Vaccines for Older Adults
Knowledge, adaptation, implementation

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Director
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- 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

Tipping point

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 models

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Towards universal coverage

- **Coverage mechanisms**
  - Reduce cost sharing and fees
  - Include other services
  - Extend to non-covered

- **Population: who is covered?**
- **Services: which services are covered?**
- **Financial protection: what do people have to pay out-of-pocket?**

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Innovation

- World Health Organization
- Centre for Health Development
Leading causes of **death**, low and middle income countries, by age.

![Pie charts showing leading causes of death by age group](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.

Source: UN, 2001
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

hospitalizations

Deaths
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.

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<th>Countries</th>
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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)
- Diptheria, 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

- Measure of infectious disease burden in elderly in DCs
- Evaluation of immunogenicity of existing vaccines in elderly in DCs
- Evaluation of immune function in elderly of DCs
- Developing and evaluating improved vaccines for elderly in DCs
- Evaluating role of immunization of healthy adults on later immune responses
- Role of exposure to infectious disease in immune function

Developing and implementing policies for immunization to ensure healthy ageing

Time: 10-15 years
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 prostaglandin 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

Ref: 13th ICID, Kuala Lumpur June 2020
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)

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<tr>
<th>Population</th>
<th>VE% (univariate)</th>
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<tr>
<td></td>
<td>TIV</td>
<td>ATIV</td>
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<tr>
<td>All</td>
<td>-12</td>
<td>35</td>
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<tr>
<td>Not in long-term care</td>
<td>42</td>
<td>73</td>
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Two SAGE(s)

- WHO Strategic Advisory Group of Experts on Immunization

- WHO Global Study on Ageing and Adult Health
WHO Study on Global Ageing and Adult Health (SAGE)

- China
- India
- Russia
- Mexico
- South Africa
- Ghana
- Kenya
- Tanzania
- Bangladesh
- Viet Nam
- Indonesia

Legend:
- Full SAGE only
- Full SAGE + at INDEPTH sites
- Short version only at INDEPTH sites
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?
      1. Prospective studies for developing countries
      2. Infectious disease burden / quality of life
      3. 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**
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
Immune senescence

Vaccinology

Public health
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