



**World Health  
Organization**

*WHO Centre for Health Development (Kobe)*

***Advancing the Agenda:***

***Vaccines for Older Adults***

***Knowledge, adaptation, implementation***

12 June 2014

**12<sup>th</sup> International Federation of Ageing**  
Hyderabad, India

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Director

# Acknowledgements

- **Dr Martin Friede**, WHO HIS Cluster/Essential Medicines Department
- **Dr Somnath Chatterji**, WHO Health Information Systems Department
- **WHO Essential Medicines Department**
- **WHO Immunization, Vaccines, Biologicals Department**
- **WHO Ageing and Life Course Department**
- **WHO Regional Office colleagues, and....**
- **WHO Kobe Centre**

# Outline

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

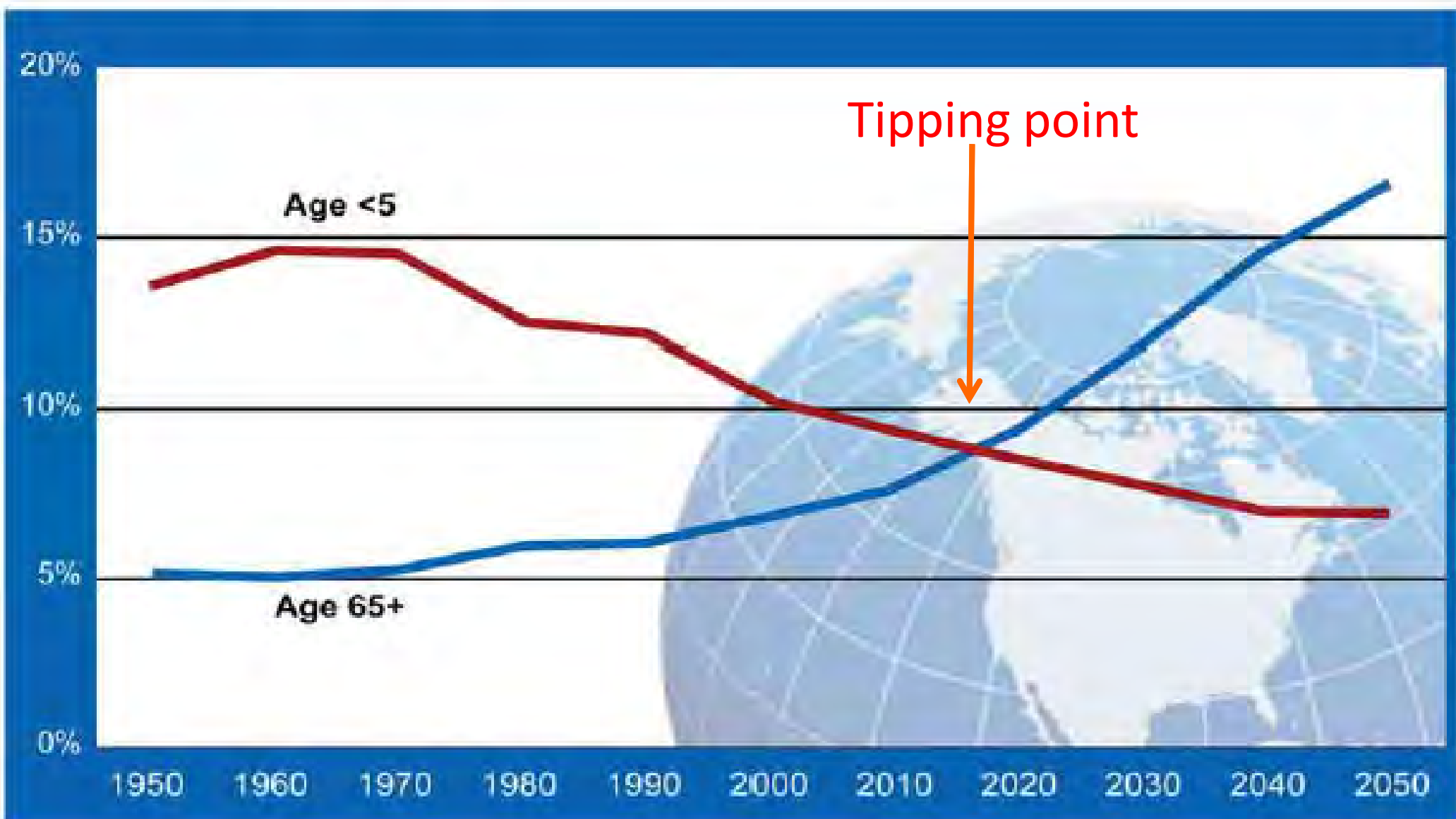
# THE NEED



# 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

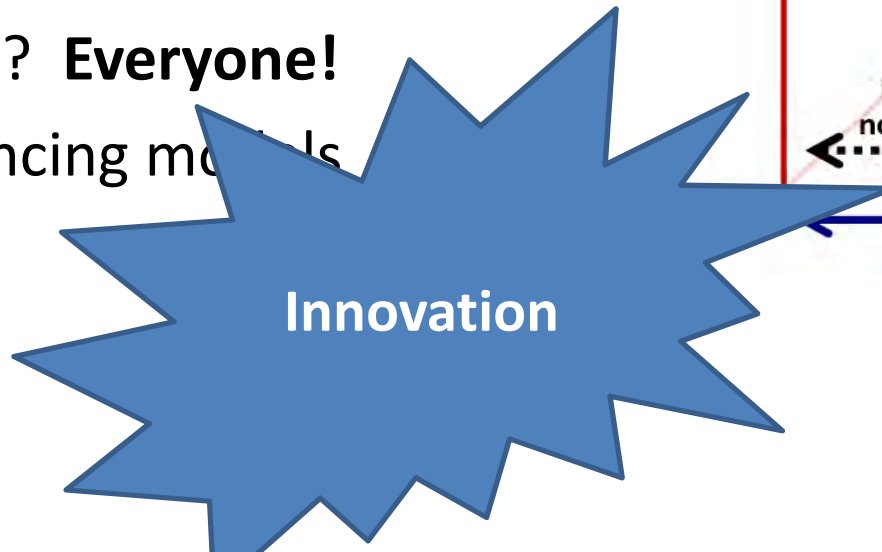
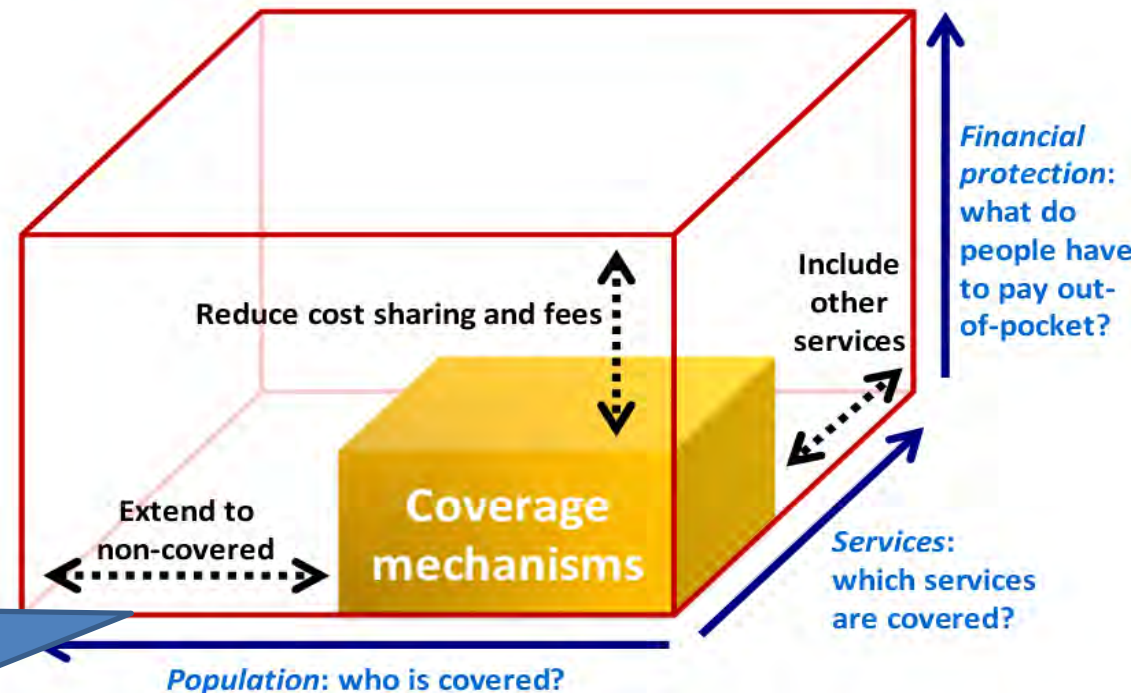


Source: United Nations. *World Population Prospects: The 2010 Revision*.  
Available at: <http://esa.un.org/unpd/wpp>.

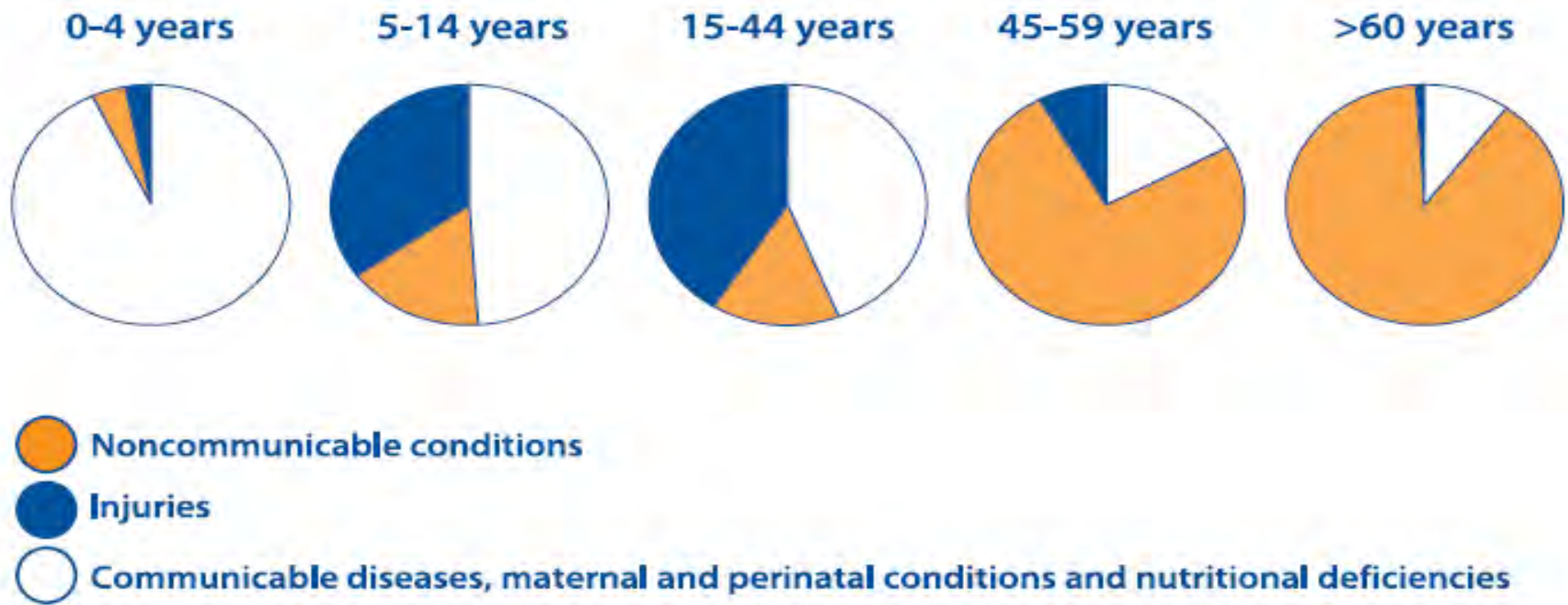
# In the context of universal health coverage

- 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



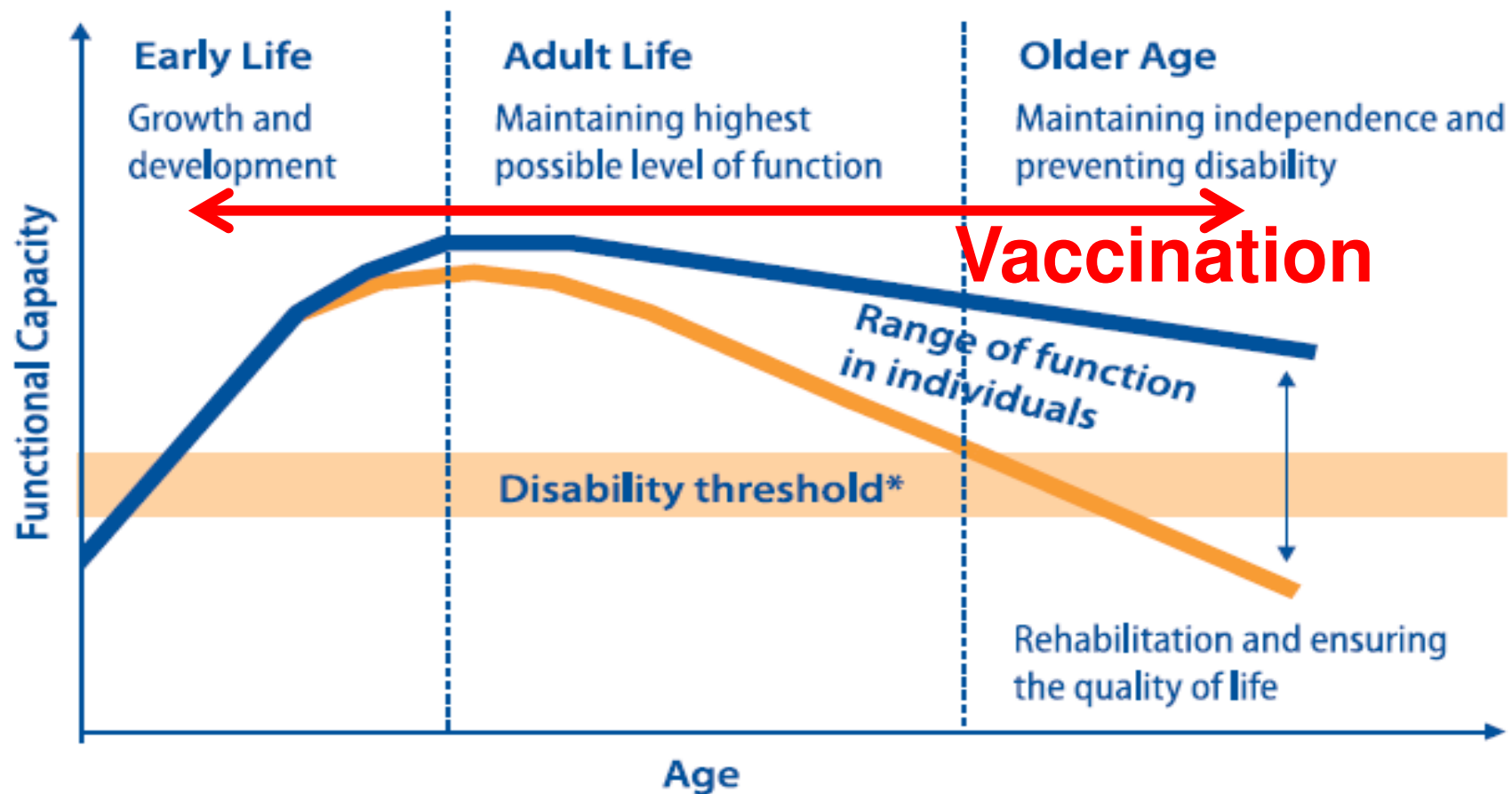
# Leading causes of death, low and middle income countries, by age.



Source: World Health Report 1999 Database

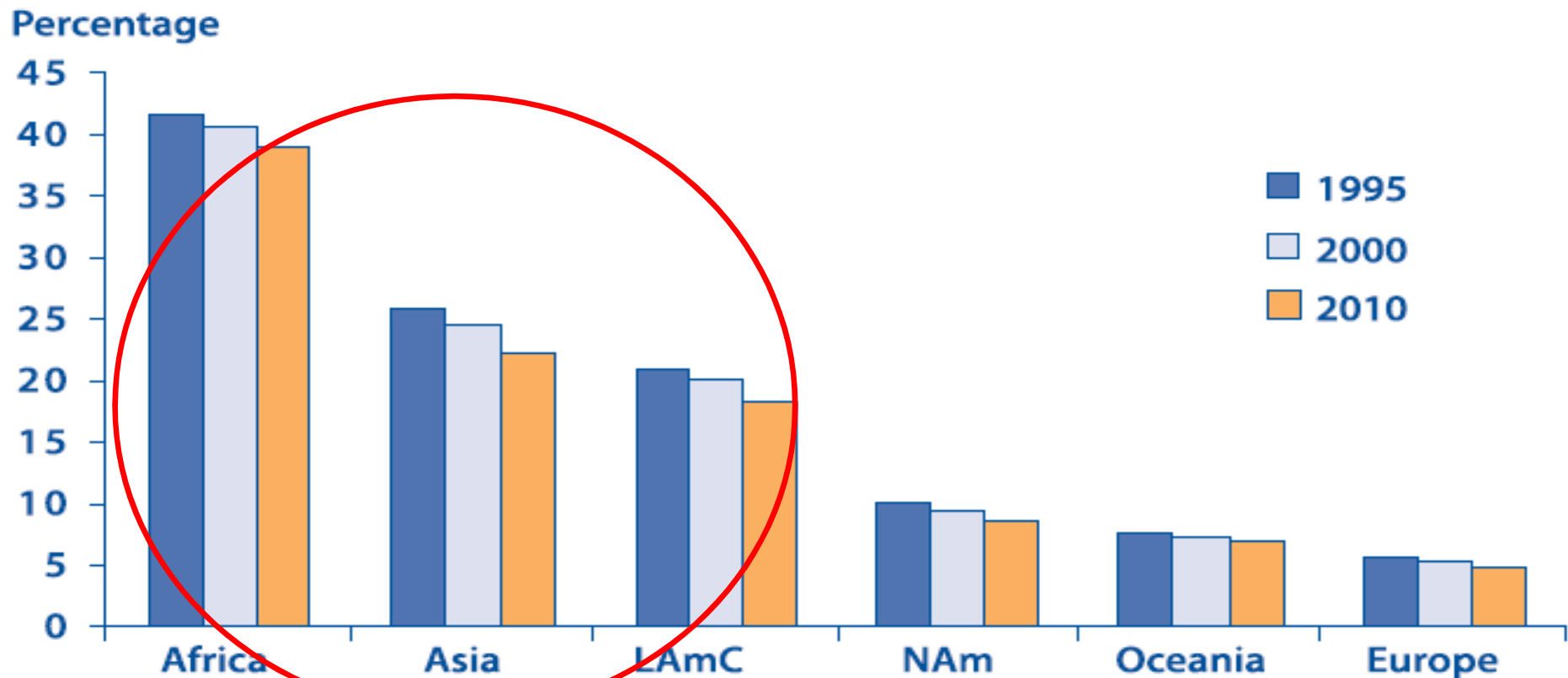


# Maintaining functional capacity over the life-course



Source: Kalache and Kickbusch, 1997

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

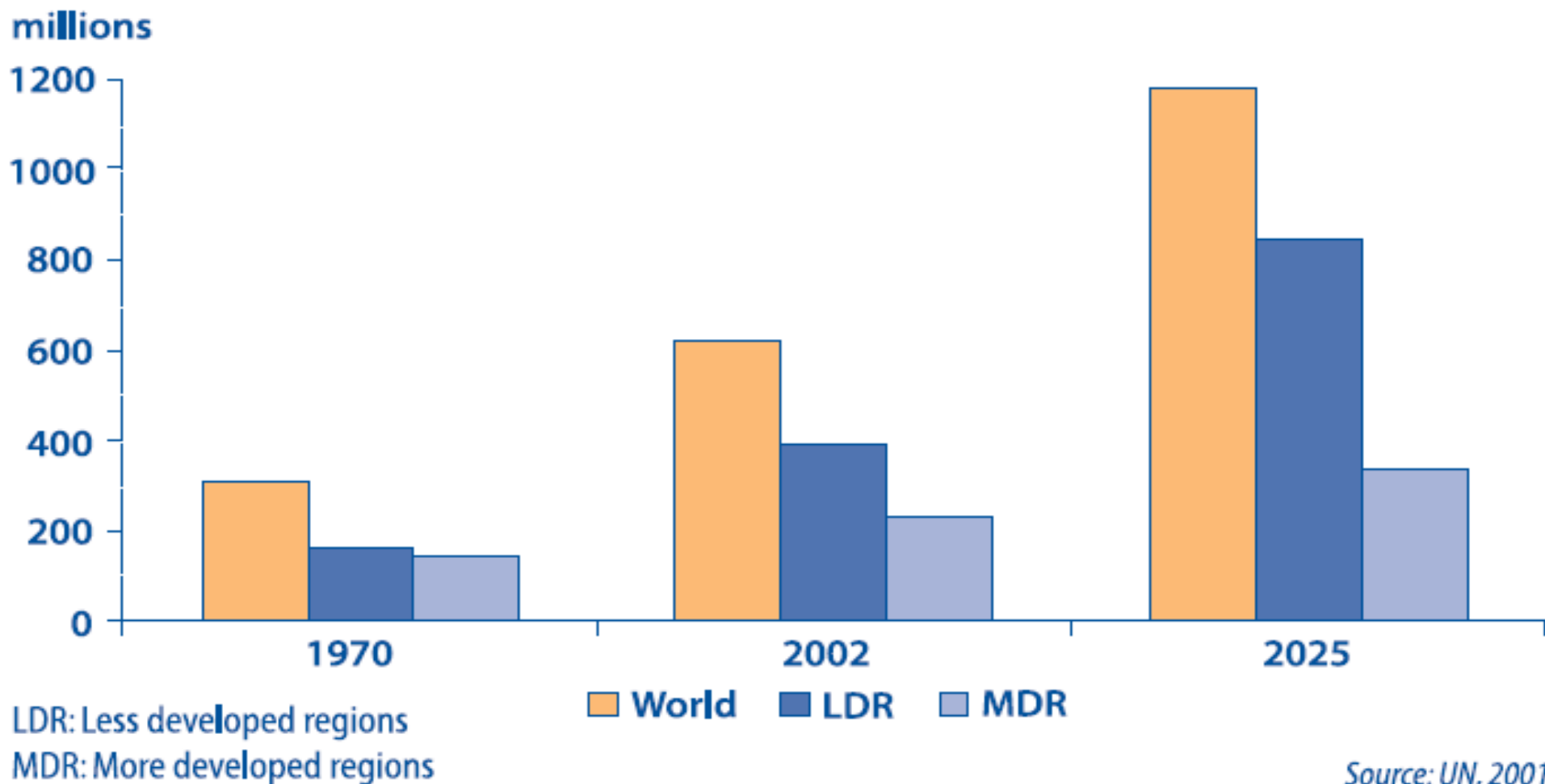


LAmC: Latin America and the Caribbean

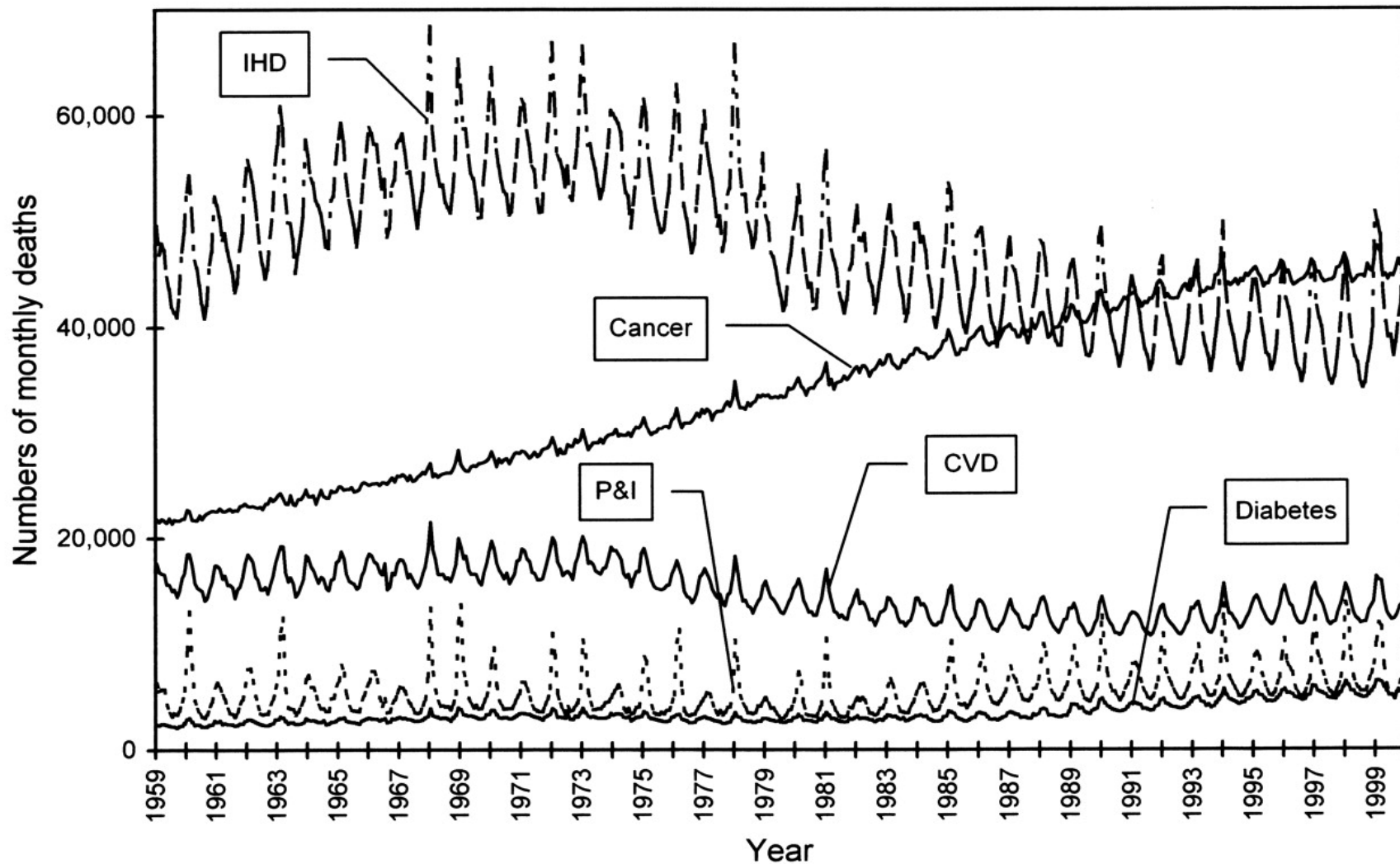
NAm: North America

Source: ILO, 2000

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



# Infection may be the trigger that kills...

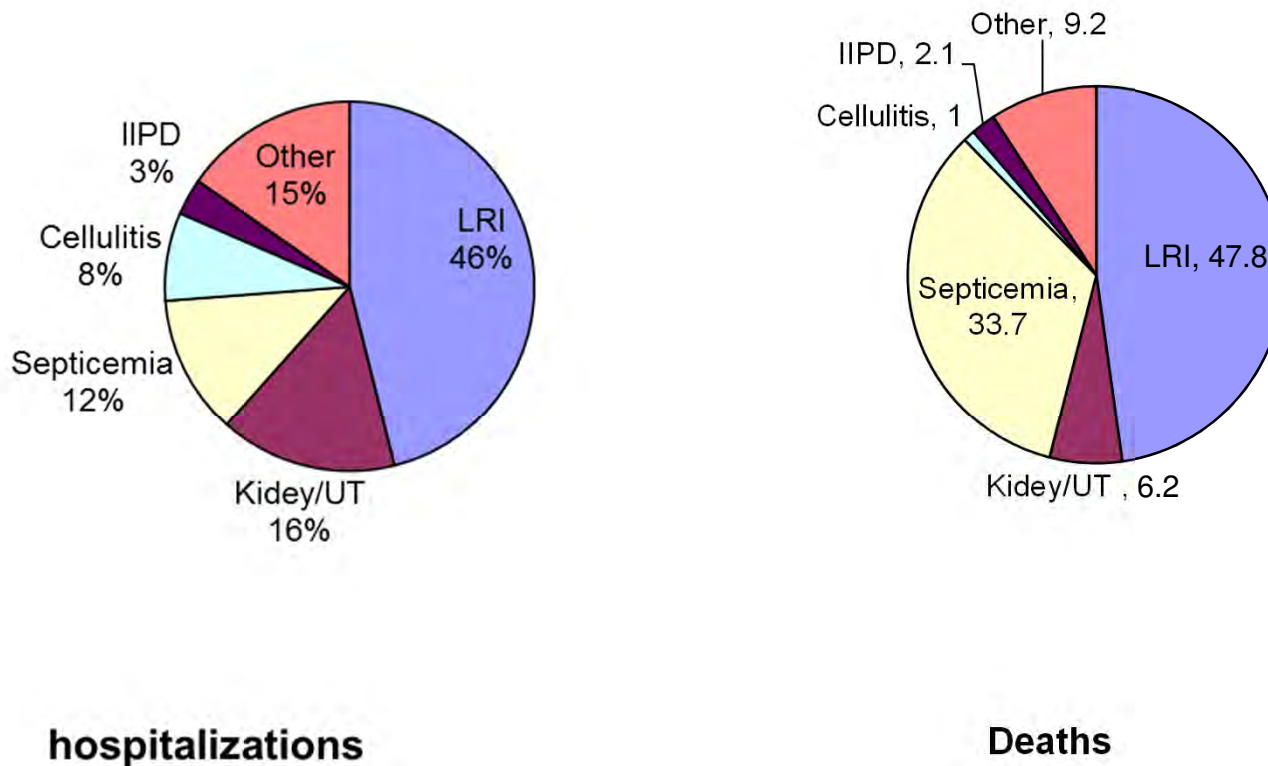


# Infection – hospitalization – catastrophic disability

- Catastrophic disability : loss of independence in  $\geq 3$  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 require more health services ...
  - 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 developing countries
- 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

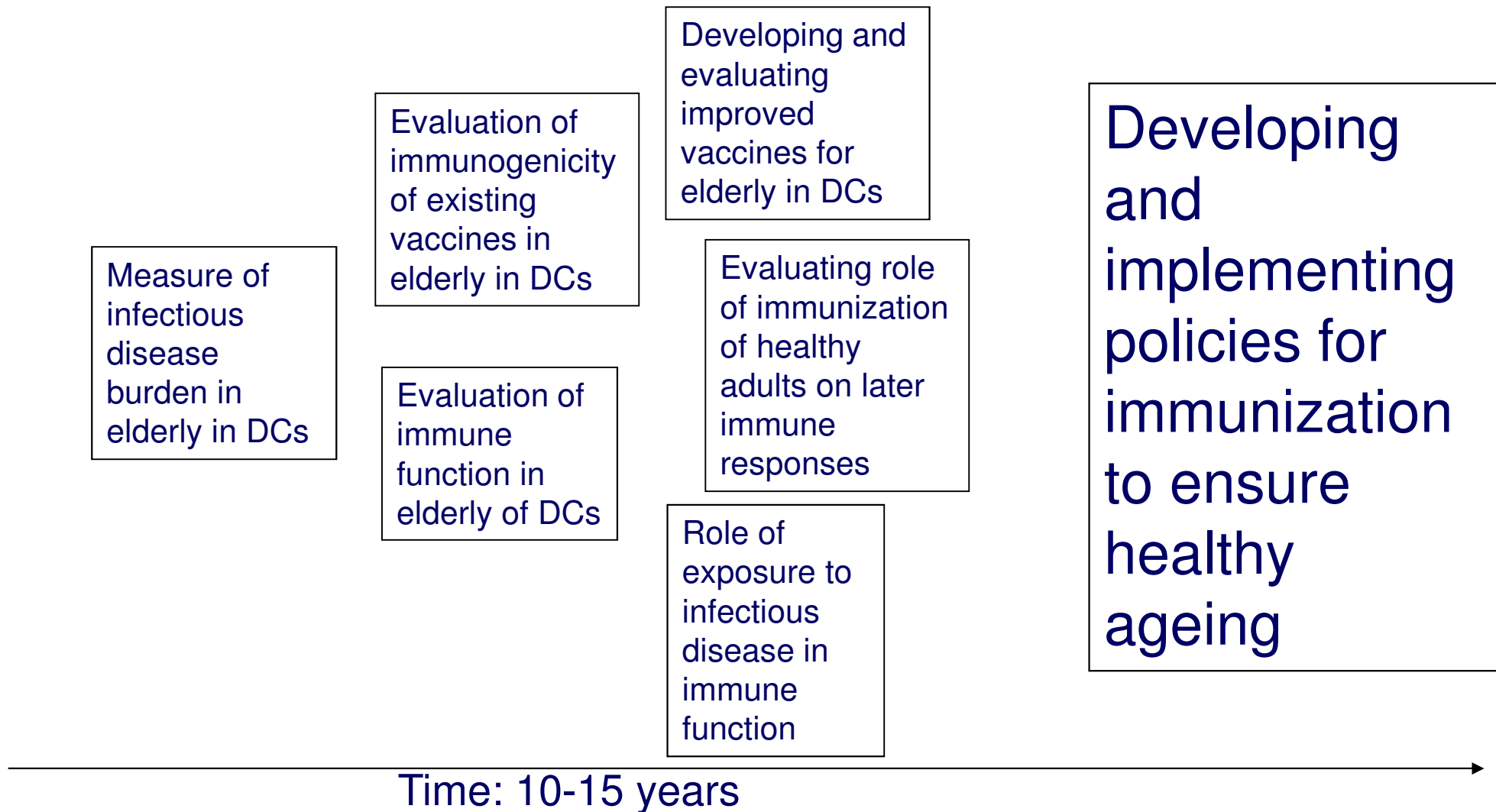
As well as...

- 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



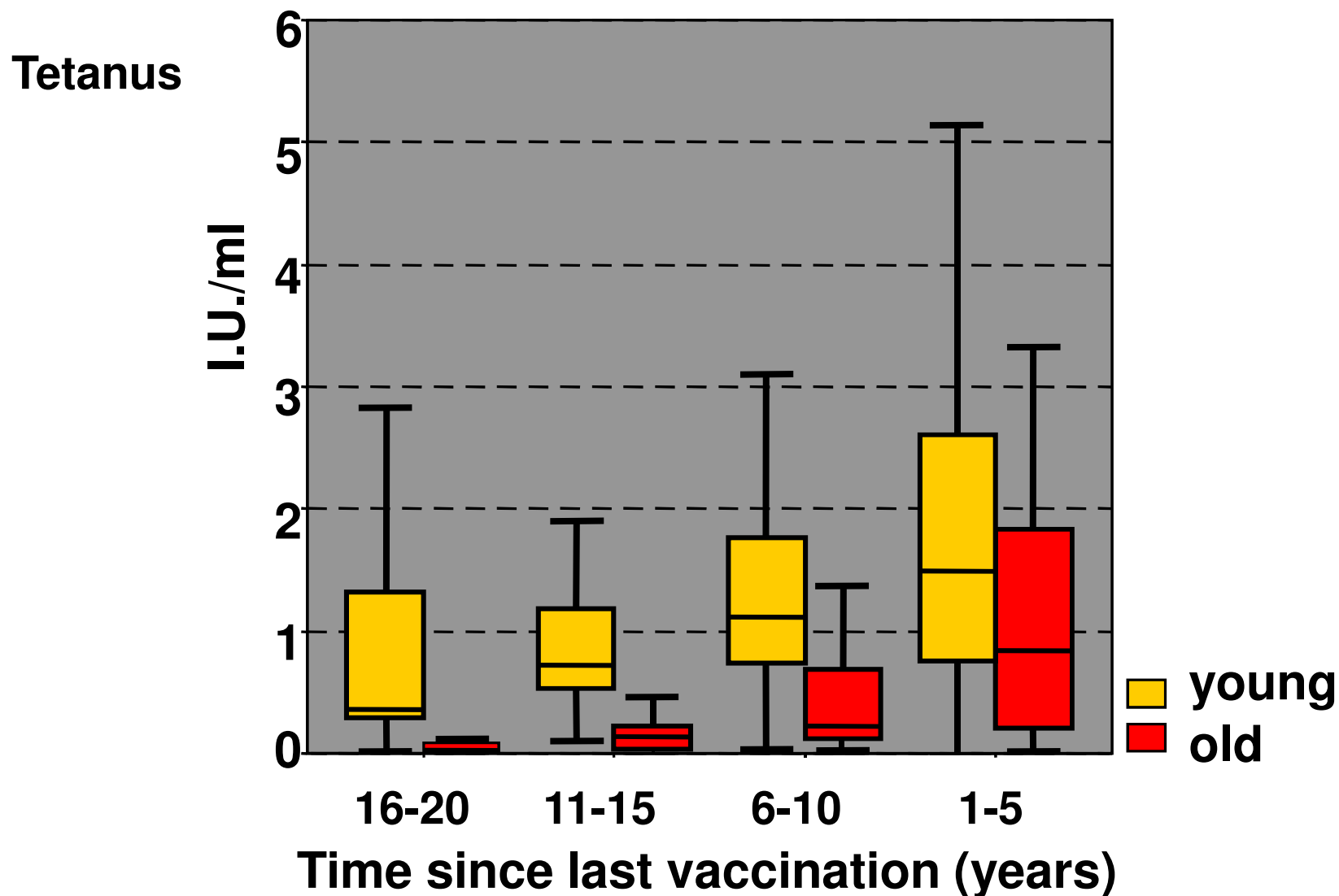
# Immunity in Older adults: "Senescence"

- 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,...

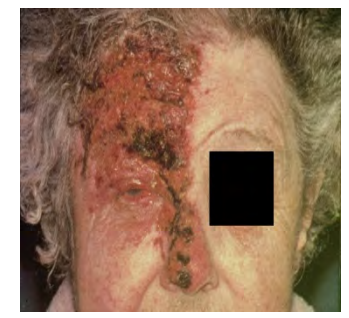
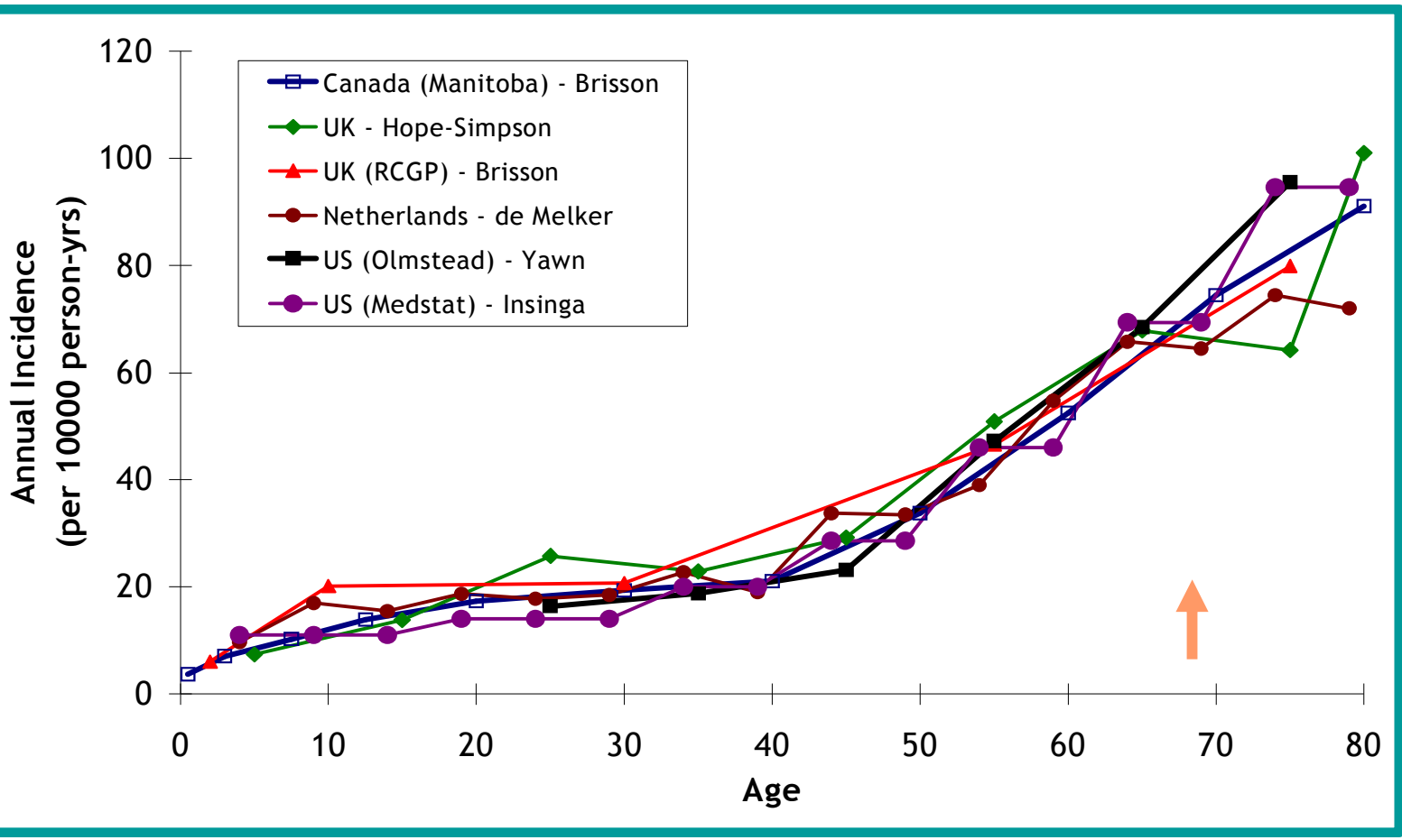
# Result

- 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

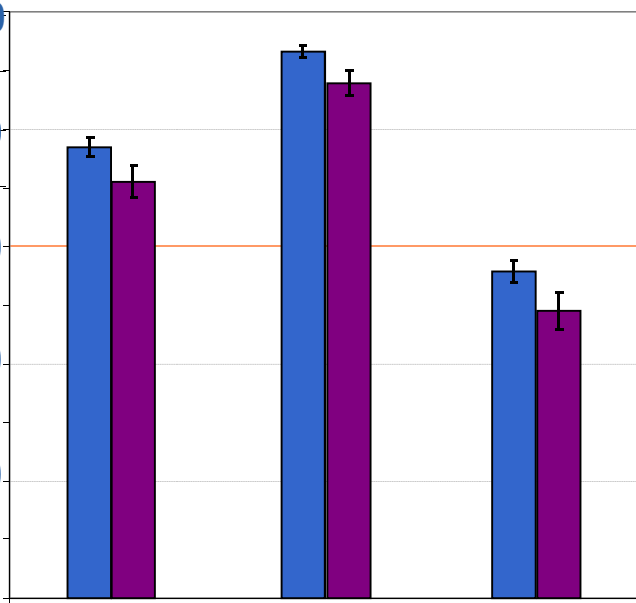
- Recombinant antigen + adjuvant (gE + AS01)
  - Phase III studies (GSK)
  - Potential:
    - overcome antibody mediated clearance of live vaccine
    - Boost CTL response
  - Will it work in those with depressed immune system ?

# Influenza vaccine: Intradermal delivery

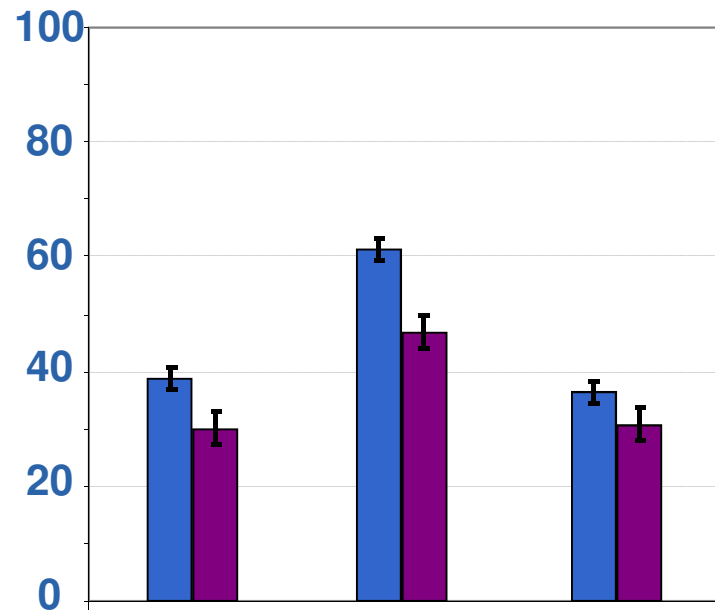
Criterion for superiority met: seroprotection rates were significantly higher with ID vaccine against all strains

EMEA criteria: immune responses significantly higher with ID for all strains and criteria

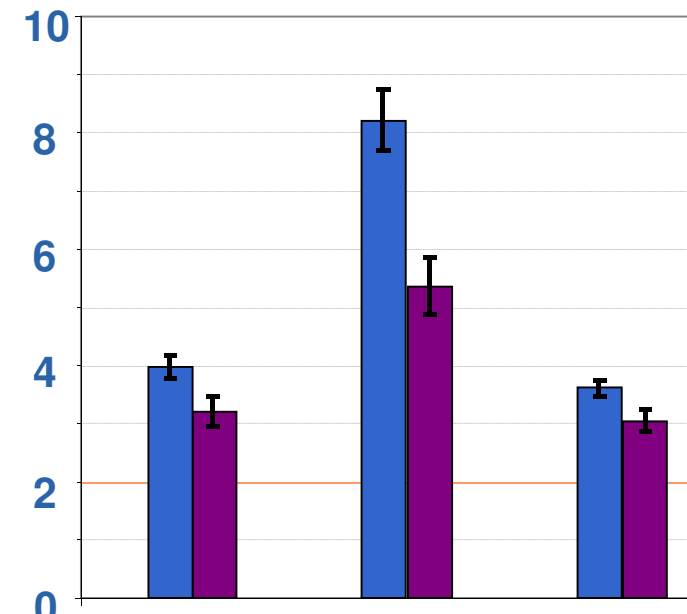
Seroprotection rate (%)



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
- Fluvad vs TIV in: 65-75, 75-85, >85 (limited numbers)

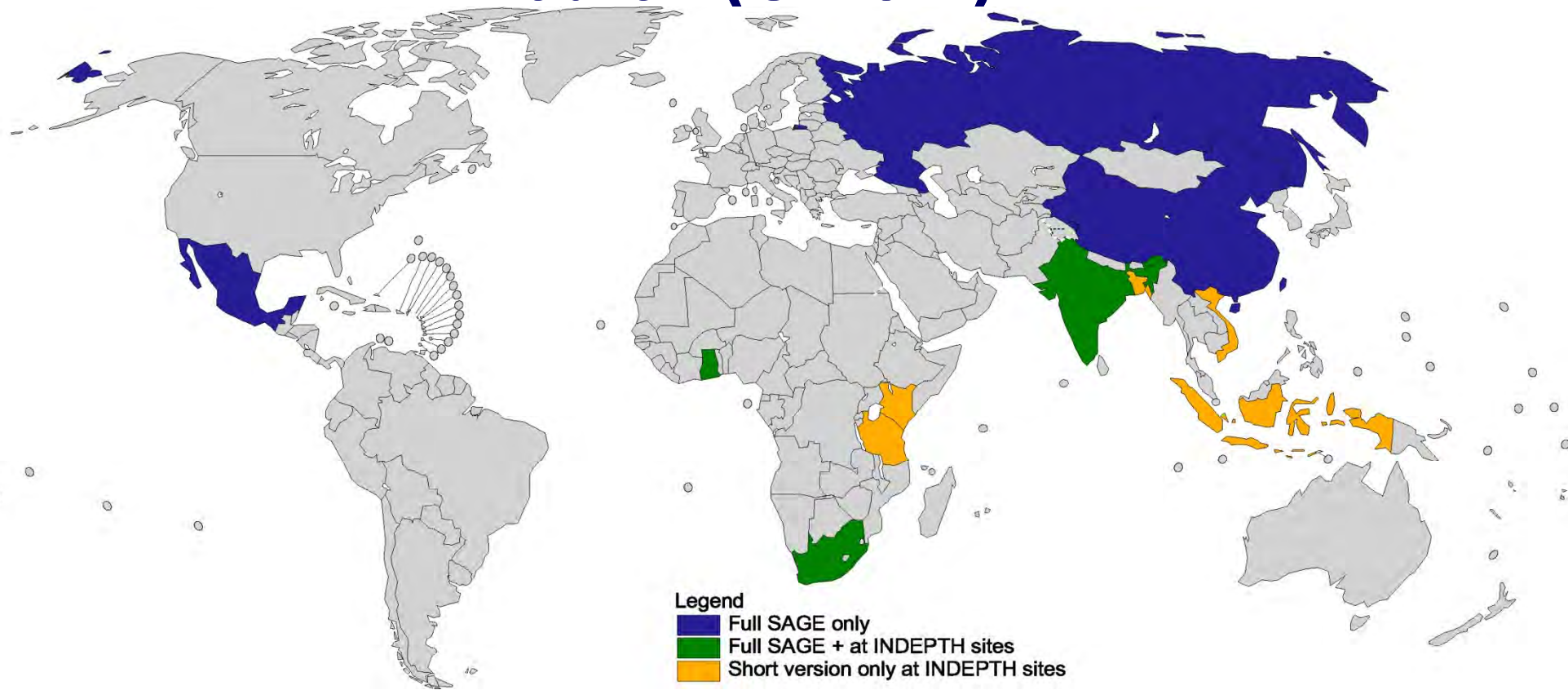
Population	VE% (univariate)	
	TIV	ATIV
All	-12	35
Not in long-term care	42	73

# 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



# A formula

**(Evidence + Demand + Affordable supply + Policies)  
x Innovation = ACTION**

# 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

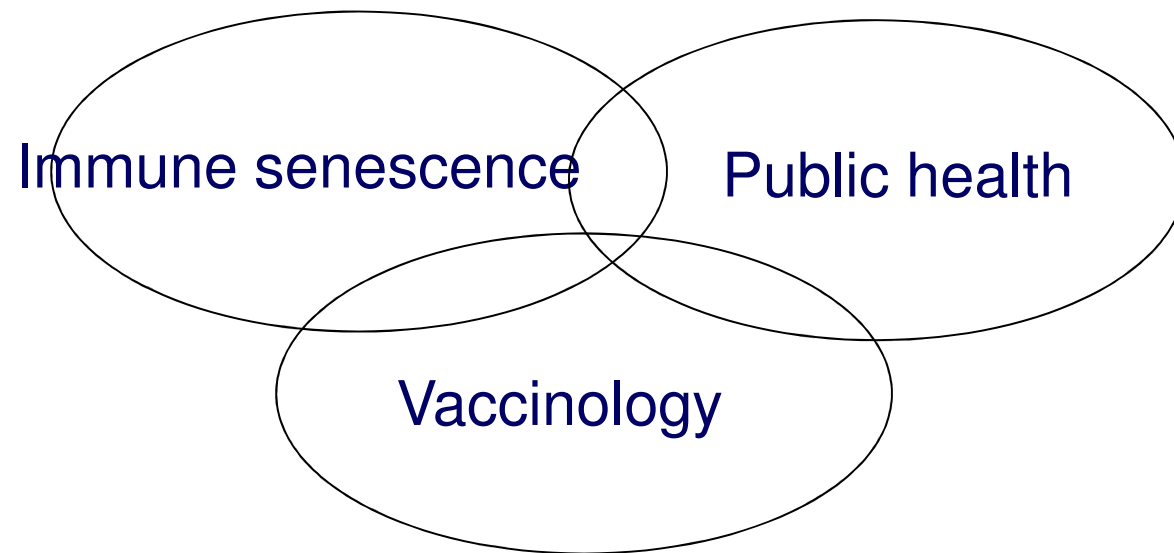
1. Understanding limitations
2. Raising awareness: public, agency / government / funder (incl insurers)
3. Role of health personnel

## 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](http://www.who.int/kobe_centre)

