Enhancing Decision Making for New Vaccine Development and Public Health Policy

Guru Madhavan, Ph.D.

DCVMN Annual Meeting, New Delhi

29 October 2014

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Advising the nation • Improving health

The Institute of Medicine

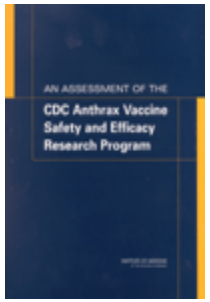
IOM asks and answers the nation's most pressing questions about health and health care.

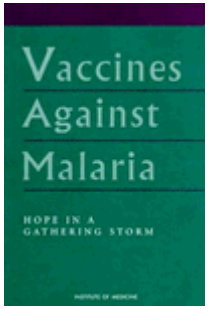
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

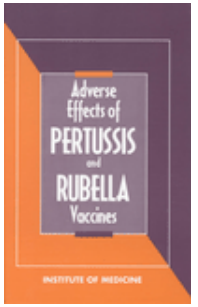
NATIONAL ACADEMY OF SCIENCES
1863–2013 • Celebrating 150 Years of Service to the Nation

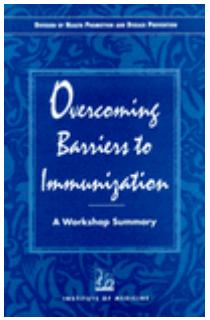
Source: The National Academies Press

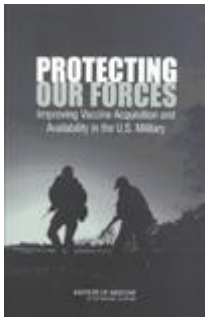
IOM and Vaccines Policy

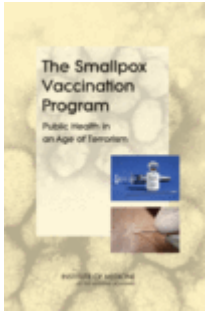


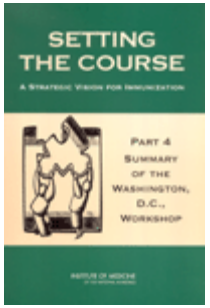


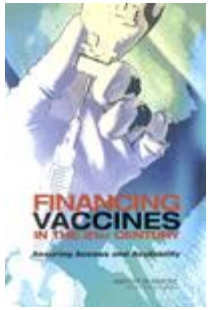




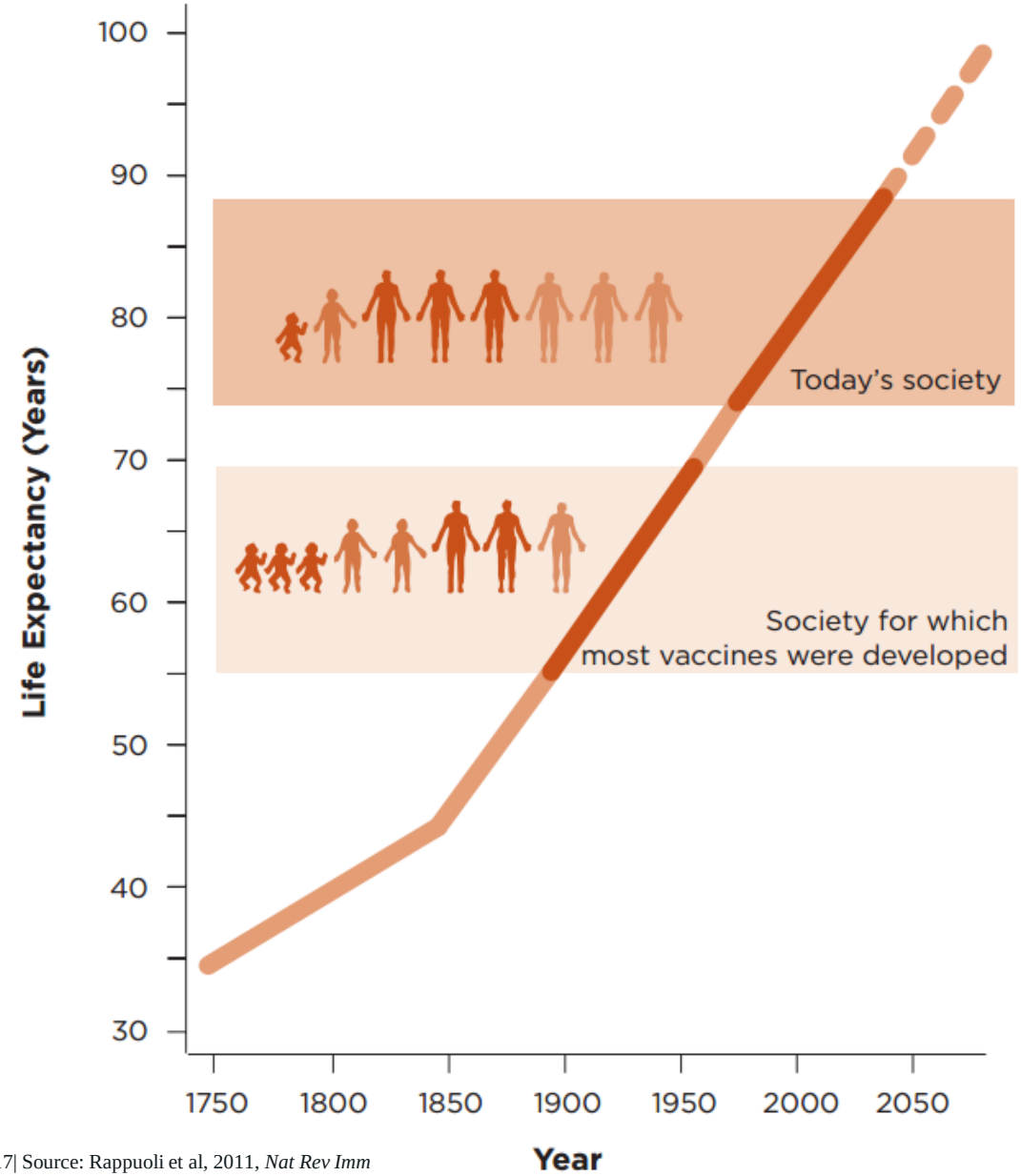






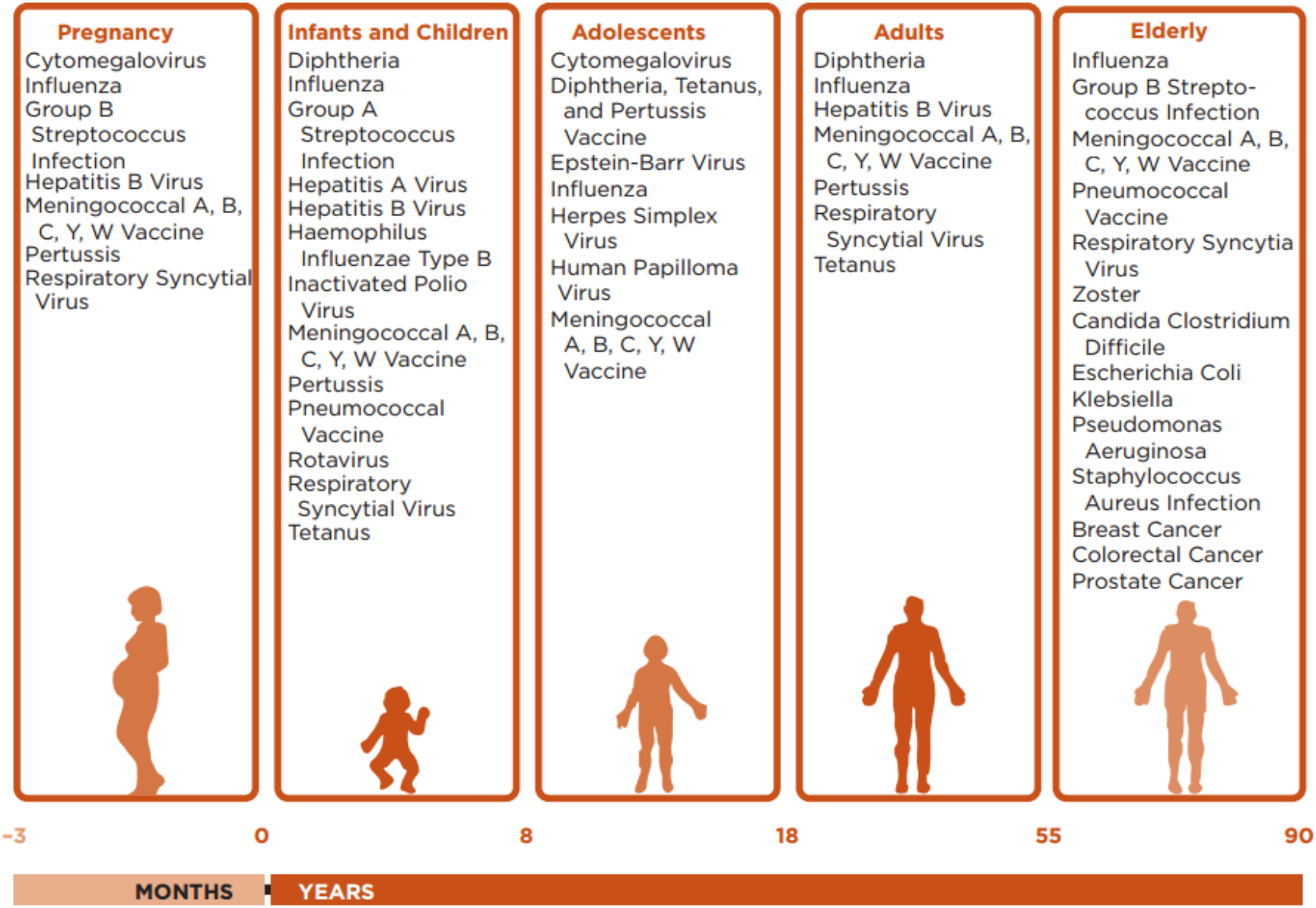


A Changing Society



From *Ranking Vaccines* (2012), p. 17| Source: Rappuoli et al, 2011, *Nat Rev Imm*

A Lifetime of Maladies



From *Ranking Vaccines* (2012), p. 18 | Source: Rappuoli et al, 2011, *Nat Rev Imm*

The Diversity of Diseases

Poverty

- Cholera
- Dengue
- Enterotoxigenic Escherichia Coli
- Hepatitis A Virus
- Hepatitis B Virus
- Influenza
- Japanese Encephalitis Virus
- Malaria
- Meningococcal A
- Parasitic Infections
- Paratyphoid
- Rabies
- Rotavirus
- Salmonella Enterica
- Salmonella Typhimurium
- Shigella
- Tuberculosis
- Typhoid Fever
- Yellow Fever

Emerging Infections

- AIDS
- Anthrax
- Avian Influenza
- Cholera
- Diphtheria
- Dengue
- Ebola
- Enterovirus 71
- Malaria
- Meningococcal X
- Severe Acute Respiratory Syndrome
- Smallpox
- Tuberculosis
- West Nile

Travelers

- Cholera
- Dengue
- Enterotoxigenic Escherichia Coli
- Hepatitis A Virus
- Hepatitis B Virus
- Influenza
- Japanese Encephalitis Virus
- Malaria
- Meningococcal A
- Paratyphoid
- Rabies
- Shigella
- Tuberculosis
- Typhoid Fever
- Yellow Fever

People with Chronic Diseases

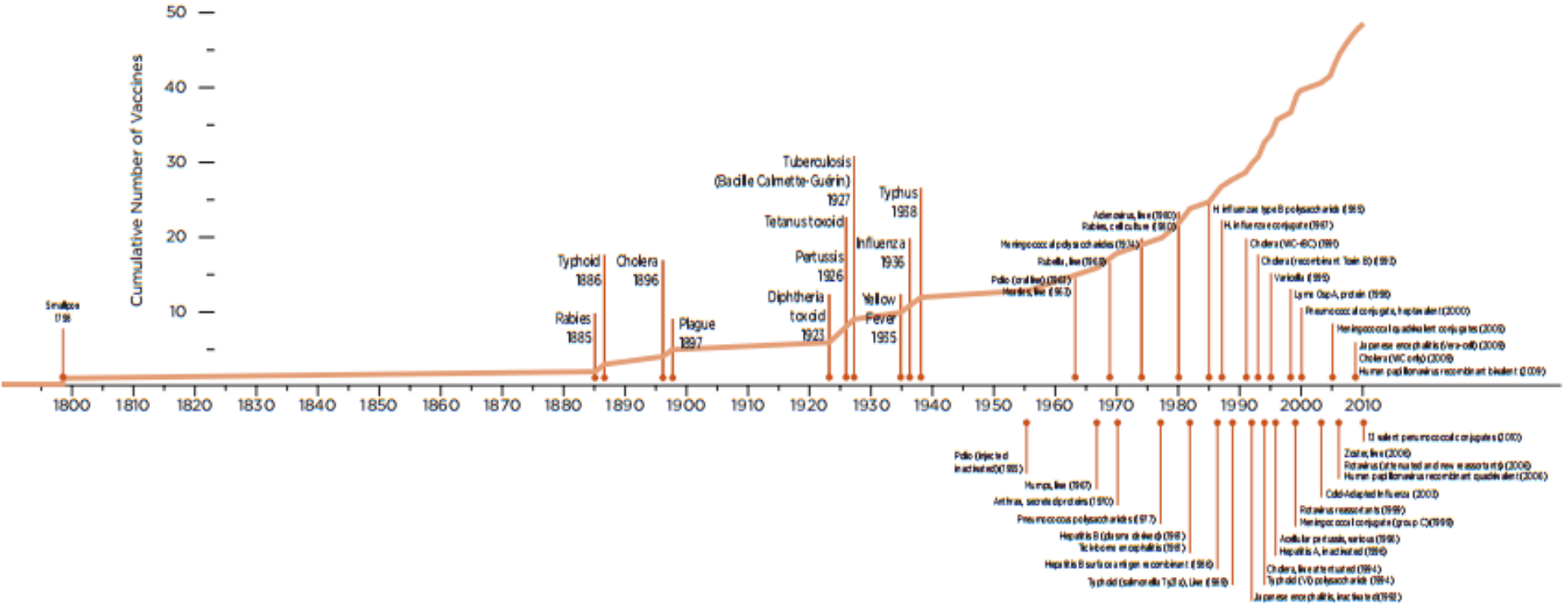
- Cytomegalovirus
- Influenza
- Fungal Infections
- Pseudomonas Aeruginosa
- Parainfluenza
- Respiratory Syncytial Virus
- Staphylococcus
- Tuberculosis

People with HIV Infection

- Influenza
- Pneumococcus
- Pneumocystis
- Tuberculosis

From *Ranking Vaccines* (2012), p. 18 | Source: Rappuoli et al, 2011, *Nat Rev Imm*

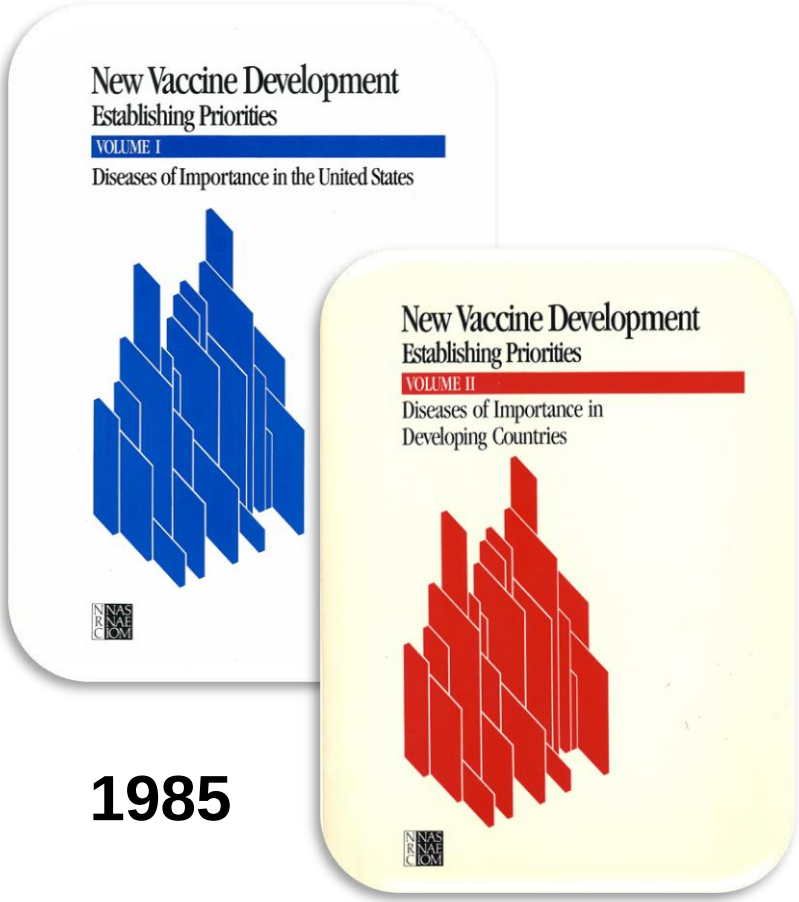
The Past and the Present of Vaccine Development



From *Ranking Vaccines* (2012), p. 19 | Source: Stanley Plotkin, Courtesy of GAVI Alliance

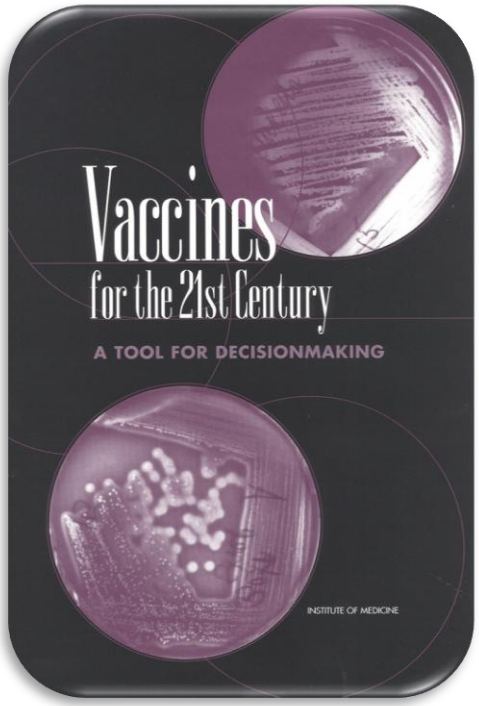
Priority setting is a challenge.

20th Century Approaches



1985

1986

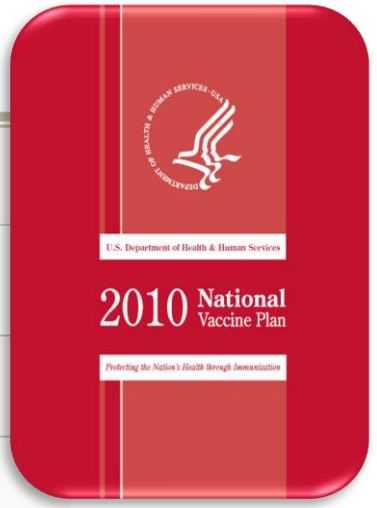


2000

Infant Mortality Equivalent

Cost-Effectiveness

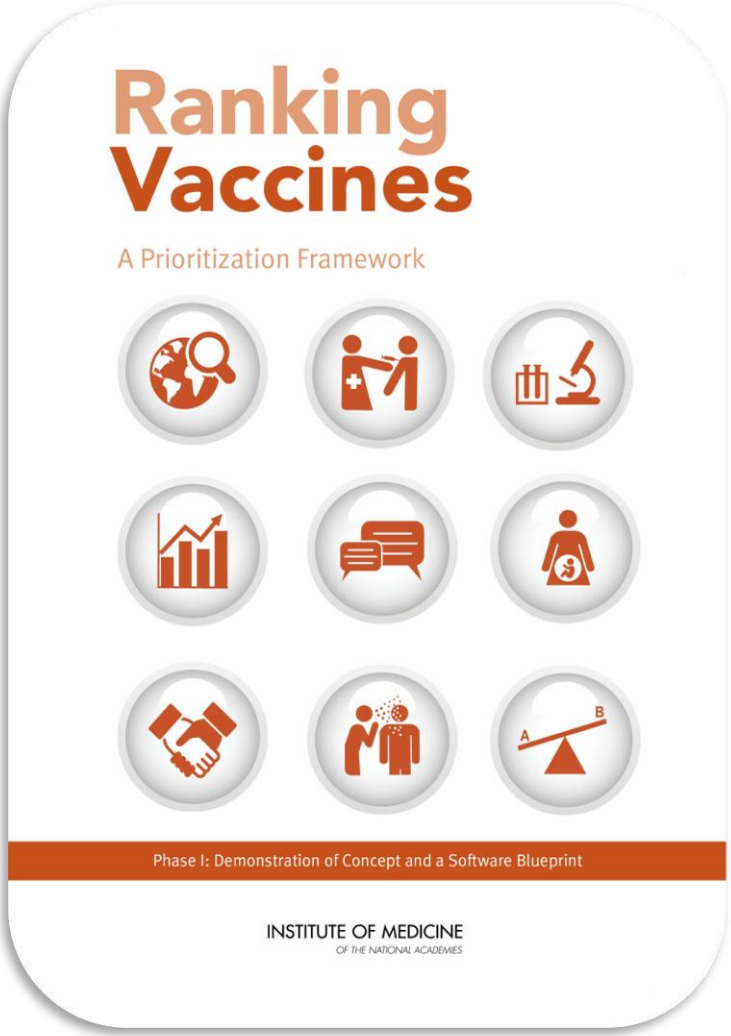
National Vaccine Plan Priorities for Implementation



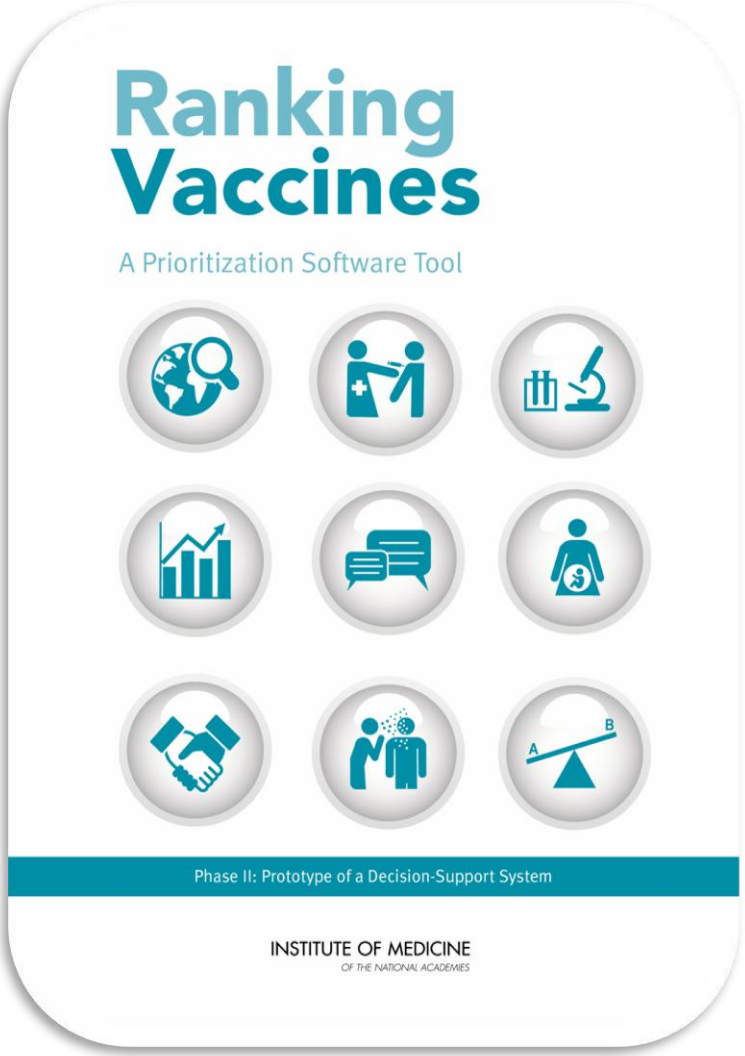
A.	Develop a catalogue of priority vaccine targets of domestic and global health importance (Goal 1).
B.	Strengthen the science base for the development and licensure of new vaccines (Goals 1 and 2).
C.	Enhance timely detection and verification of vaccine safety signals and develop a vaccine safety scientific agenda (Goal 2).
D.	Increase awareness of vaccines, vaccine-preventable diseases, and the benefits/risks of immunization among the public, providers, and other stakeholders (Goal 3).
	access to routinely recommended vaccines (Goal 4).
G.	Create an adequate and stable supply of routinely recommended vaccines and vaccines for public health preparedness (Goal 4).
H.	Increase and improve the use of interoperable health information technology and electronic health records (Goal 4).
I.	Improve global surveillance for vaccine-preventable diseases and strengthen global health information systems to monitor vaccine coverage, effectiveness, and safety (Goal 5).
J.	Support global introduction and availability of new and under-utilized vaccines to prevent diseases of public health importance (Goal 5).

A. Develop a catalogue of priority vaccine targets of domestic and global health importance (Goal 1).

A Multi-User Approach



2012



2013

A Multi-Criteria Approach

Health Considerations	• Premature Deaths Averted per Year • Incident Cases Prevented per Year • QALYs Gained or DALYs Averted
Economic Considerations	• Net Direct Costs (Savings) of Vaccine Use per Year • Workforce Productivity Gained per Year • One-Time Costs • Cost-Effectiveness ($/QALY or $/DALY)
Demographic Considerations	• Benefits Infants and Children • Benefits Women • Benefits Socioeconomically Disadvantaged • Benefits Military Personnel • Benefits Other Priority Population
Public Concerns	• Availability of Alternative Public Health Measures • Potential Complications Due to Vaccines • Disease Raises Fear and Stigma in the Public • Serious Pandemic Potential
Scientific and Business Considerations	• Likelihood of Financial Profitability for the Manufacturer • Demonstrates New Production Platforms • Existing or Adaptable Manufacturing Techniques • Potential Litigation Barriers Beyond Usual • Interests from NGOs and Philanthropic Organizations
Programmatic Considerations	• Potential to Improve Delivery Methods • Fits into Existing Immunization Schedules • Reduces Challenges Relating to Cold-Chain Requirements
Intangible Values	• Eradication or Elimination of the Disease • Vaccine Raises Public Health Awareness
Policy Considerations	• Interest for National Security, Preparedness, and Response • Advances Nation's Foreign Policy Goals
User-Defined Attributes	• Up to Seven Attributes

SMART Vaccines Demo

Demographic Information

SMART Vaccines

Specify: ● Population ○ Disease ○ Vaccine

Evaluate: ○ Attributes ○ Weights ○ Priorities

Select a population.

Continue

Population: United States

Subpopulation: female

Demographic Characteristics:

Age Group (Year)	Population (N)	Living (lx)	Life Years (nLx)	Life Expectancy (ex)	Standard Life Expectancy (sx)	Health Utilities Index 2 (HUI2)	Hourly Wage Rate (USD)
<1	2183518	100000	99452	80.90	86.50	0.99	17.90
1-4	8456004	99391	397326	80.40	85.70	0.99	17.97
5-9	10228540	99292	496309	76.50	81.70	0.99	23.50
10-14	10309899	99232	495991	71.60	76.80	0.99	24.57
15-19	10910307	99164	495387	66.60	71.80	0.99	8.45
20-24	10862866	98991	494371	61.70	66.90	0.99	10.90
25-29	10634528	98758	493104	56.90	62.00	0.95	16.40
30-34	10326394	98484	491541	52.00	57.10	0.90	16.47
35-39	10441258	98133	489384	47.20	52.20	0.86	18.20
40-44	10944157	97621	486111	42.40	47.30	0.86	18.20
45-49	11697857	96823	481067	37.70	42.50	0.84	18.50
50-54	11270132	95603	473634	33.20	37.80	0.84	18.50
55-59	9904308	93850	463085	28.80	33.10	0.81	18.70
60-64	8297733	91384	447776	24.50	28.50	0.81	18.70
65-69	6266131	87726	425003	20.40	24.00	0.83	16.07
70-74	4919414	82275	391682	16.60	19.70	0.83	16.00
75-79	4159980	74398	344041	13.10	15.50	0.82	16.00
80-84	3493449	63218	278259	9.90	11.80	0.82	16.00
85-89	2397331	48086	195937	7.30	8.50	0.82	16.00
90-94	1194178	30289	104147	5.10	5.80	0.82	15.00

Disease Burden

SMART Vaccines

Specify: ● Population ◉ Disease ● Vaccine
Evaluate: ● Attributes ● Weights ● Priorities

Specify disease characteristics.

Continue

Population: United States

Select Disease: Flu

Subpopulation: female

Burden:

Age Groups (years)	Population (N)	Annual Incidence (per 100,000)	Case Fatality Rate (probability)
Infants < 1	2183518	20300.00	0.000037
Children 1 to < 20	39904750	11872.00	0.000024
Adults 20 to < 65	94379233	6600.00	0.000415
Elderly >= 65	22853007	9000.00	0.011141

Save

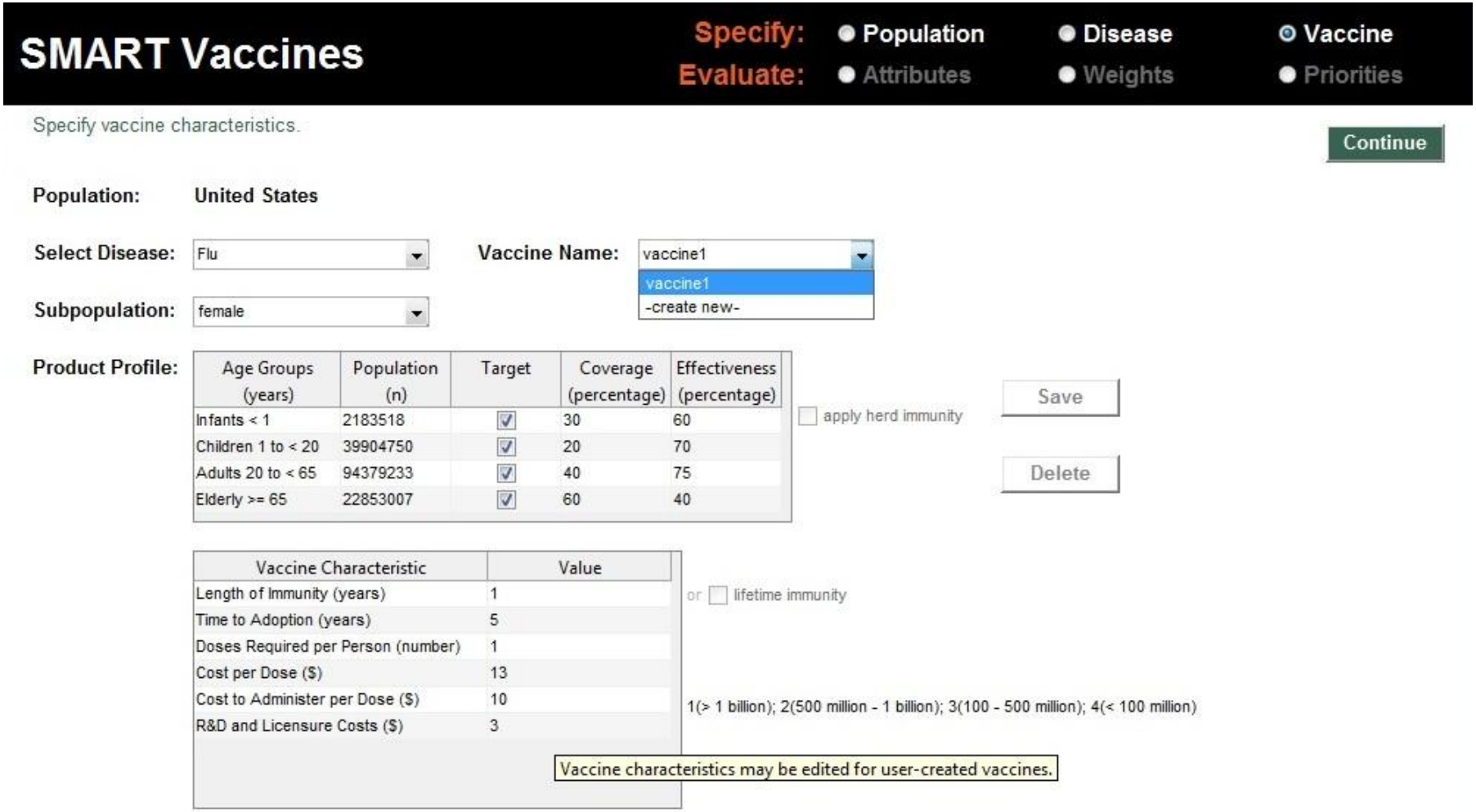
Delete

Outcome	Illness Type	Percent of Cases	Disutility (Tolls)	Disability (Weight)	Duration (Days)	Hospital Costs	Outpatient Costs	Medicat Costs
death by disease	death	--	--	--	--	6000	250	0
influenza without outpatient visit	morbidity	59.5	0.09	0.01	5	0	0	3
influnenza with outpatient visit	morbidity	40.0	0.13	0.10	5	0	250	3
influenza with inpatient visit	morbidity	0.5	0.20	0.30	5	6000	250	3

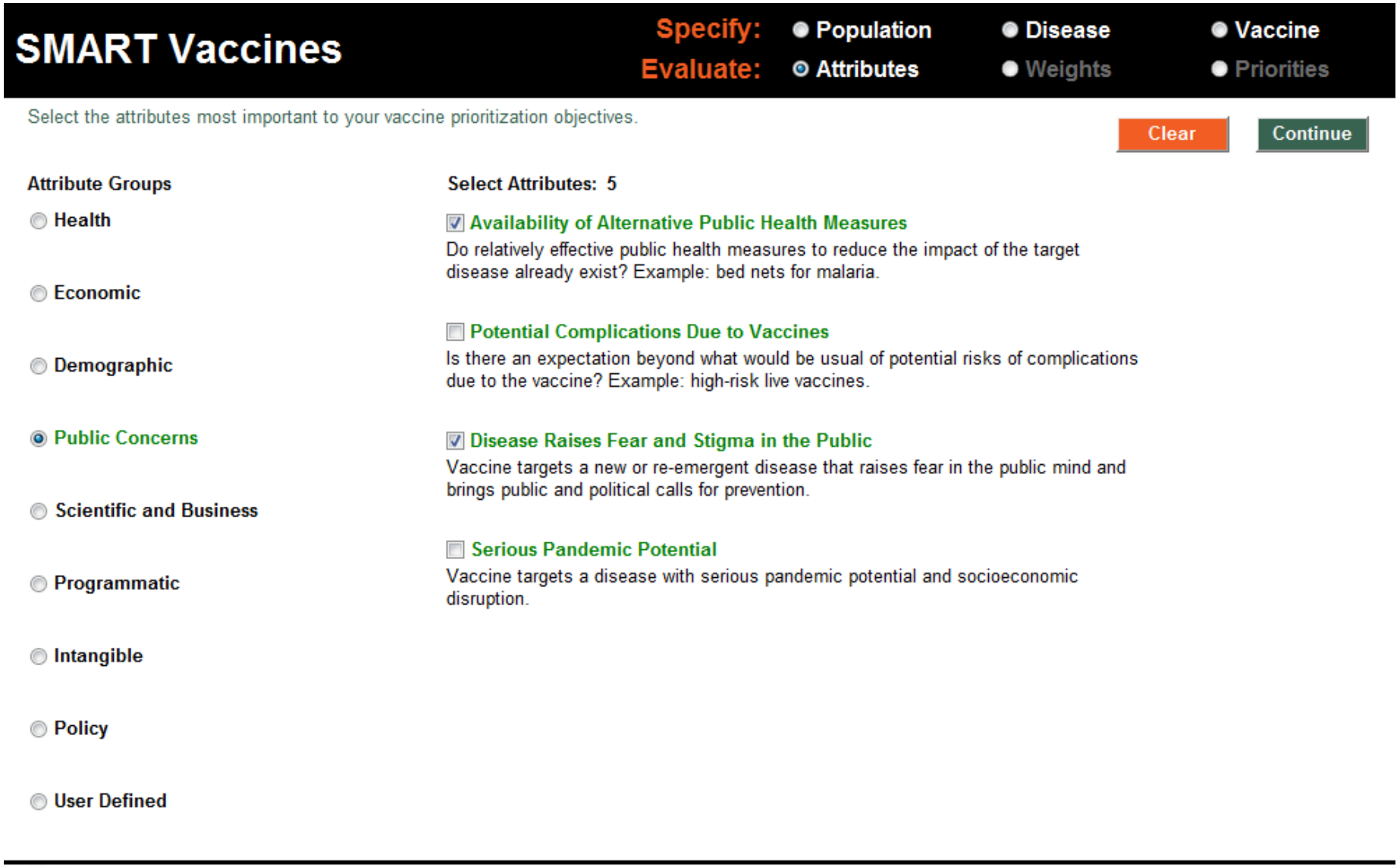
Outcomes, illness types, and corresponding health and cost measures may be edited for user-created diseases This information must be complete for processing.

Cell data populated with '--' are not applicable for illness types (i.e., death, permanent impairment, morbidity) specified and need not be entered.

Product Profile



Attribute Selection



User A: Government Official

SMART Vaccines

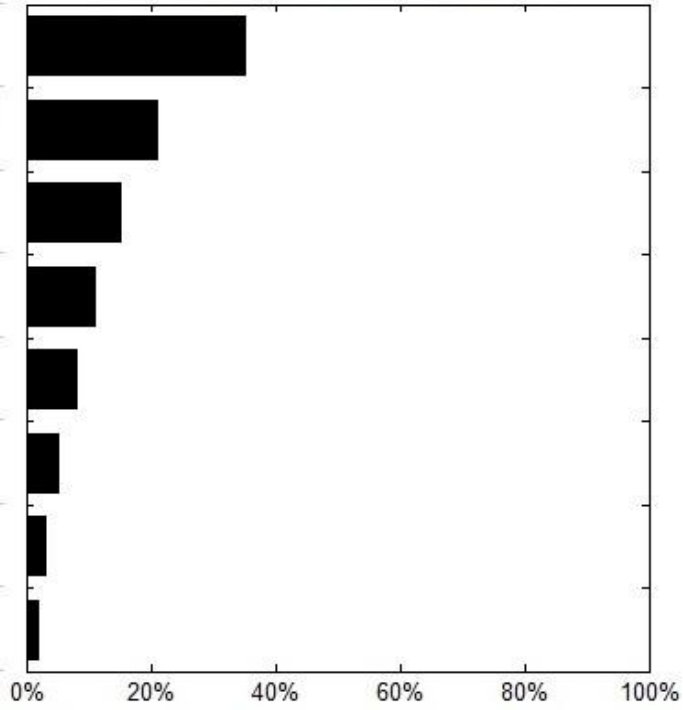
Specify: ● Population ● Disease ● Vaccine

Evaluate: ● Attributes ◉ Weights ● Priorities

Rank attributes in order of importance (1 = MOST IMPORTANT) and fine tune weights.

Continue

Attributes Selected	Least Favorable	Most Favorable	Rank	Modify	Weight
Premature Deaths Averted per Year	0	5000	1		35%
Incident Cases Prevented per Year	0	100000	2		21%
Net Direct Costs (Savings) of Vaccine Use per Year (Millions)	1000	0	3		15%
Benefits Socioeconomically Disadvantaged	no	yes	4		11%
Potential Complications Due to Vaccines	yes	no	5		8%
Disease Raises Fear and Stigma in the Public	no	yes	6		5%
Fits into Existing Immunization Schedules	no	yes	7		3%
Vaccine Raises Public Health Awareness	no	yes	8		2%



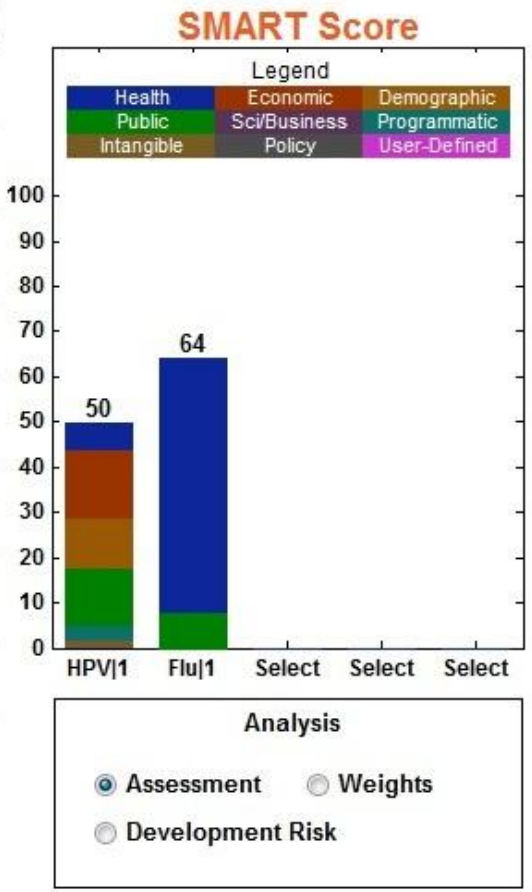
SMART Scores for User A

SMART Vaccines

Specify: ● Population ● Disease ● Vaccine
Evaluate: ● Attributes ● Weights ● Priorities

Select vaccine candidates to compare. Set attributes and scores (least favorable 0 to most favorable 100). View SMART Score.

Attributes Selected	United States Vaccine Candidates: Values (Scores)				
	HPV|vaccine1	Flu|vaccine1	Select	Select	Select
Premature Deaths Averted per Year	740 (15)	11233 (100)			
Incident Cases Prevented per Year	2340 (2)	6119401 (100)			
Net Direct Costs (Savings) of Vaccine Use per Year (Millions)	-42 (100)	1801 (0)			
Benefits Socioeconomically Disadvantaged	yes (100)	no (0)			
Potential Complications Due to Vaccines	no (100)	no (100)			
Disease Raises Fear and Stigma in the Public	yes (100)	no (0)			
Fits into Existing Immunization Schedules	yes (100)	no (0)			
Vaccine Raises Public Health Awareness	yes (100)	no (0)			



User B: Vaccine Manufacturer

SMART Vaccines

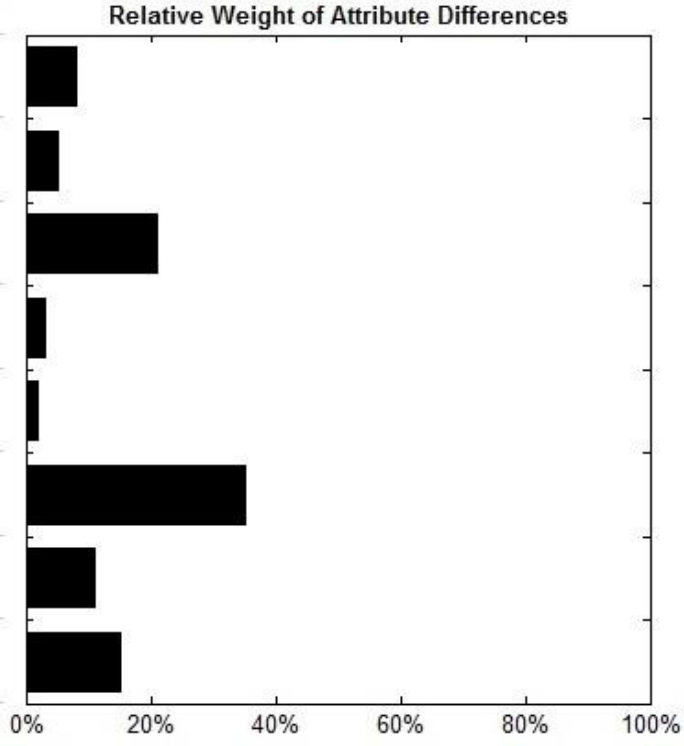
Specify: ● Population ● Disease ● Vaccine

Evaluate: ● Attributes ◉ Weights ● Priorities

Rank attributes in order of importance (1 = MOST IMPORTANT) and fine tune weights.

Continue

Attributes Selected	Least Favorable	Most Favorable	Rank	Modify	Weight
Premature Deaths Averted per Year	0	5000	5		8%
Incident Cases Prevented per Year	0	100000	6		5%
Net Direct Costs (Savings) of Vaccine Use per Year (Millions)	1000	0	2		21%
Potential Complications Due to Vaccines	yes	no	7		3%
Disease Raises Fear and Stigma in the Public	no	yes	8		2%
Likelihood of Financial Profitability for the Manufacturer	level 1	level 5	1		35%
Existing or Adaptable Manufacturing Techniques	no	yes	4		11%
Potential Litigation Barriers Beyond Usual	yes	no	3		15%



SMART Scores for User B

SMART Vaccines

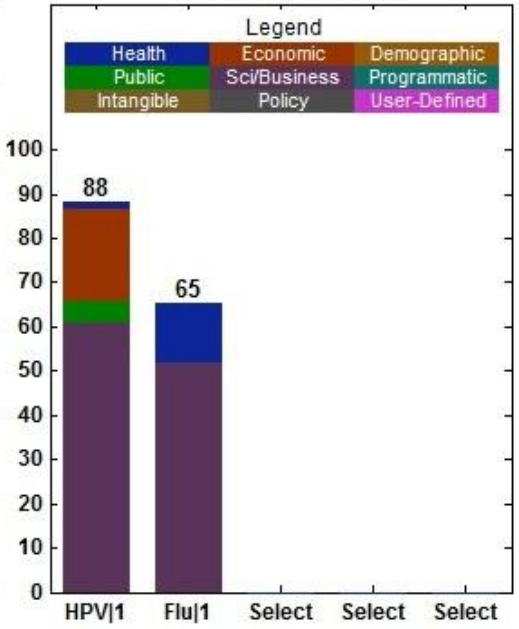
Specify: ● Population ● Disease ● Vaccine

Evaluate: ● Attributes ● Weights ◉ Priorities

Select vaccine candidates to compare. Set attributes and scores (least favorable 0 to most favorable 100). View SMART Score.

Attributes Selected	HPV|vaccine1	Flu|vaccine1	Select	Select	Select
United States Vaccine Candidates: Values (Scores)					
Premature Deaths Averted per Year	740 (15)	11233 (100)			
Incident Cases Prevented per Year	2340 (2)	6119401 (100)			
Net Direct Costs (Savings) of Vaccine Use per Year (Millions)	-42 (100)	1801 (0)			
Potential Complications Due to Vaccines	no (100)	yes (0)			
Disease Raises Fear and Stigma in the Public	yes (100)	no (0)			
Likelihood of Financial Profitability for the Manufacturer	5 (100)	4 (75)			
Existing or Adaptable Manufacturing Techniques	yes (100)	yes (100)			
Potential Litigation Barriers Beyond Usual	no (100)	no (100)			

SMART Score



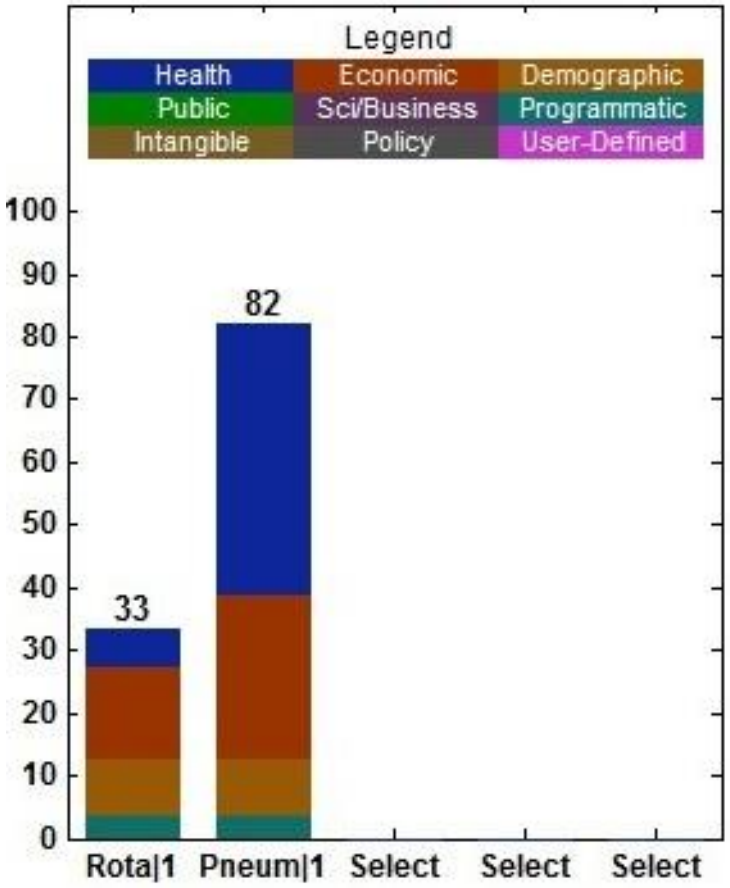
Analysis

◉ Assessment ○ Weights

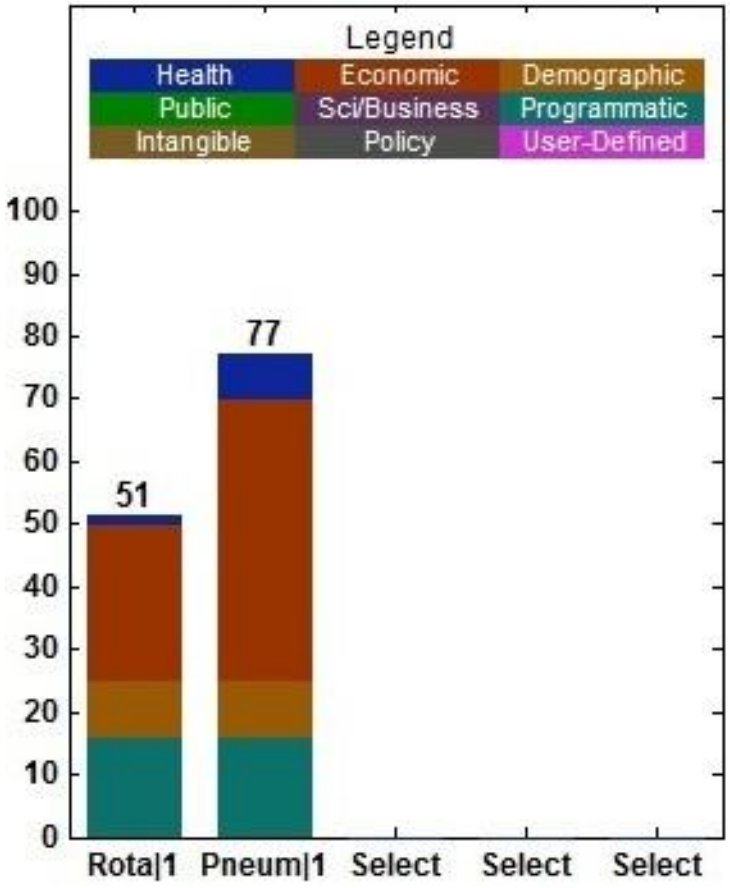
○ Development Risk

Comparative SMART Scores

User X



User Y



Health Minister

Commerce Minister

Expected Benefits of SMART Vaccines

1. Transparency
2. Discussion Facilitation
3. Decision Convergence

Guiding Principle

SMART Vaccines will have the greatest potential and value if it is programmed as a dynamic, continuously evolving software application and made freely available in an open-source environment to all decision makers and developers around the world.

Guiding Strategy

- **To identify a host for SMART Vaccines and its future versions.**
- **To help create a data warehouse and expand data collection for use in SMART Vaccines.**

Work in Progress

SMART Vaccines

Specify: ● Population ● Disease ● Vaccine
Evaluate: ● Attributes ● Weights ◉ Priorities

Examine vaccine profile effects on attributes and SMART Score.

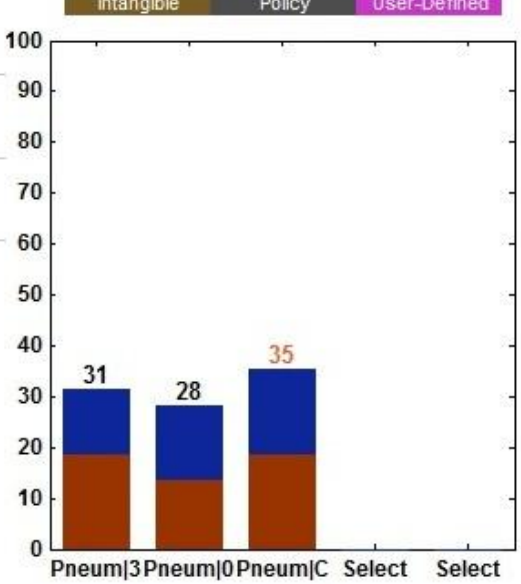
SouthAfrica Vaccine

Vaccine				
	Pneumo|PC			
Likelihood of Licensure within 10 Years	0%	100%	100%	
Coverage (%)	0%	100%	80%	
Effectiveness (%)	0%	100%	80%	
Length of Immunity (Years)	1Yr	Life	15Yrs	
Doses per Person	1	5	2	
Cost per Dose	$1	$1,000	$20	
Cost to Administer per Dose	$1	$1,000	$20	
R&D and Licensure Costs ($100 Millions)	<$1	>$10	$5-10	

Update Vaccine updated

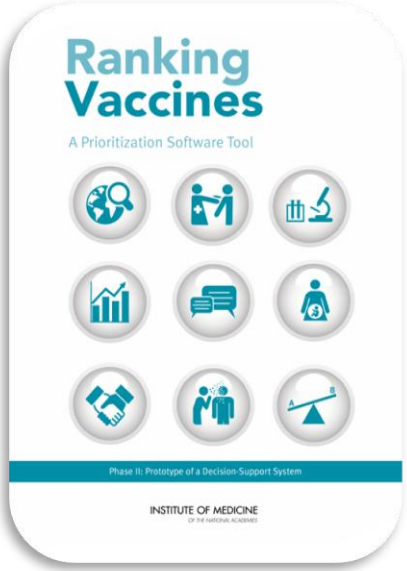
Attributes	Values (Scores)
Premature Deaths Averted per Year	1693 (34)
Quality adjusted life-years (QALYs) Gained	22423 (22)
Net Direct Costs (Savings) of Vaccine Use per Year (Millions)	28 (44)
Cost-Effectiveness ($/QALY)	4050 (60)

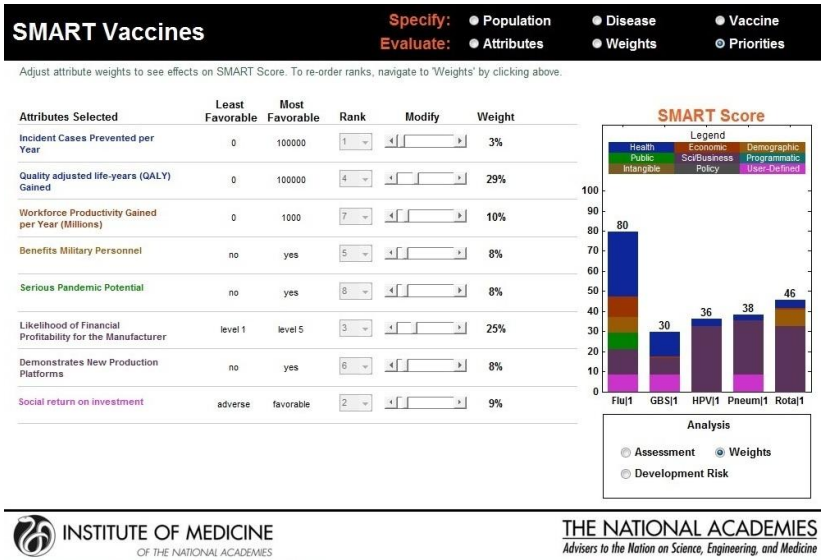
SMART Score



Analysis
● Assessment ● Weights
◉ Vaccine Profile ● Print

Discussion and Feedback





www.nap.edu/smartvaccines

GMadhavan@nas.edu