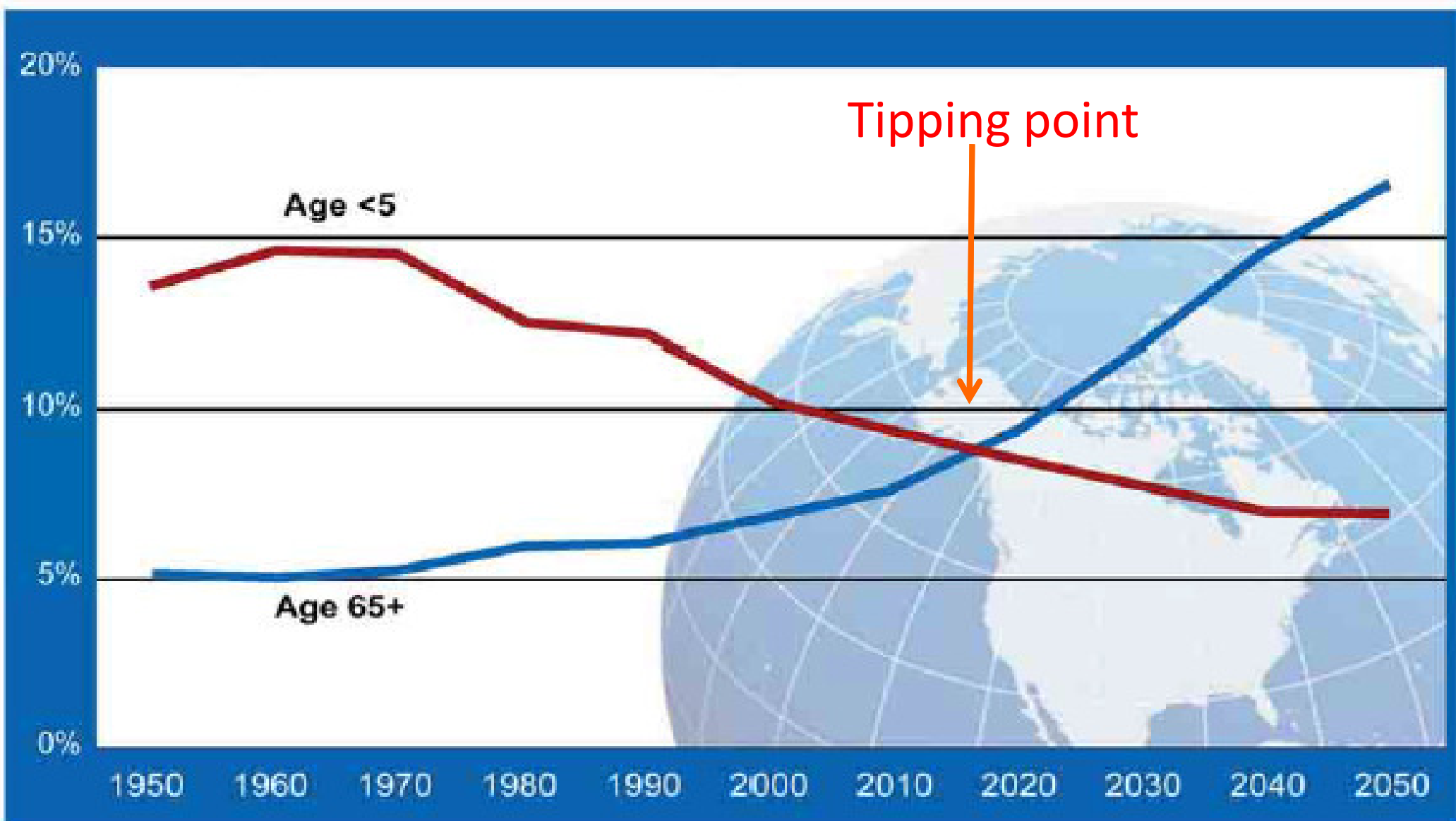
THE NEED



Why vaccinate older persons?

- Proven public health prevention
- Life course approach
- Reduce morbidity, frailty, and early death
- Reduce hospitalizations, suffering
- Enable productivity and ability to work
- Protect carers and youth

Young Children and Older People as a Percentage of Global Population: 1950-2050

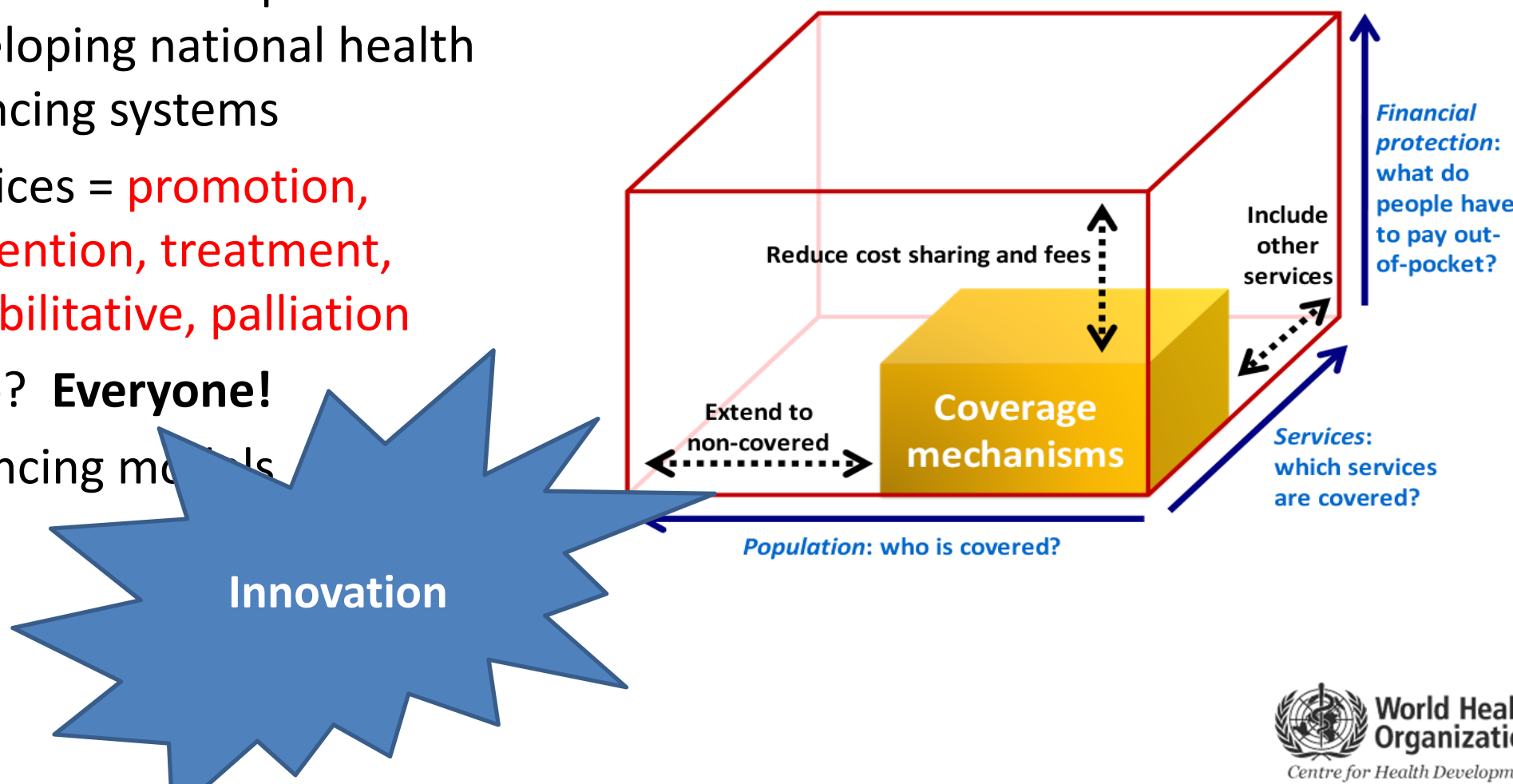


Source: United Nations. *World Population Prospects: The 2010 Revision*.
Available at: <http://esa.un.org/unpd/wpp>.

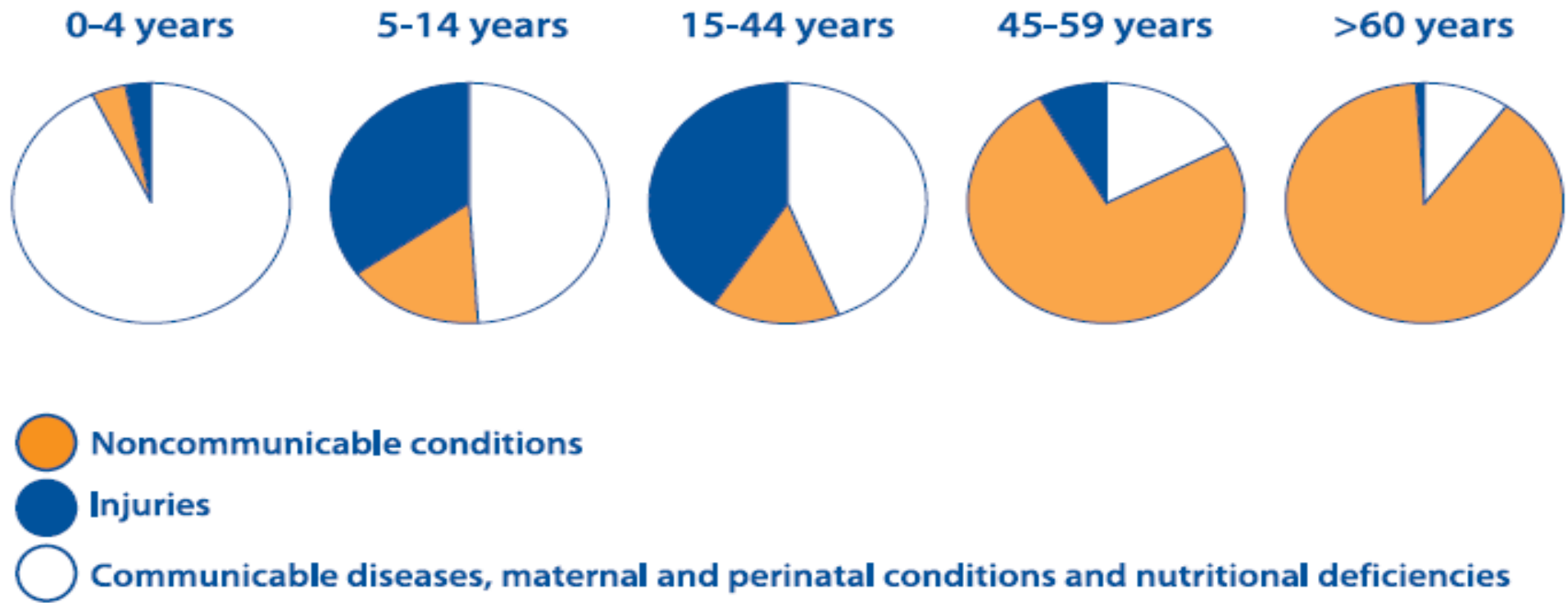
In the context of universal health coverage

- Current increased attention on universal coverage has created some kind of momentum and platform for developing national health financing systems
- Services = **promotion, prevention, treatment, rehabilitative, palliation**
- Who? **Everyone!**
- Financing mechanisms

Towards universal coverage

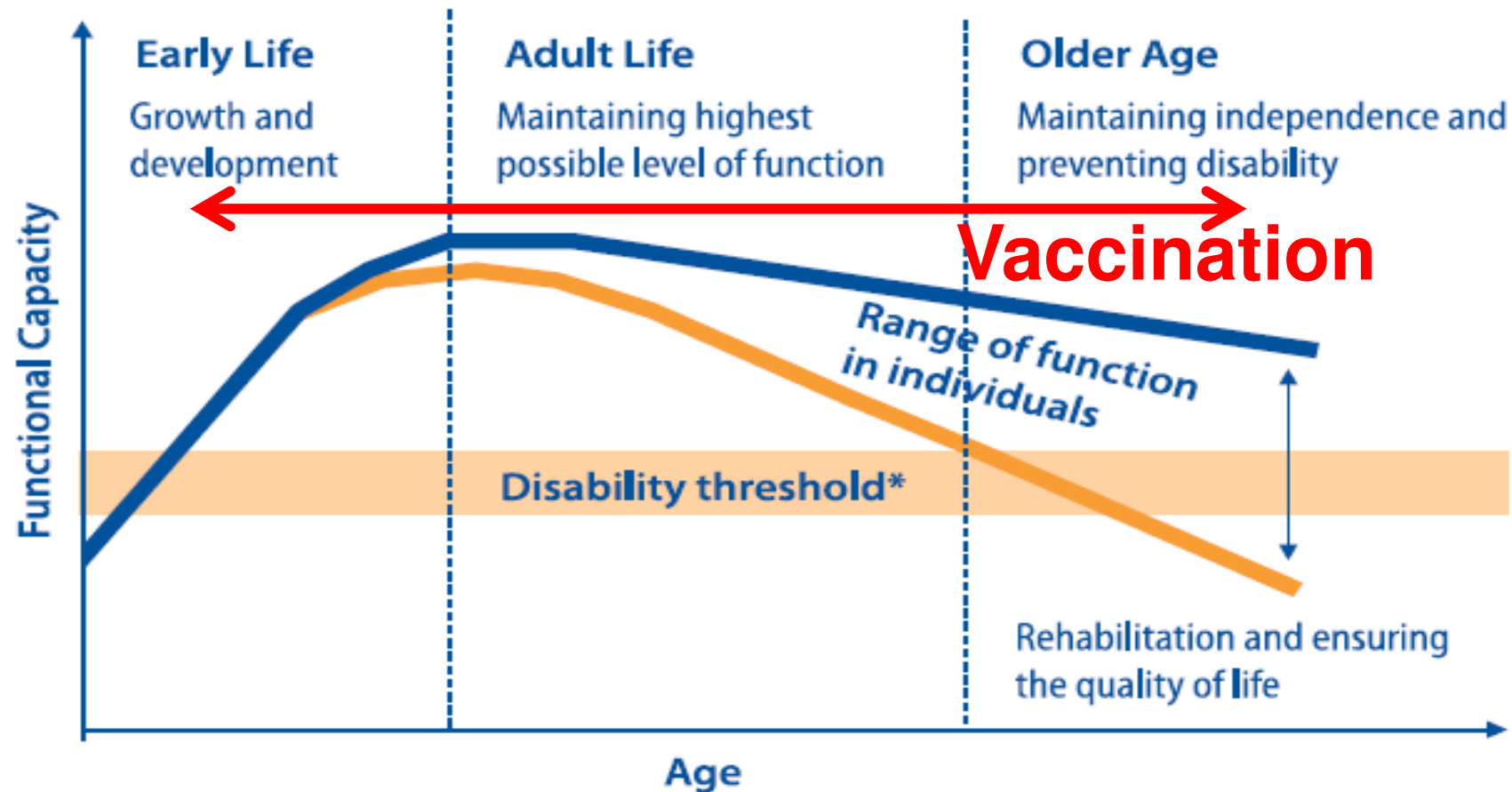


Leading causes of death, low and middle income countries, by age.



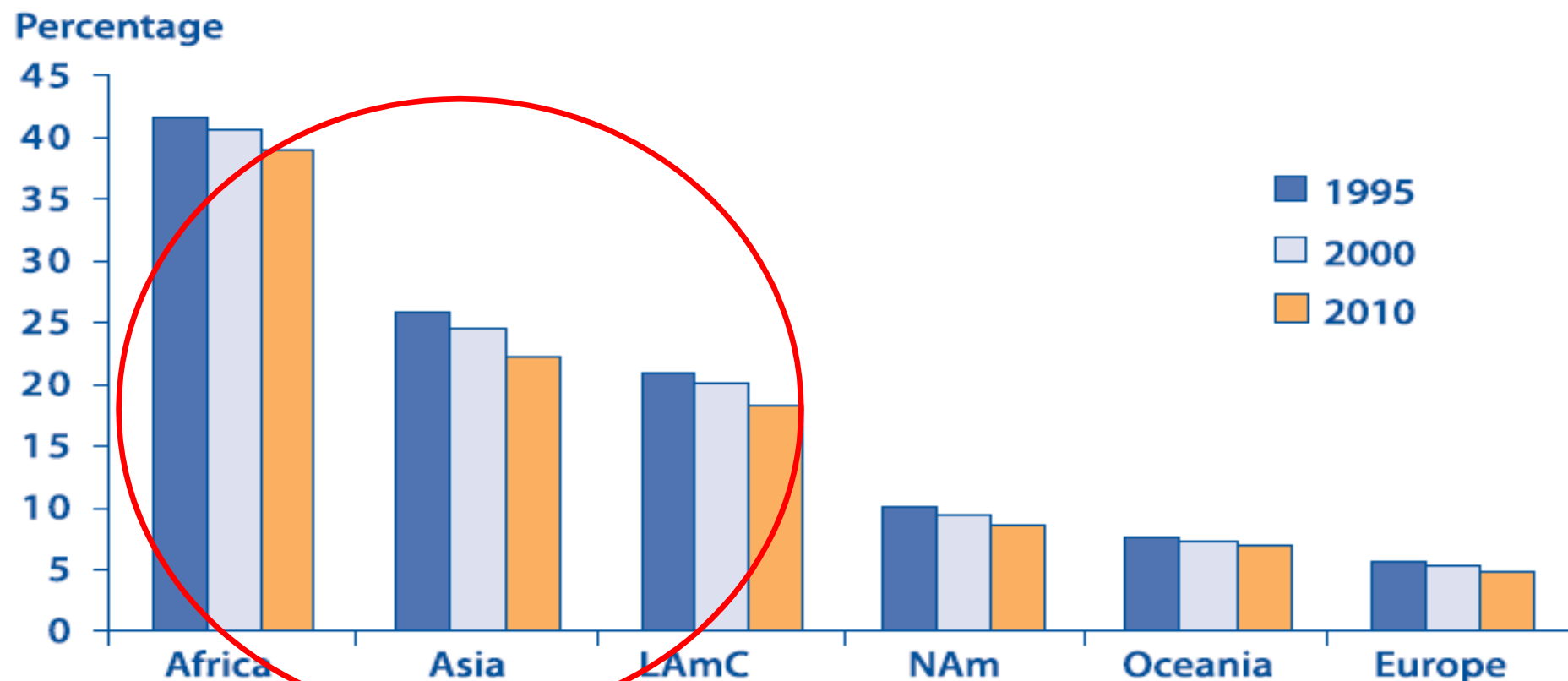
Source: World Health Report 1999 Database

Maintaining functional capacity over the life-course



Source: Kalache and Kickbusch, 1997

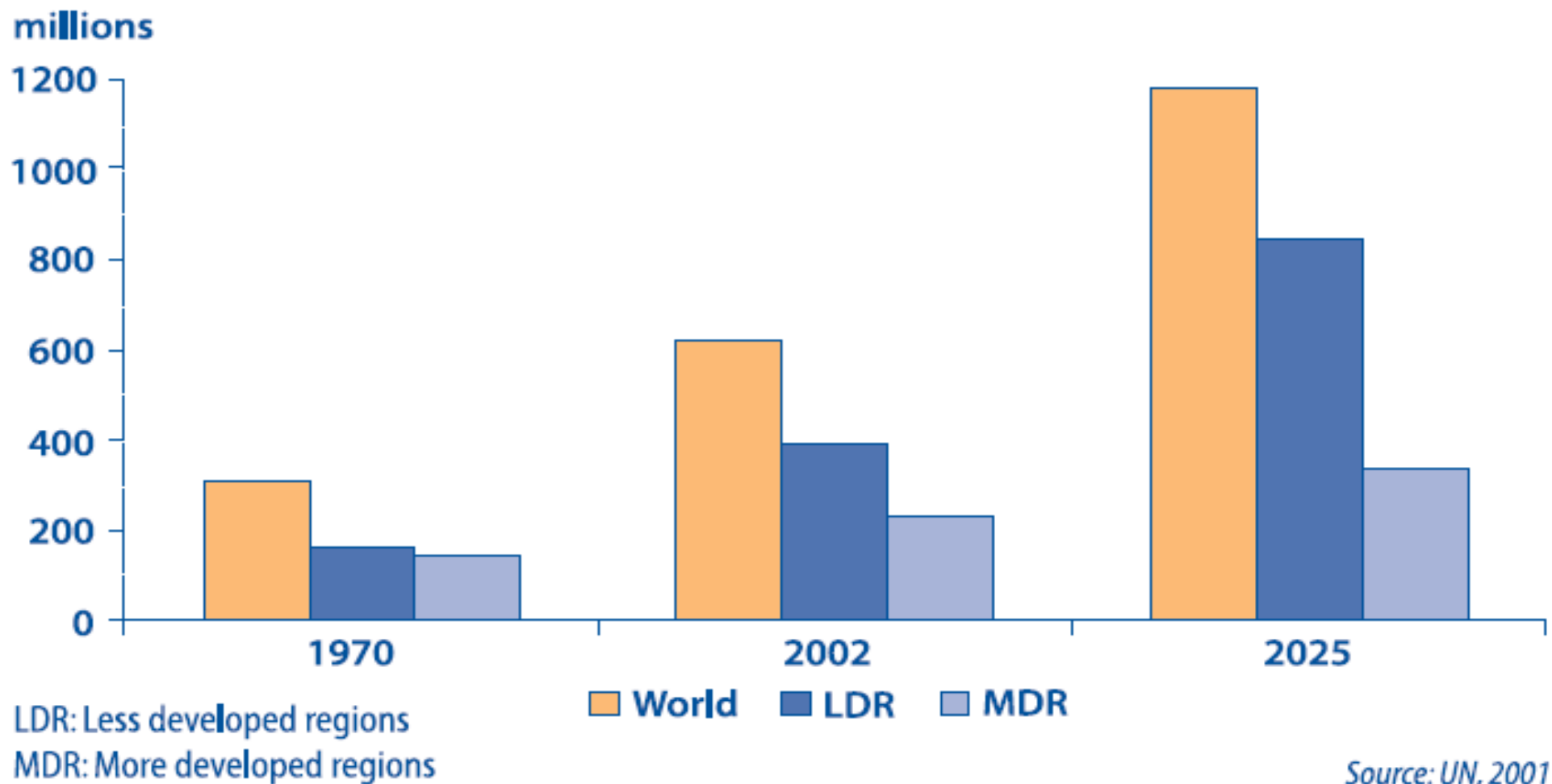
Percentage of labour force participation by people 65 and older, by region



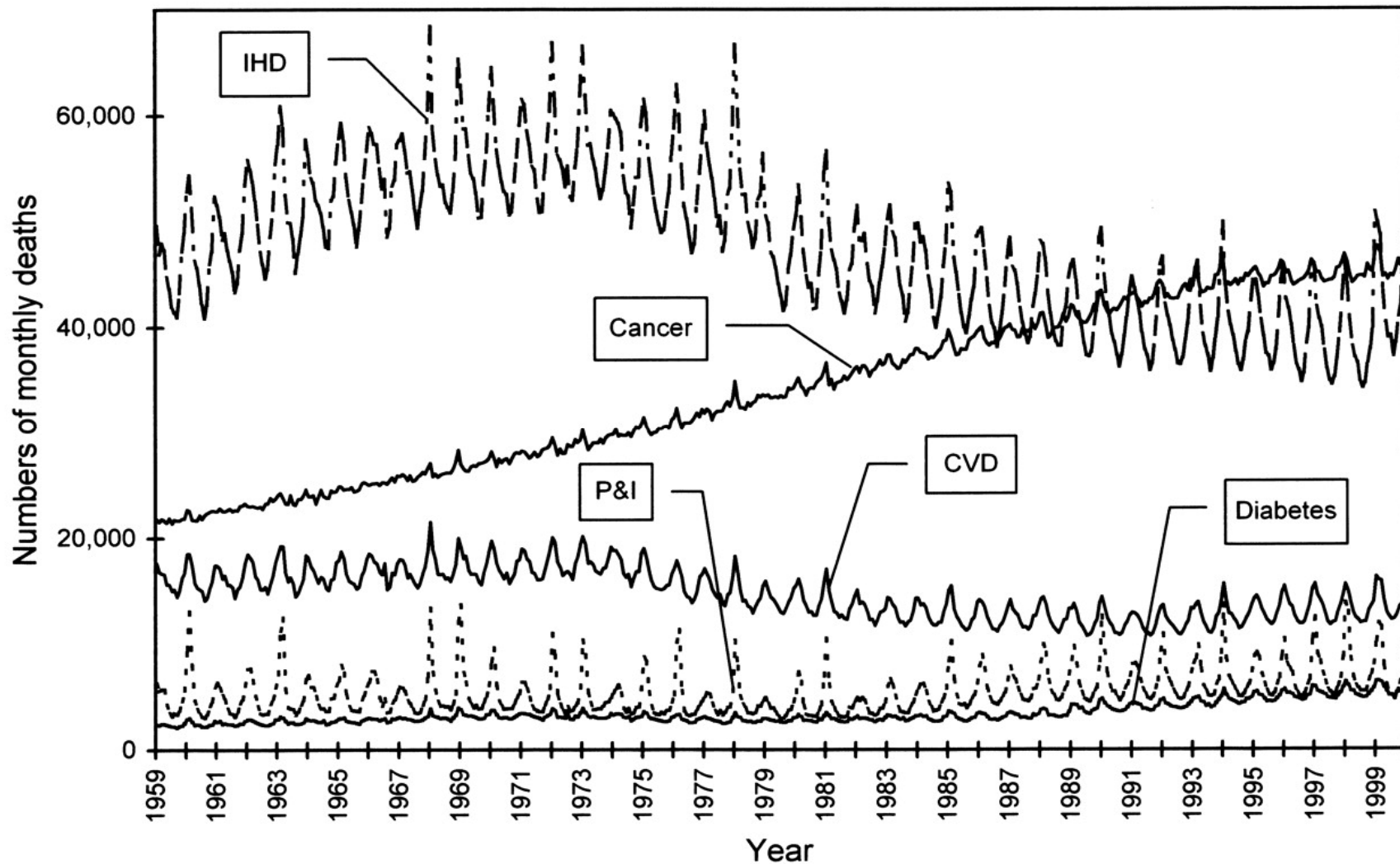
LAmC: Latin America and the Caribbean
NAm: North America

Source: ILO, 2000

The number of people over 60, in less and more developed regions.



Infection may be the trigger that kills...

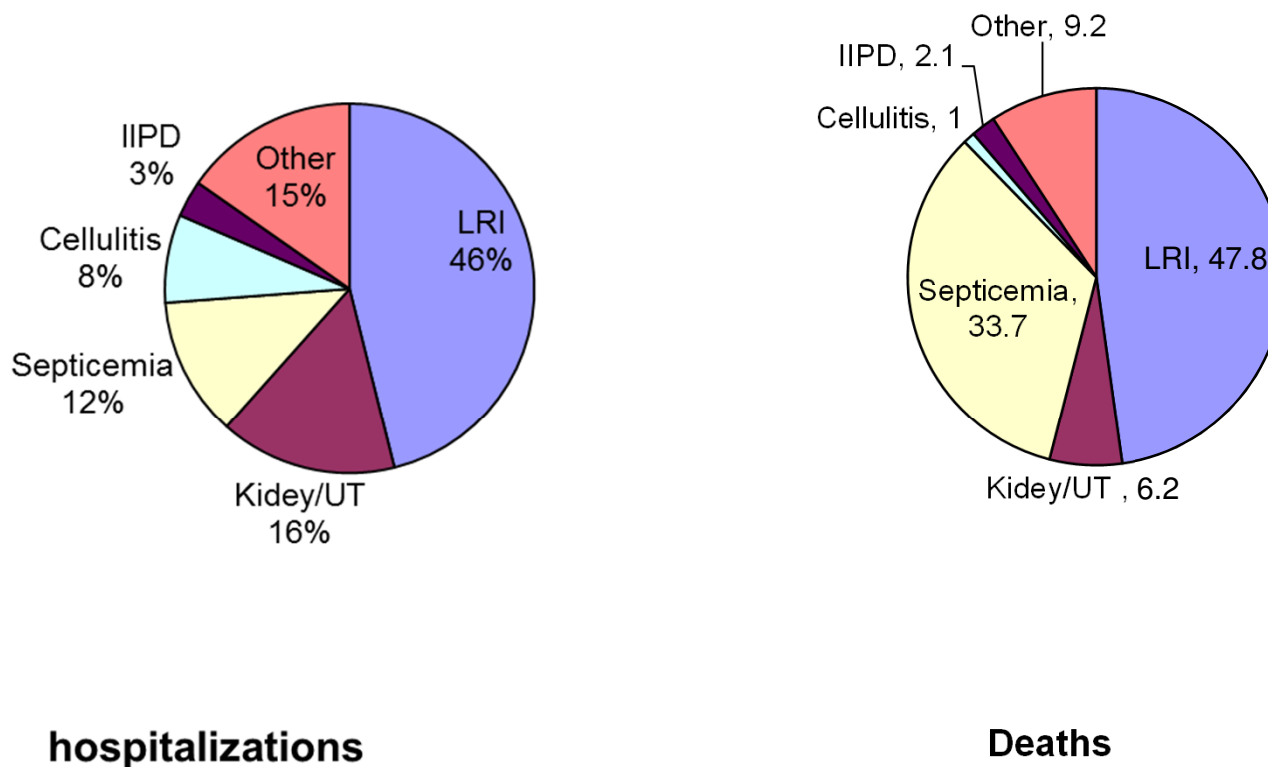


Infection – hospitalization – catastrophic disability

- Catastrophic disability : loss of independence in ≥ 3 ADL
 - 72% who experience catastrophic disability have been hospitalized
- Leading causes of catastrophic disability
 - Strokes
 - CHF
 - Pneumonia and influenza
 - Ischemic heart disease
 - Hip fracture



Infectious disease causing hospitalization or death



In all countries, and in developing countries in particular, measures to help older people remain healthy and active are a necessity, not a luxury.

..and everywhere the final years are spent in poor health

YEARS IN POOR HEALTH

Life Expectancy at Birth minus Healthy Life Expectancy at Birth

Countries	Males	Females
Brazil	9	11
Canada	8	8
China	7	8
Congo	8	8
Costa Rica	10	11
Greece	7	8
India	7	9
Jamaica	7	8
Japan	6	7

Countries	Males	Females
Lebanon	9	10
Mexico	9	9
Mozambique	8	8
Norway	7	8
Russia	5	8
Saudi Arabia	8	9
South Africa	5	5
Switzerland	7	8
USA	8	9

Source: World Health Report WHO 2004

So...

- Many years of ill-health in elderly in all regions...
- In all societies the aged will be a burden on the health systems...
- But... the industrialised world became rich before it became old, while developing countries are becoming old before they become rich.
 - ➔ Proportional financial / infrastructure burden greater in DCs
 - ➔ Occupying health systems at expense of infant/child survival ?

Key vaccines

(Reviewed against local epidemiology and other criteria)

- Influenza – seasonal/annual
- Pneumococcal (Strep pneumonia; conjugate or polysaccharide)
- Diphtheria, pertussis, tetanus
- Herpes zoster
- Hepatitis B
- Future vaccines?
 - *Respiratory Syncytial Virus (RSV)*, Staphylococcus, CMV

Adaptation



Adaptation of existing vaccines?

- To adapt, one must first understand
- Research agenda
 - Epidemiology (infectious diseases) and burden of disease; long term morbidity;
 - Serotypes
 - Previous immunization in early life patterns
 - Immune system
 - Hospitalizations, long term disability, frailty patterns

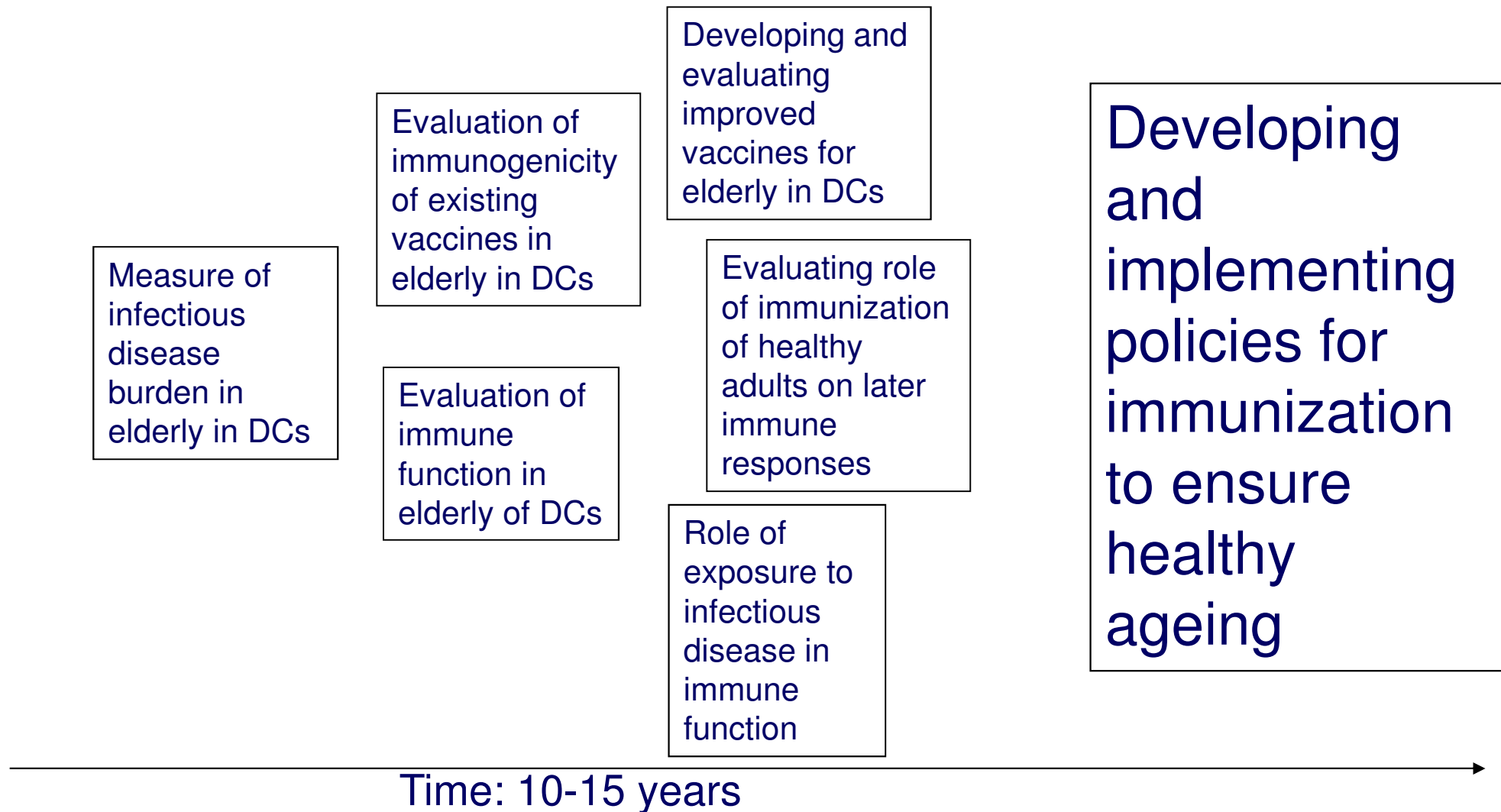
As well as...

- Demand
- Financing system
- Delivery science

The known unknowns

- To what extent do infectious diseases contribute to loss of independence and death in older adults in developing countries ?
 - At what ages ?
 - Affected by what environmental parameters ?
- Are these potentially vaccine preventable ?
 - Which vaccines ? Vaccination at what age ?
 - Is age of onset of immune-senescence affected by other infections
- How cost-effective will these vaccines be ?

Potential elements of a research strategy



Measuring infectious disease burden in elderly in developing countries

- Not so easy.....
 - Hospitalization – misses large part of population
 - Death – misses measurement of dependency effect
 - Questionnaire – misses lots
- Large longitudinal cohorts required in different countries and environmental settings

Limitations and potential future directions

- No infectious disease burden laboratory data
 - 50,000 blood samples (dried spots)
 - What data can be extracted ?
- Prospective studies in selected SAGE cohorts
 - Clinical trial design ?
 - WHO ad-hoc expert committee TBD
 - Funding

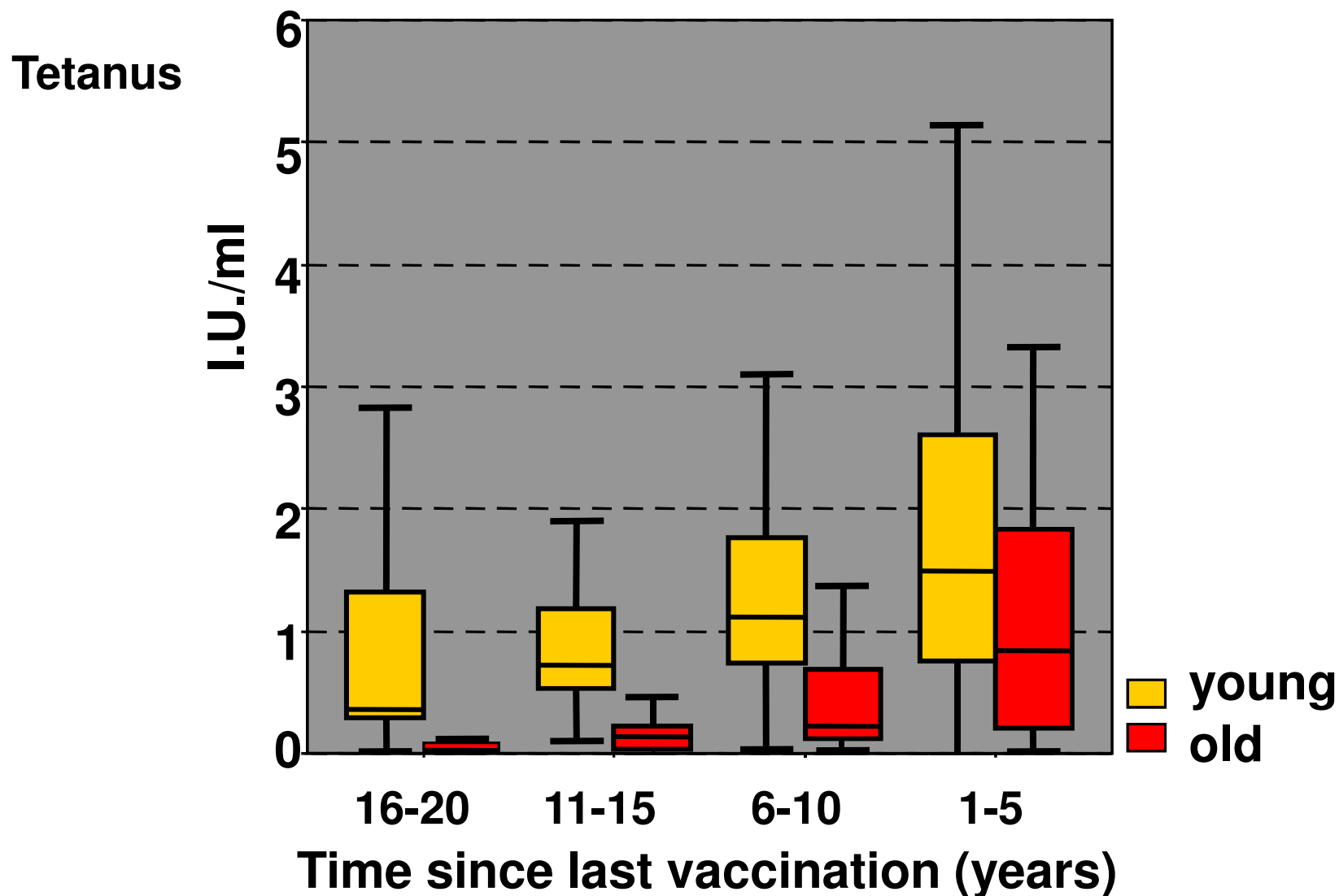
Immunity in Older adults: "Senescence"

- Hematopoietic stem cells stop proliferating
 - Decrease in number of lymphocytes
- Thymic involution : no new naive T cells
 - CD8>>CD4
- Leaky intestine, chronic infection, CMV:
 - constant exposure to inflammatory signals
 - 'Inflammageing', decreased response to danger signals
 - 'using up' remaining naive cells
- Increase in lung prostoglandin D2, reduced bone marrow,...

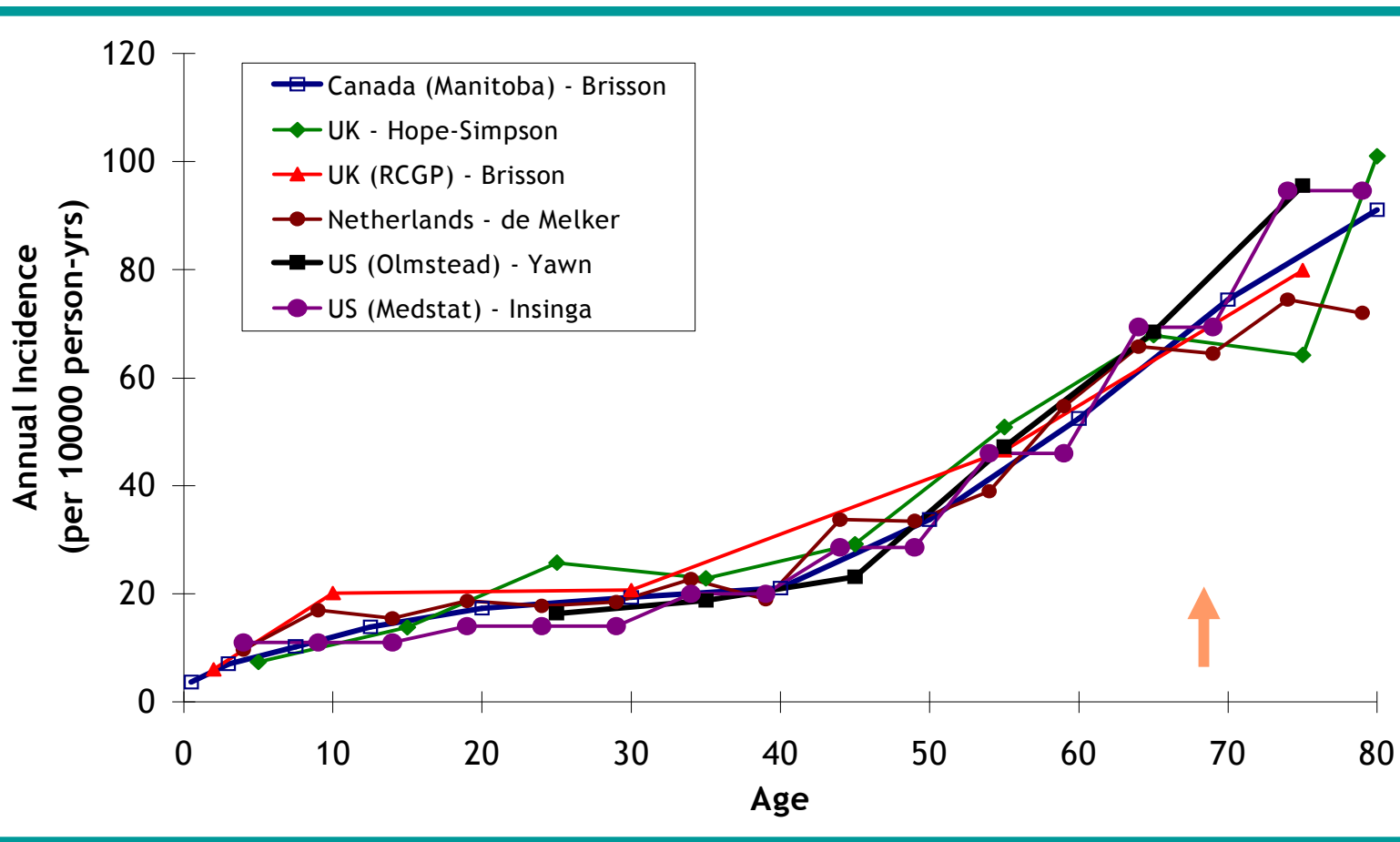
Result

- Increased susceptibility to infection
 - Fewer naive T cells, fewer new B cells: inability to respond to new pathogens
 - Skewed immune response
- Decreased response to vaccines
 - Lower response to danger signals
 - Impaired proliferative response

Antibody concentrations in young and elderly adults depending on the timepoint of the last vaccination



Herpes Zoster Incidence by Age



*Estimated 1 million cases per year in the United States**

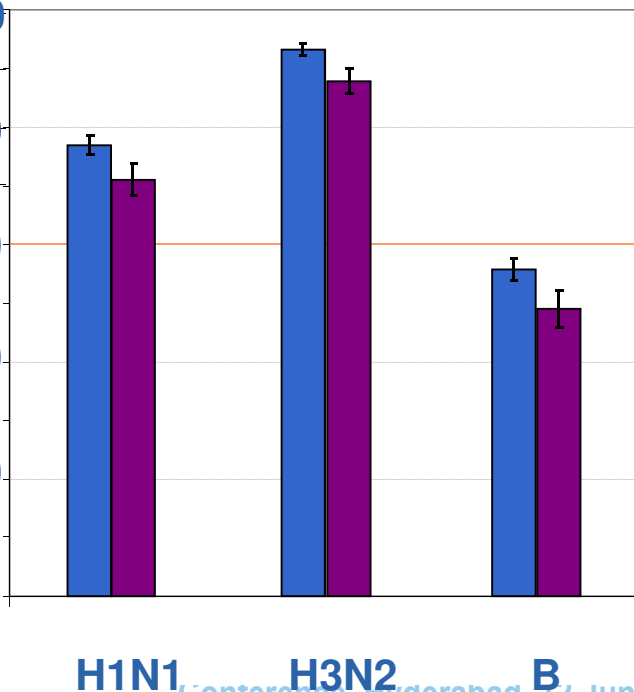
Innovative approaches for Herpes Zoster

- Recombinant antigen + adjuvant (gE + AS01)
 - Phase III studies (GSK)
 - Potential:
 - overcome antibody mediated clearance of live vaccine
 - Boost CTL response
 - Will it work in those with depressed immune system ?

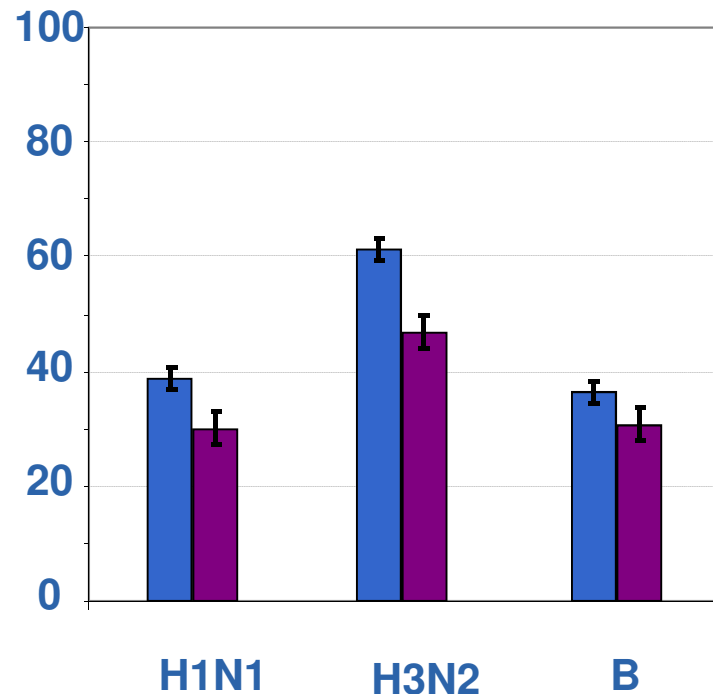
Influenza vaccine: Intradermal delivery

- Criterion for superiority met: seroprotection rates were significantly higher with ID vaccine against all strains
- EMA criteria*: immune responses significantly higher with ID for all strains and criteria

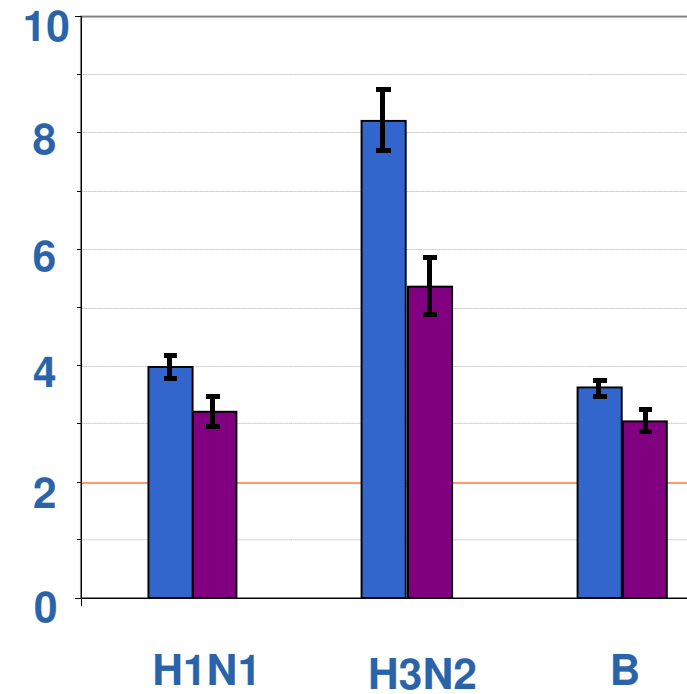
Seroprotection
rate (%)



Seroconversion or
4x increase (%)



GMTR **ID** **IM**



Efficacy of adjuvanted influenza vaccine in old and very old

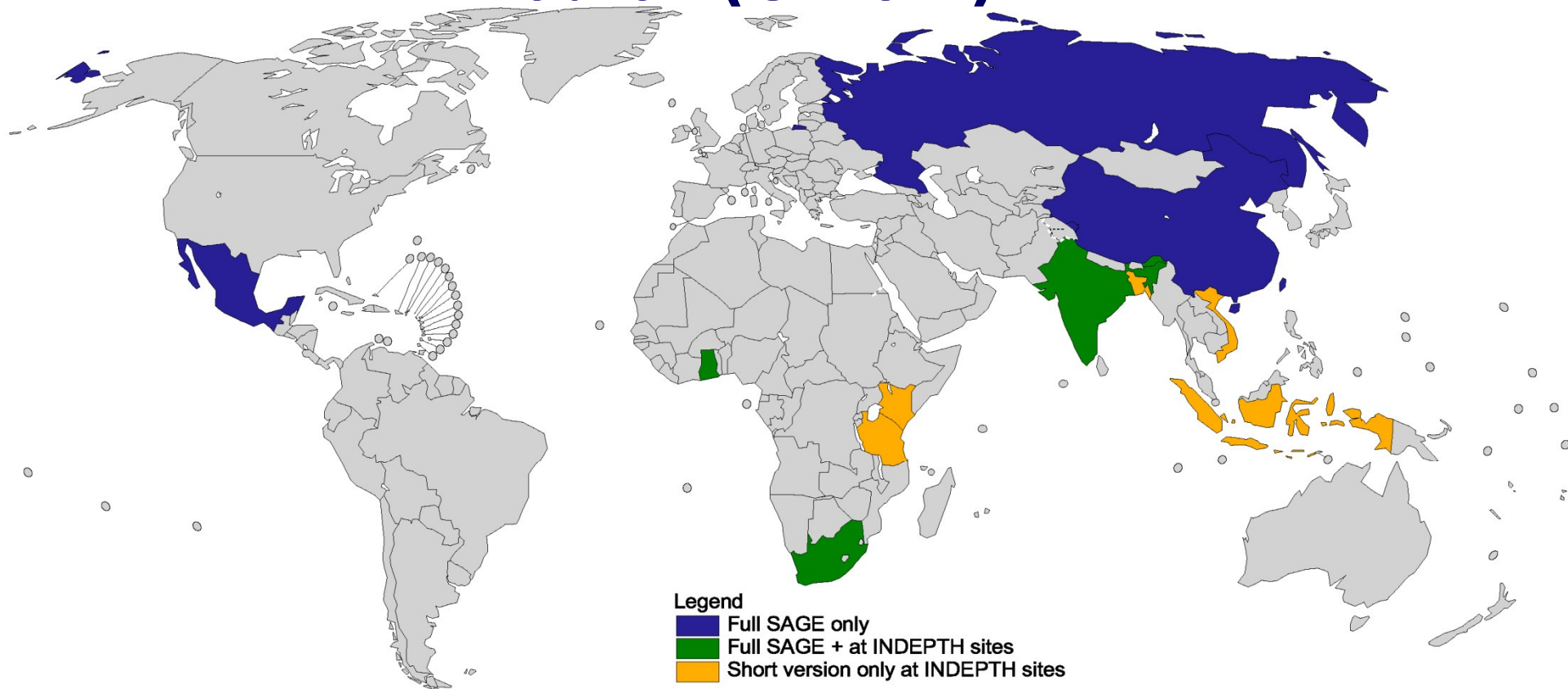
- Van Buynder et al. 2013 Vaccine 31, 6122
- Fluad vs TIV in: 65-75, 75-85, >85 (limited numbers)

Population	VE % (univariate)	
	TIV	ATIV
All	-12	35
Not in long-term care	42	73

Two SAGE(s)

- WHO Strategic Advisory Group of Experts on Immunization
 - <http://www.who.int/immunization/policy/sage/en/>
- WHO Global Study on Ageing and Adult Health
 - <http://www.who.int/healthinfo/sage/en/>

WHO Study on Global Ageing and Adult Health (SAGE)



- China
- India
- Russia

- Mexico
- South Africa
- Ghana

- Kenya
- Tanzania
- Bangladesh

- Viet Nam
- Indonesia

CALL TO ACTION -- IMPLEMENTATION



Actions - 1

1. EVIDENCE NEEDED

1. Science – immunology; Public health – epidemiology
2. Who is vaccinated? If, when were they previously vaccinated?
3. When to vaccinate – age: 50-60; older?
 - I. Prospective studies for developing countries
 - I. Infectious disease burden / quality of life
 - II. Measure of immune function (requires simple diagnostics)
4. **Financing:** cost of vaccine and delivery; strategies

2. DEMAND

1. Understanding limitations
2. **Raising awareness:** public, agency / government / funder (incl insurers)
3. Role of health personnel

3. POLICIES NEED TO BE DEVELOPED: OLDER ADULTS

4. IDENTIFY FINANCING, PROCUREMENT, DELIVERY MECHANISMS

Actions - 2

5. **Prioritized list** of diseases to vaccinate

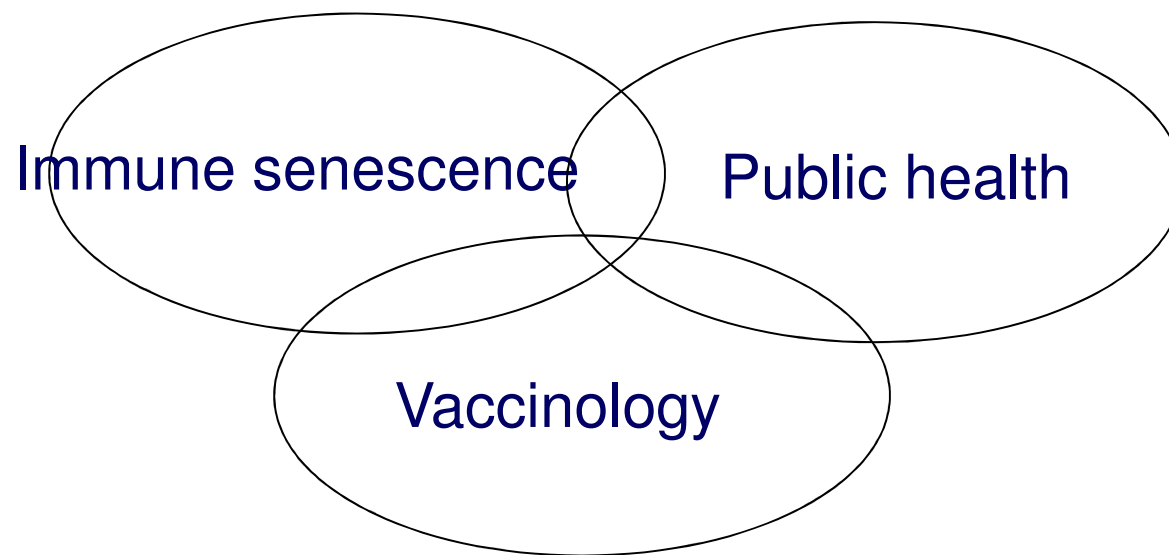
6. **Innovations**

A. **Adapt vaccines/manufacturing & delivery**

- Adjuvants
- Intradermal application
- High dose vaccines

B. **Financing & related regulatory**

- Affordability
- Safety



Conclusions

- Immune changes in older adults makes them more susceptible to infection
 - Contributes to death and catastrophic disability
- Vaccines less effective in older population - Innovative mechanisms to address this:
 - adjuvants, high dose, viral vectors, better delivery,... Etc
- Waiting till >65 years to begin 'elderly vaccination' may be too late – start earlier while immune system still viable
 - Needs policy
- World population that is ageing demands that we ACT

Thank you

http://www.who.int/kobe_centre

