# Vaccine Innovation Across the Life-Cycle

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# **Innovation in Vaccines**



- Growth areas
- Competitive advantage
- Public health benefit

CONS

Risk

- Sustainability and ROI
- Barriers
  - Biology
  - Regulatory
  - IP
  - Human stupidity



# **Innovation in Vaccines**







# **Innovation in many forms**

New vaccine (no vaccine against pathogen exists)

- Improved Vaccines:
  - Simplified production (cost of goods, supply, speed)
  - New technology (DNA, RNA, viral vectors)
  - Breadth of protection
  - Longer lasting
  - Reduced schedule
  - Combination vaccines
  - Simplified delivery

# Vaccines, the Life Cycle, and Global Opportunities

Birth	Childhood	Adolescent Young Adult	Maternal	Older Adult	
Existing					
BCG, HepB	D,T,P,HepB, HiB,PCV,Rota MR, Influenza	HPV	Influenza	Influenza Zoster (PCV, tetanus)	
Desired					
RSV	GAS Pertussis +	HIV, TB, HSV, Chlamydia Gonorrhoea	RSV GBS Zika ?	Pneumonia E.Coli S. Aureus Pseudomonas	

And.. Better influenza vaccines, Shigella, ETEC, Norovirus,...



# **Maternal Immunization**





# **GBS vaccines**

- Maternal antibody to capsular polysaccharide reduces risk of disease
  - Capsular polysaccharide conjugate vaccines in development (phase II)
    - 5-valent or higher
  - Common protein phase 1.

#### Issues:

- Phase III trial designs (endpoints)
- Standardised immunogenicity
- Cost, and cost effectiveness





# **Respiratory Syncytial Virus (RSV)**

- 34 million episodes/yr under 5 yr
- 3.4 million hospitalizations
- 200,000 deaths
- No effective drugs
- Palivizumab monoclonal for highrisk preterms (\$10,000/course)





**Drganization** 

# RSV vaccines vaccinate mother or child ?

- 1960s: inactivated virus on alum
  - Severe immunopathology in immunized infants (Th2 response)
- 2000s: multiple candidates
  - Live attenuated (infant)
  - virus-like particle (maternal, infant or elderly)
  - Subunit (maternal or infant)
  - Viral vector (eg chimp adenovirus)
  - and passive immunization with monoclonals



# 63 candidates in pipeline



http://sites.path.org/vaccinedevelopment/respiratory-syncytial-virus-rsv/

# **Infant Immunization**





# **WHO EPI Schedule 1984**

Age	Vaccines	
Birth	BCG	
6 weeks	DPT, OPV	
10 weeks	DPT, OPV	
14 weeks	DPT, OPV	
9 months	Measles	



# Since then...

- Hep B 2-3
- Rubella 1-dose
- HiB 3 doses
- PCV 3 doses
- Rotavirus 2-3 doses
- Meningitis



#### Source: MSF Access Campaign

IPV, mumps, varicella, JE, typhoid,...



### **DTP3 coverage 2010-2015**



(WUENIC), 2010-2015

(WUENIC), 2010-2015

14

DCVMN, Seoul, 2017

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# Improving coverage through technology







# Some childhood vaccines in the pipeline

- Group A Streptococcus major source of antibiotic use
  - Rheumatic heart disease, soft tissue infection.
  - Phase III: endpoint ?
- Enterovirus 71
  - one approved (Sinovac),
  - others in development
- Norovirus, shigella, ETEC,
- Improved pertussis, 'flu...





# Adolescents, young adults



• HPV

Pertussis

- New TB
- HIV
- Herpes
- Chlamidya..



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# HPV: The challenge is to ensure that girls are protected in areas where the risk is greatest



#### Risk of cervical cancer

#### HPV vaccine introduced



Data Source: WHO/IVB Database, as at 23 January 2014

Map production: Immunization Vaccines and Biologicals, (IVB), World Health Organization

The boundaries and remes shown and the designations used on this map do not imply the expression of any opinion whatsbever 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

# Vaccines for sexually transmitted infections

#### Issues

- Limits to progress with condoms,
- Asymptomatic
- Anti-microbial resistance

### Status: Global roadmap to move forward

- Herpes Simplex
- Chlamydia trachomatis
- Neisseria gonorrhoeae
- Trichomonas vaginalis
- Treponema pallidum (syphilis)





### **Older adults**



- Tetanus
- Influenza
- Pertussis ?
- Herpes Zoster
- Pneumonia



# We are living in an Ageing world-wide: contrasting realities



 Is the immune response of the average 65 year-old rural Kenyan the same as that of the average 65 year-old urban Japanese ? How do you develop policy ??



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# Leading causes of <u>death</u>, low and middle income countries, by age.



Noncommunicable conditions
Injuries
Communicable diseases, maternal and perinatal conditions and nutritional deficiencies

Source: World Health Report 1999 Database



# Infectious diseases as triggers of excess mortality ?





### **Tetanus cases by age (EU)**

Figure 3.5.17. Age-specific notification rates of tetanus cases in EU and EEA/EFTA countries, 2006 (n = 163)



Source: Country reports: Belgium, Bulgaria, Denmark, France, Greece, Hungary, Italy, Lithuania, Poland, Portugal, Romania, Slovenia, Spain, Sweden and UK. Cyprus, Czech Republic, Estonia, Ireland, Latvia, Luxembourg, Malta, Slovakia, Iceland and Norway reported zero cases.

Importance of a life course vaccination programme

# Pneumonia hospital admissions by age



Pneumonia hospitalisations across age groups

• Griffin NEJM 2013. 369(2) 155-159



### Aging and T Cell Homeostasis

Age-dependent decline in thymic output



Naylor, K et al. J Immunol. 2005 Jun 1; 174(11):7446-52

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



Forum on Innovation, Kobe, 2013 Hainz et al., Vaccine (2005)

# Improving efficacy through technology

- Intradermal delivery of influenza
- High dose influenza vaccines
- Adjuvants (Herpes Zoster)





rganization

# **Herpes Zoster**

### Risk factors

- History of chickenpox<sup>1</sup>
- Advancing age and waning immunity<sup>1</sup>
  - VZV-specific immunity • declines with age<sup>1</sup>



1. Gnann JW, Whitley RJ. N Engl J Med. 2002;347:340-346.



Image courtesy of Charles E. Crutchfield III, MD. Crutchfield Dermatology, Eag World Health



# **Herpes Zoster Vaccines**







#### Cunningham NEJM 2016



# Other vaccines needed for older adults

- Clostridium difficile
- E. coli
- S. Aureus
- Pseudomonas
- Cancers, Alzheimer's,

### Driven by AMR



ization

# And then there are surprises which hit all ages... where vaccines are needed









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# Conclusions

- Vaccines can have a huge impact on health at all ages.
- Innovation will expand the number of vaccines which will permit prevention of a wider number of infectious diseases and antimicrobial use.
- Reaching the populations and sustaining high-level coverage is and will be a challenge that will require innovation, investment and support from all health care sectors.



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