# Quality of Medicines for Non-Communicable Diseases (NCD): opportunities to improve the evidence

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Quality of Medical Products and Public Health
Boston July 14 2017

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    - Framework to measure quality of medicines in public and privately funded access to medicines programs

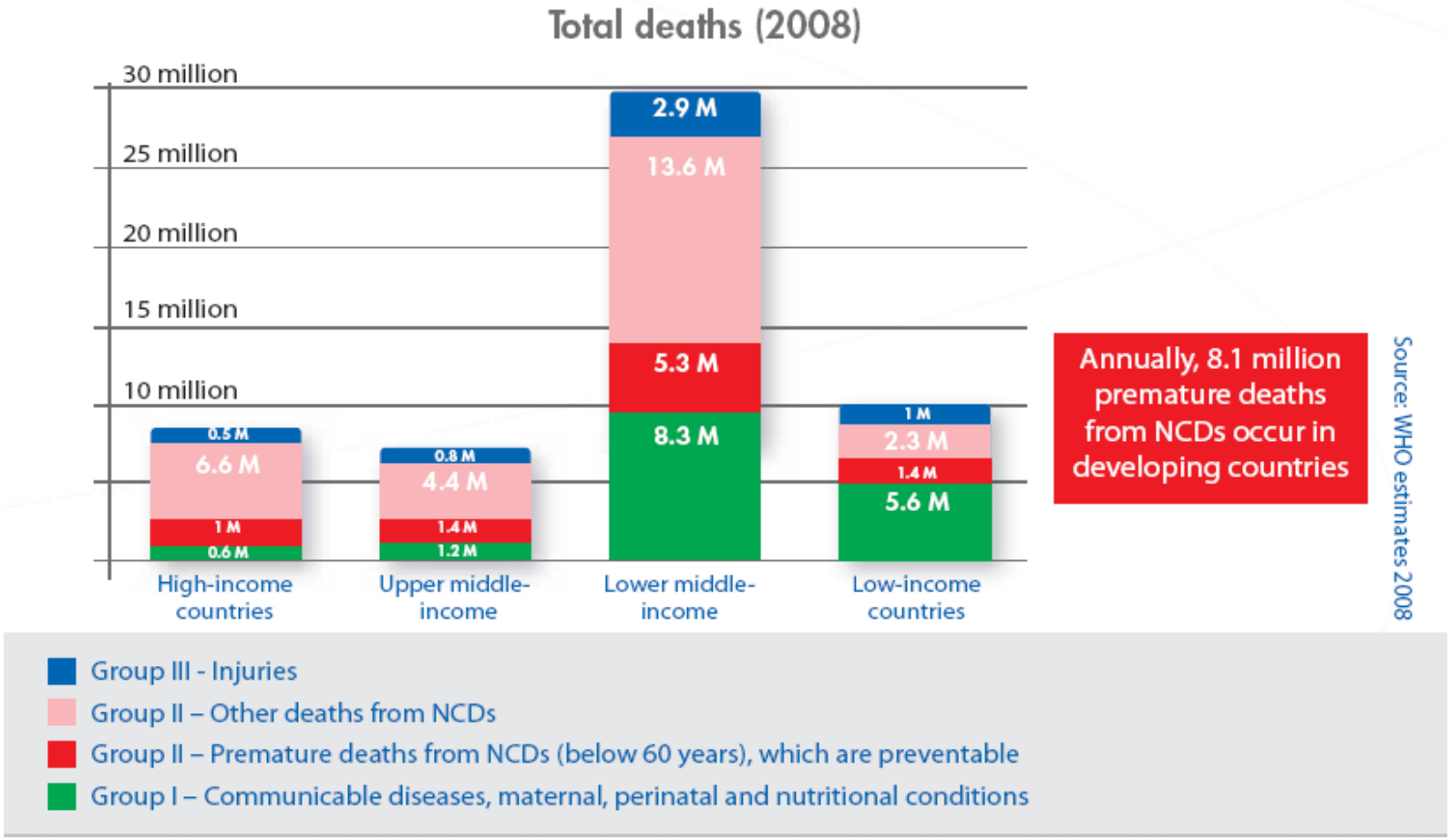
**Part 1: Veronika Wirtz**

Overview

# QUALITY OF NCD MEDICINES

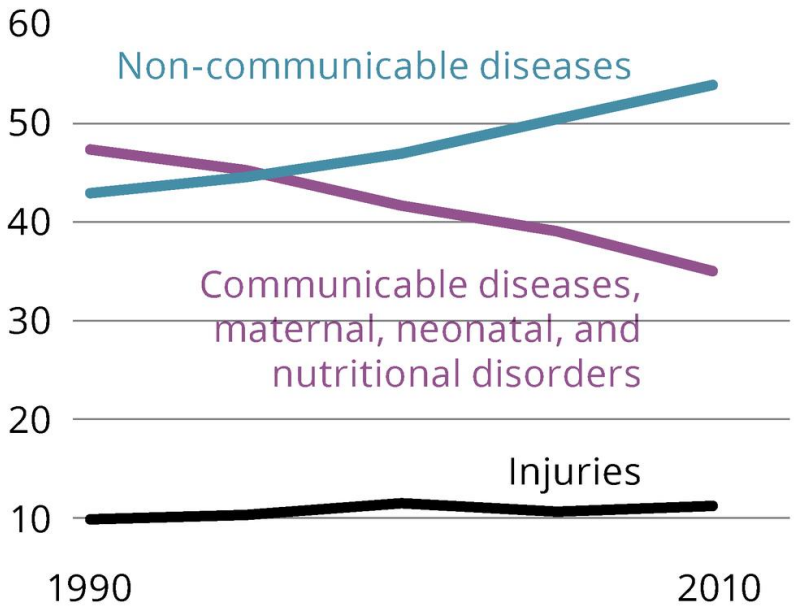
# The NCD gap: People in LMIC develop NCDs at younger ages, suffer more – often with preventable complications – and die sooner than those in high-income countries

**29%** of deaths from NCDs in LMIC occur in people < 60 years versus **13%** in high income countries

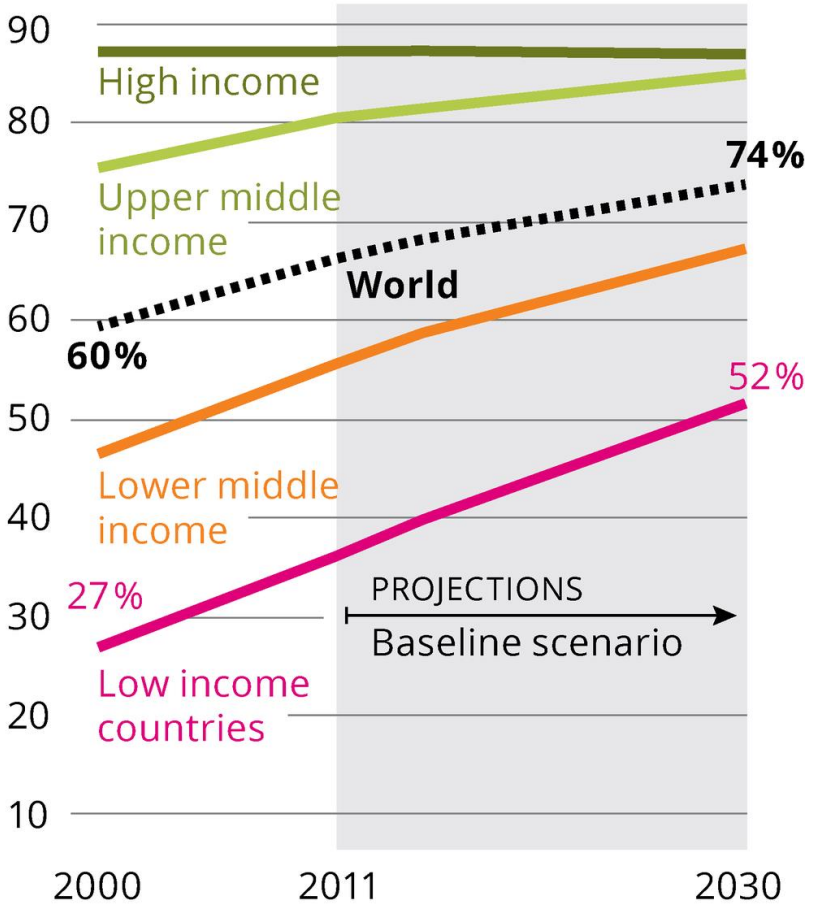


# Loss of healthy life year and death related to NCDs

Loss of healthy life years
(in percentage of total DALY)




Deaths related to non-communicable diseases (in percentage of total deaths)




Noncommunicable diseases, Factsheet, World Health Organization, Geneva, Switzerland

# WHO Global NCD Action Plan 2013-2020

- Target on NCDs
  - "**25 by 25**" target -- a 25 percent reduction in mortality from NCDs by year 2025
- Target #9:

  "an 80% availability of the affordable basic technologies and essential medicines, including generics, required to treat major non-communicable diseases in both public and private facilities"

# Access challenges to NCD medicines

1. **Appropriate selection and use** including adherence
   - Underuse, overuse, misuse, unnecessary expensive use
2. **Affordability**
   - Chronic use, continuous expenditure
   - NCD medicines not included in benefit packages
3. **Sustainable financing**
4. **Reliable supply systems**
5. **Quality and Safety**
   - **Many knowledge gaps**

THE LANCET

## Non-Communicable Diseases 5

# Promotion of access to essential medicines for non-communicable diseases: practical implications of the UN political declaration

*Hans V Hogerzeil, Jonathan Liberman, Veronika J Wirtz, Sandeep P Kishore, Sakthi Selvaraj, Rachel Kiddell-Monroe, Faith N Mwangi-Powell, Tido von Schoen-Angerer, on behalf of* The Lancet *NCD Action Group*

**Access to medicines and vaccines to prevent and treat non-communicable diseases (NCDs) is unacceptably low worldwide. In the 2011 UN political declaration on the prevention and control of NCDs, heads of government made several commitments related to access to essentia of experience with policies for essential medicine knowledge needed to address barriers to long-tern be acquired within existing budgets with efficient s**

Published Online
February 12, 2013

Circulation

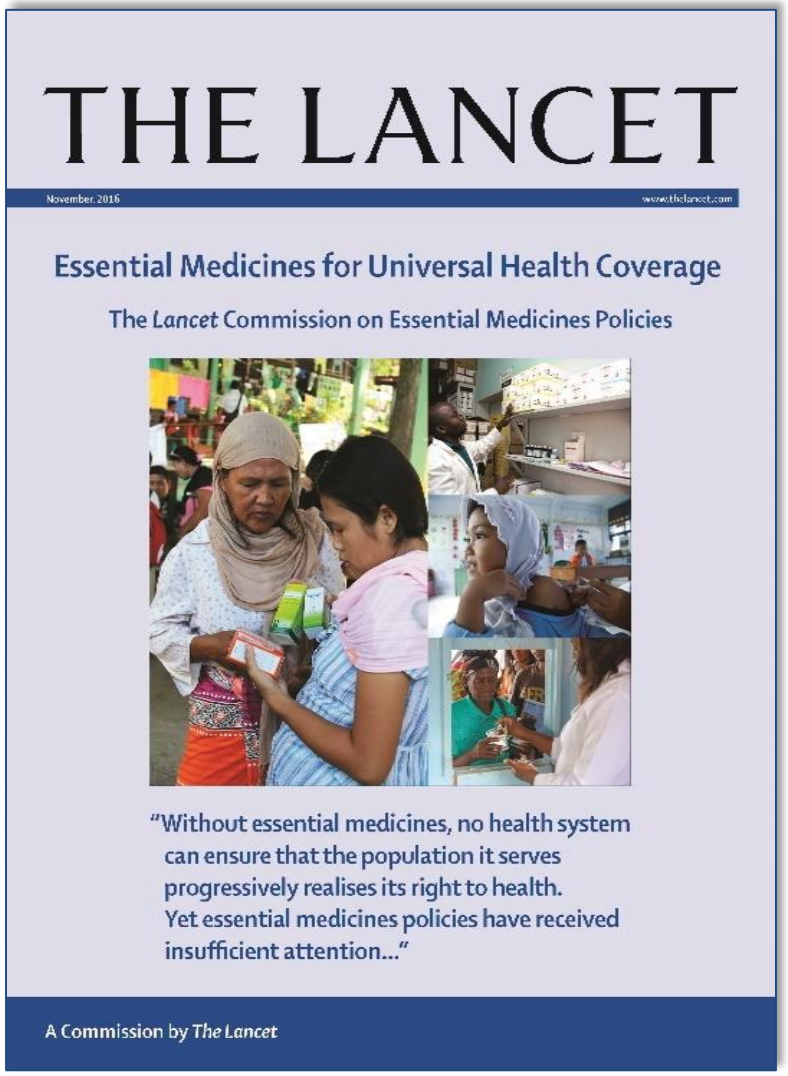
**Global Burden of Cardiovascular Disease**

# Access to Medications for Cardiovascular Diseases in Low- and Middle-Income Countries

Veronika J. Wirtz, MSc, PhD; Warren A. Kaplan, PhD, JD, MPH; Gene F. Kwan, MD, MPH; Richard O. Laing, MB, ChB, MSc, MD

*tract*—Cardiovascular diseases (CVD) represent the highest burden of disease globally. Medicines are a critical intervention used to prevent and treat CVD. This review describes access to medication for CVD from a health system perspective and strategies that have been used to promote access, including providing medicines at lower cost, improving medication supply, ensuring medicine quality, promoting appropriate use, and managing intellectual property issues. Using key evidence in published and gray literature and systematic reviews, we summarize advances in access to cardiovascular medicines using the 5 health system dimensions of access: availability, affordability, accessibility, acceptability, and quality of medicines. There are multiple barriers to access of CVD medicines, particularly in low- and middle-income countries. Low availability of CVD medicines has been reported in public and private healthcare facilities. When patients lack insurance and pay out of pocket to purchase medicines, medicines can be unaffordable. Accessibility and acceptability are low for medicines used in secondary prevention; increasing use is positively related to country income. Fixed-dose combinations have shown a positive effect on adherence and intermediate outcome measures such as blood pressure and cholesterol. We have a new opportunity to improve access to CVD medicines by using strategies such as efficient procurement of low-cost, quality-assured generic medicines, development of fixed-dose combination medicines, and promotion of adherence through insurance schemes that waive copayment for long-term medications. Monitoring progress at all levels, institutional, regional, national, and international, is vital to identifying gaps in access and implementing adequate policies. (*Circulation*. 2016;133:2076-2085. DOI: 10.1161/CIRCULATIONAHA.115.008722.)

# The Lancet Commission Report
# Section 3: Assuring quality of essential medicines




- **Effective national regulatory agencies** are a core component of improving the safety and quality of effective medicines;
- **Good procurement practices** that incorporate effective and transparent quality assurance mechanisms;
- **Concrete targets and public accountability mechanisms** for the performance of national regulatory.

# Quantifying the problem of substandard NCD medicines

- Lack of systematic review to quantify the problem of substandard quality in NCD medicines

- Recent review by Hamilton et al HPP 2016 says “Safeguarding the quality of commonly used medicines for non-communicable chronic illnesses such as statins, antidiabetics, and anti-hypertensives will be of increasing relevance to these countries”

# Recent publications on quality of NCDs medicines

- 3,468 samples collected in Benin, Burkina-Faso, Congo-Brazzaville, the Democratic Republic of Congo, Guinea, Côte d'Ivoire, Mauritania, Niger, Togo and Senegal
- Out of the 1,530 samples randomly tested
- Probability of substandard products increased in products
  - from Asia
  - which are generic
  - containing amlodipine and captopril
  - sold on street-markets were found higher

Antignac et al, International Journal of Cardiology, 2017

# Systematic review of quality of oxytocin in LMIC

- The proportion of low fails was higher in samples collected in Africa than in Asia or Latin America (57.5% versus 22.3% versus 0%, respectively, $P < 0.0001$)
- in private than in public sectors (34.0% versus
- 25.3%, $P = 0.032$)
- and in facilities than in central distributors (37.9% versus 22.0%, $P=0.030$).

Torloni et al BJOG 2016; DOI: 10.1111/1471-0528.13998

# Focus on medicines for maternal and child health

- Of 204 samples tested, 157 (77%) complied with the specifications set for this survey.
- The highest proportion of non-compliant samples was found for oxytocin injection (64%)
- Relatively high failure rates:
  - 41% gentamicin injection
  - 35% ampicillin injection
  - 32% dexamethasone injection


WHO, 2015

**UN Commission on Life-Saving Commodities for Women and Children (UNCoLSC):**

- oxytocin injection,
- magnesium sulfate injection,
- gentamicin injection,
- procaine benzylpenicillin injection,
- ampicillin injection,
- ceftriaxone injection,
- dexamethasone phosphate injection,
- amoxicillin dispersible tablets,
- zinc sulfate dispersible tablets/syrup,
- levonorgestrel tablets, and
- mifepristone tablets.

# Studies examining the quality of medicines for reproductive health

- Oxytocin and ergometrine purchased in Ghana
  - pharmacies, chemical shops and stationary and mobile sellers
  - Among ergometrine ampoules purchased
    - None were within British Pharmacopoeia standards
  - Among oxytocin ampoules purchased,
    - only 11 (26%) were within British Pharmacopoeia standards

Ghana study:

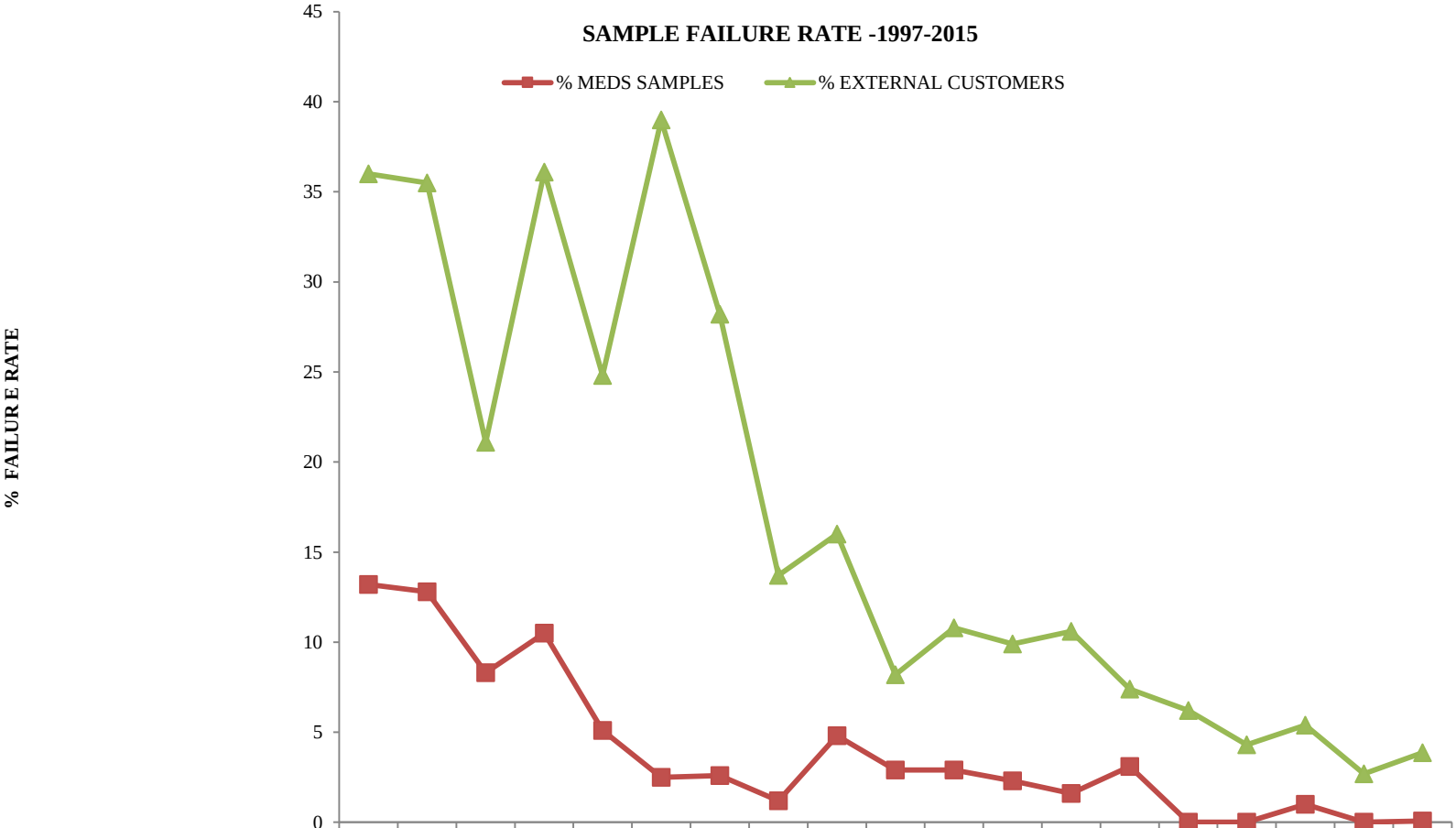
| Assay percentage | Oxytocin 10 IU (%) | Ergometrine 0.5 mg (%) |
|---|---|---|
| 0 | 0 | 1.8 |
| 1–39 | 23.9 | 23.7 |
| 40–59 | 8.7 | 50.8 |
| 60–89 | 41.3 | 21.9 |
| 90–110 | 26.1 | 0 |
| >110 | 0 | 1.8 |
| Total % (N) | 100 (46) | 100 (55) |
| Median % | 64 | 50.5 |
| Per cent expired | 4.3 (2) | 0 (0) |

Stanton et al, BMJ Open 2012

- Similar study done in India also reports problems regarding the quality of oxytocin and methyl-ergometrine

Stanton et al, BMC Preg and Child 2014

# Quality testing at Mission for Essential Drugs and Supplies (MEDS), Kenya




| | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| % EXTERNAL CUSTOMERS | 22.8 | 22.7 | 12.8 | 25.6 | 19.7 | 36.5 | 25.6 | 12.5 | 11.2 | 5.3 | 7.9 | 7.6 | 9 | 4.3 | 6.2 | 4.3 | 4.4 | 2.7 | 3.8 |
| % MEDS SAMPLES | 13.2 | 12.8 | 8.3 | 10.5 | 5.1 | 2.5 | 2.6 | 1.2 | 4.8 | 2.9 | 2.9 | 2.3 | 1.6 | 3.1 | 0 | 0 | 1.0 | 0 | 0.07 |

Source: http://meds.or.ke/images/downloads/EPNFORUM2016.pdf

# Summary of anti-falsification strategies

## National initiatives

- Establish adequate NMRA and PV capacity
- Report to NMRA and global reporting system
- Drug screening at entry ports and throughout supply chain
- Medicines certified by recognised bodies
- Public awareness campaigns
- Government interdepartmental coordination
- Tackling corruption
- Protect pharmaceutical security in disrupted regions
- Police/ security involvement if required
- Legislation to bring medicine falsifiers to justice

## International stage

- Open access global reporting system
- Data-mining drug safety reports
- International support and guidance for developing NMRA and PV capacity
- Strong international leadership (e.g. WHO, INTERPOL, UNODC)
- Coordination between stakeholders including public health, pharmaceutical and law enforcement
- Active funding and participation by supranational bodies
- Global trade agreements that tackle poor quality medicines without disrupting legitimate generics

## Securing medicine authenticity


## Local pharmacy

- Pharmacist and CHW training and education
- Check medicine registration
- Check medicine packaging and product quality (e.g. WHO Checklist)
- Educate the public
- Internet pharmacists required to display registration certification

## Improved diagnostics

- Invest in R&D for medicine quality testing
- Encourage technique applicability to LMIC
- Field studies to assess new technologies

## Consumer verification

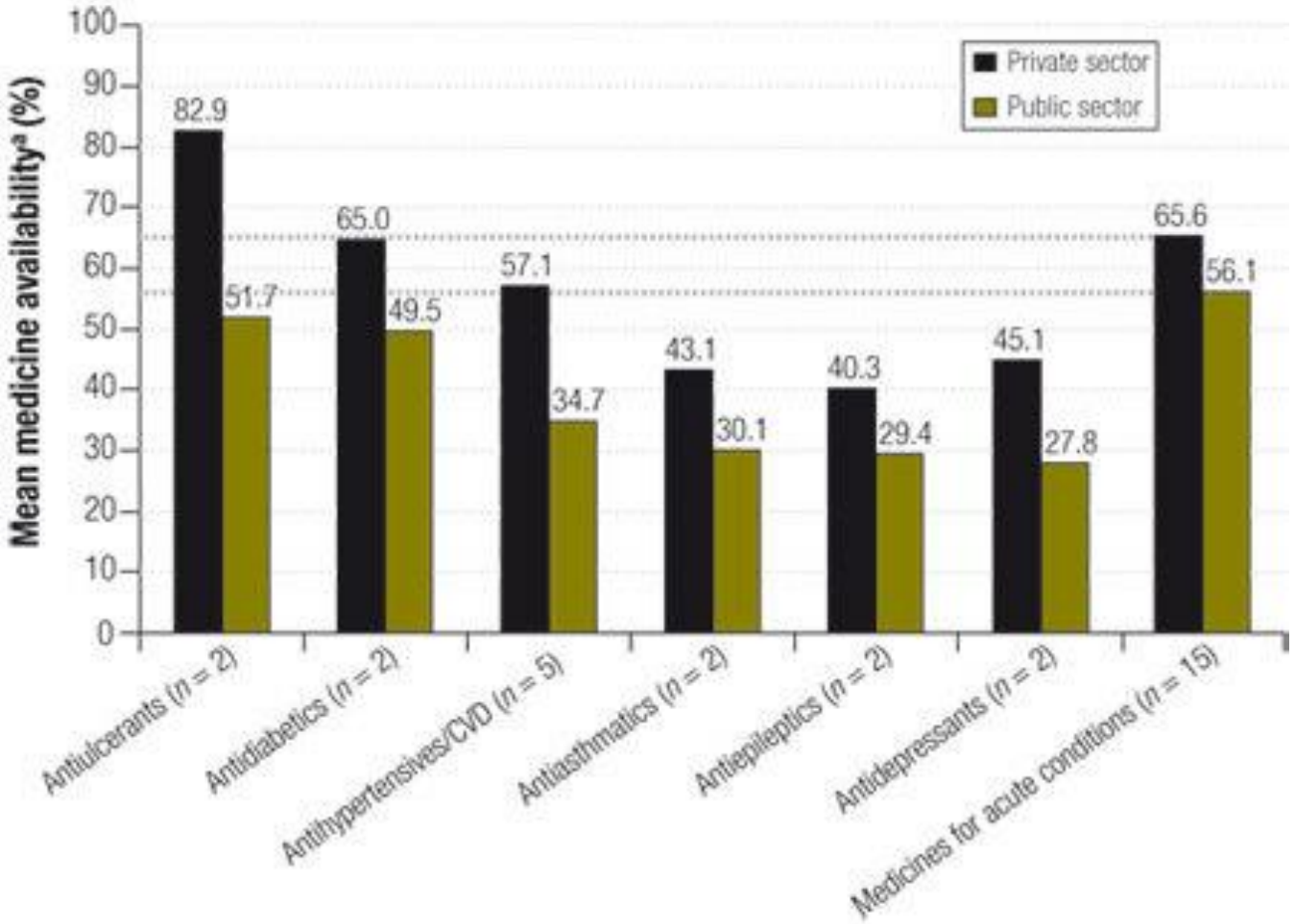
- Holograms/ packaging inspection
- Mobile Authentication Services
  - Subsidise MAS expansion
  - Link with adherence/ mHealth initiatives?
  - Monitor coverage and effectiveness

Hamilton et al Health Policy & Planning, 2016

# Monitoring availability, price and affordability of medicines


- A reliable method of comparing prices and availability across the healthcare sector in country
- Price transparency; allowing international comparisons
- Large database with over 80 surveys publically accessible

# Comparison of mean availability of individual medicines for chronic conditions, by therapeutic class, and of 15 medicines for acute conditions, in 40 LMIC




Availability is expressed as the percentage of facilities where a product was found on the day of data collection

Cameron et al, 2012

# Routine quality testing by procurement agencies or NMRA

- MEDS as an example => are there other examples
- Ecumenical Pharmaceutical Network (EPN): network of mini-lab testing specimen
- Tamil Nadu Medical Services Corporation Ltd. (TNMSC)
- Delhi E-Procurement

**National Medicines Regulatory Authorities (NMRA)**

- ANVISA, Brazil => quality reports
- Thailand => quality testing
- Mexico => not publically available, requests should be made

**RICHARD LAING**

Opportunity to collaborate with the private sector on quality of medicines related issues

# ACCESS TO MEDICINES PROGRAMS

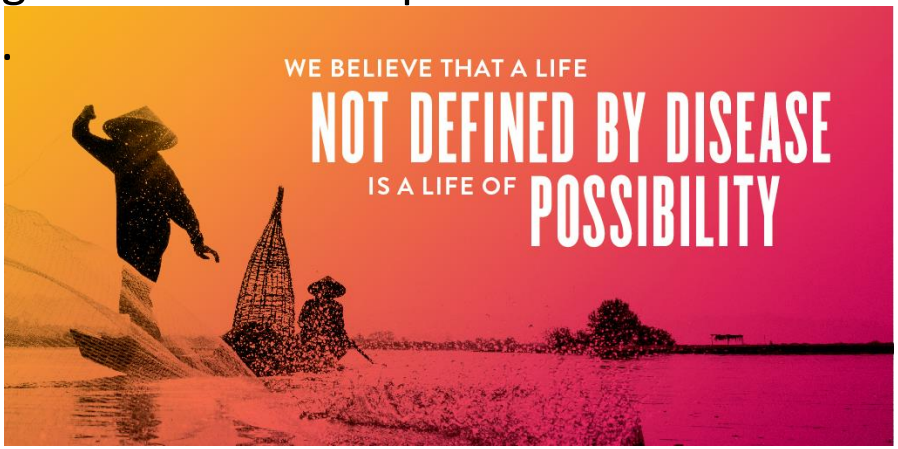
# Access-to-medicines programs

- Opportunities to collaborate with public and privately funded programs
  - To monitor quality
  - To evaluate program outcomes and impact

# What is Access Accelerated?

Access Accelerated is a global initiative to address the rise of NCDs. Its overarching aim is to work towards the United Nations Sustainable Development Goal target to reduce premature deaths from NCDs by one-third by 2030.

- multi-stakeholder collaboration involving 23 biopharmaceutical companies
- working with partners to help overcome access barriers to NCD medicines in LMICs.
- Access Accelerated supports on-the-ground work to improve NCD prevention, diagnosis and treatment.



# BU SPH independent evaluators

to develop and implement an evaluation framework for industry-led NCD medicine access initiatives

ACCESS ACCELERATED

*Moving NCD Care Forward*

THE WORLD BANK
IBRD • IDA

uicc
global cancer control
A MEMBERSHIP ORGANISATION
FIGHTING CANCER TOGETHER

IFPMA
International Federation of Pharmaceutical Manufacturers & Associations

# 4 core project activities of the Access Accelerated evaluation

Development of common framework and metrics

Tracking of progress

Training in metrics and evaluation

Proposal for innovative evaluations

## TAXONOMY OF BARRIERS

| Level | Barrier |
|---|---|
| **International and regional policies** | Research and development |
| | Intellectual property rights |
| | International donor agenda |
| **National health sector policies** | Financing |
| | Regulation and legislation |
| | Institutional arrangements and management |
| | Government priority setting |
| **Health service delivery** | Service quality |
| | Medicine quality |
| | Cost |
| | Irregular availability |
| | Geographic and physical accessibility |
| **Individuals, households, communities** | Affordability |
| | Knowledge, awareness, and perception |
| | Culture and social |

## TAXONOMY OF STRATEGIES

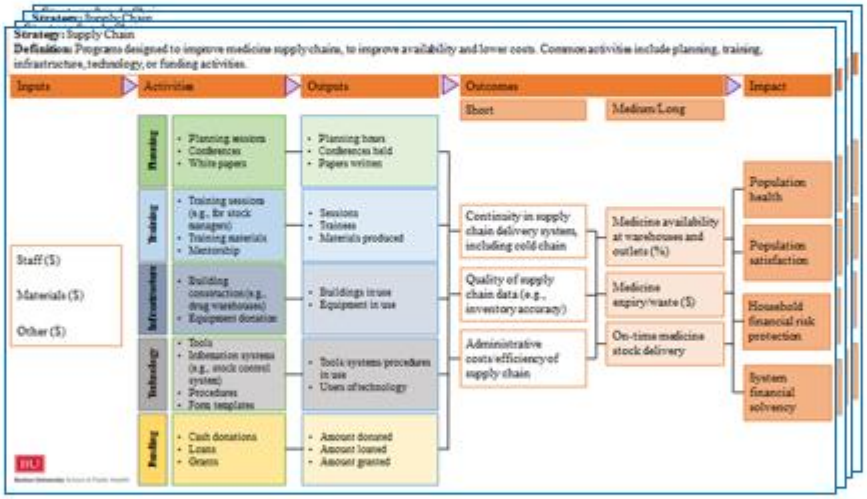
| Strategy type | Strategy |
|---|---|
| **Price Strategy** – Strategies with a primary focus on reducing the price of medicines. | Price Reduction |
| | Medicine Donation |
| **Production Strategy** – Strategies with a primary focus on increasing the production of medicines. | Licensing Agreements |
| | Manufacturing |
| | Drug Development Research |
| **Systems Strategy** – Strategies with a primary focus on aspects of the health system that affect availability and access to medicines. | Regulation |
| | Financing |
| | Supply Chain |
| | Health Service Delivery |
| **Demand Strategy-** Strategies with a primary focus on increasing consumer demand for medicines. | Community Awareness |

# Metrics Progress To Date

## TAXONOMIES DRAFTED

- Taxonomy of Barriers to Access
- Taxonomy of Strategies

## 10 LOGIC MODELS DRAFTED




## EARLY DRAFTS

- Core Indicators
- Link to SDGs

## STILL TO COME (MOSTLY SOW2)

- Repository
- Data Collection Process
- Report Template
- Actual Year 1 Report

# Commitment to transparency

BU School of Public Health
Evaluation of Access Accelerated

Home | Methods | Data | Agreements | Resources | Contact us

## Agreements

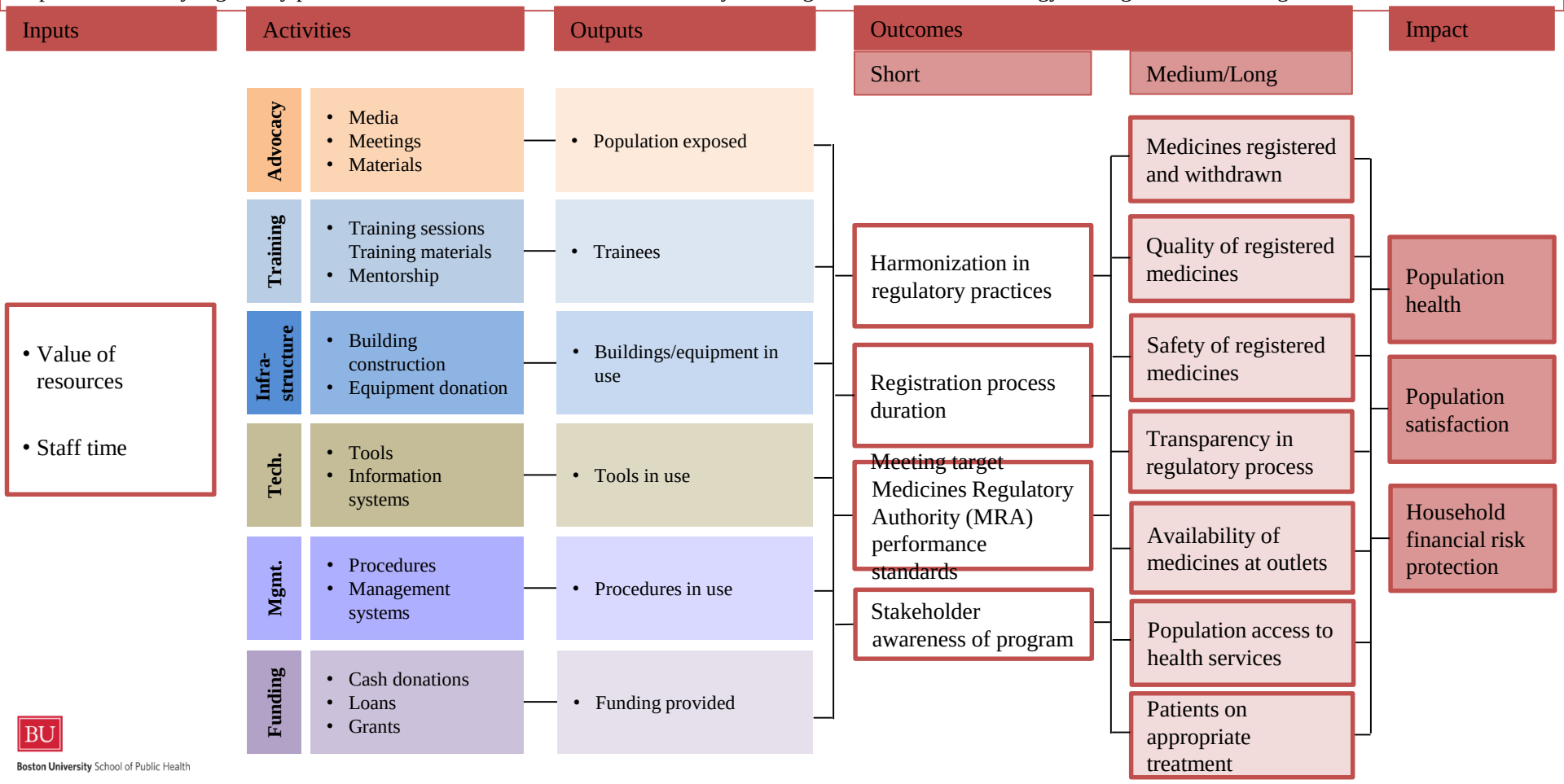
Please see the following agreements between Boston University and International Federation of Pharmaceutical Manufacturers & Associations (IFPMA):

- Master Service Agreement
- Scope of Work 1
- Scope of Work 2

# Defining the program: A Logic Model

- Tool to align all stakeholders on common understanding of program
- Program/project road map
  - Where are you going?
  - How will you get there?
  - What will tell you that you've arrived?
- Provides framework with specific constructs to evaluate
- A series of "if-then" relationships that, if implemented as intended, lead to the desired outcomes
- The core of program planning and evaluation

**Strategy:** Regulation and Legislation
**Definition:** Programs designed to improve and harmonize pharmaceutical regulatory systems, improve government coverage of and access to treatments, and/or improve in-country regulatory processes. Common activities include advocacy, training, infrastructure, technology, management or funding activities.

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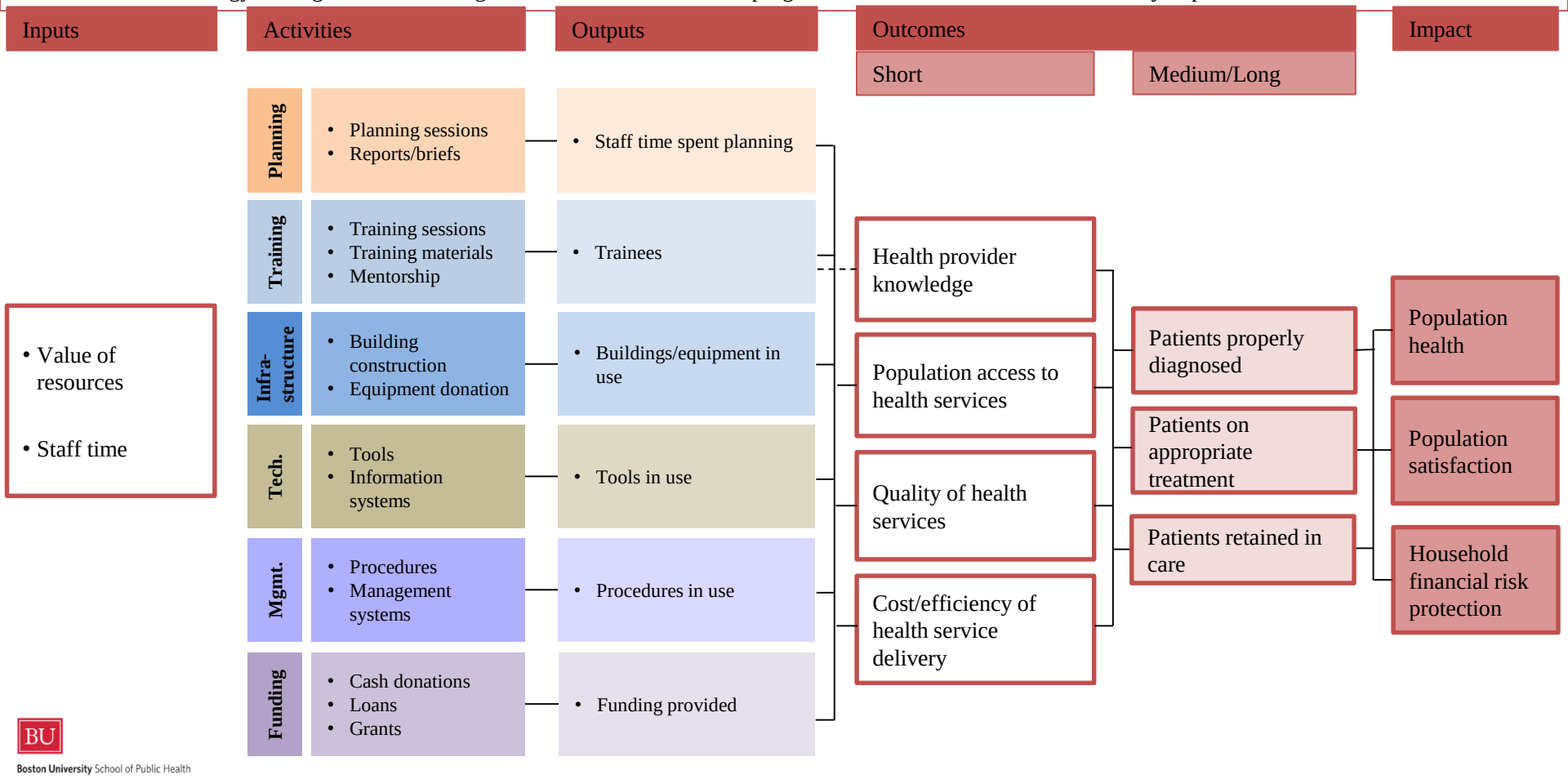
**Strategy:** Health Service Delivery

**Definition:** Programs designed to improve the availability, and affordability, and quality of health services. Common activities include planning, training, infrastructure, technology, management, or funding activities. Also included are programs that deliver health services directly to patients.

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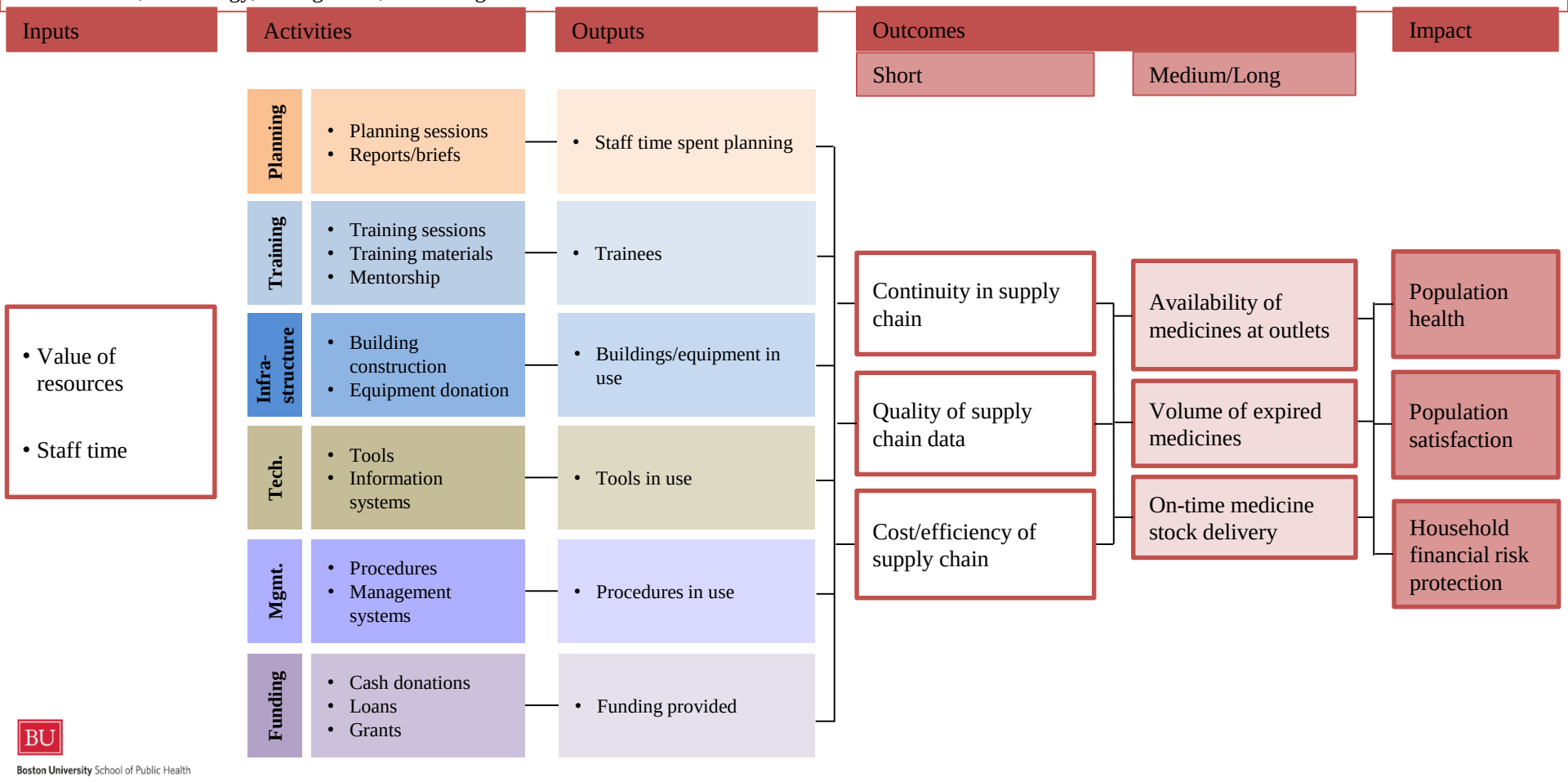
**Strategy:** Supply Chain
**Definition:** Programs designed to improve medicine supply chains, to improve availability and lower costs. Common activities include planning, training, infrastructure, technology, management, or funding activities.

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# Metadata Example: Availability of medicines at outlet

*See Handout*

| | |
|---|---|
| Abbreviated name | Availability of medicines at outlets |
| Definition | Percentage of outlets with medicine available at the time of visit |
| Numerator | Number of facilities that have medicine on stock at the time of visit |
| Denominator | Number of facilities visited |
| Disaggregation | Level of facility (primary/secondary/tertiary)<br>Geographical region (urban/rural) |
| Method of measurement | Data on the availability of a certain medicine are collected from a survey of a sample of facilities. Availability is reported as the percentage of medicine outlets where a particular medicine was found on the day of the survey. Health facility reports may also include stock outs indicators but require regular independent verification. |
| Method of frequency | Monthly or quarterly |
| Monitoring and evaluation | Outcome |
| Preferred data source | Facility surveys |
| Other possible source | Routine facility information systems |
| Further info | Draft comprehensive global monitoring framework and targets for the prevention and control of non-communicable diseases, including a set of indicators. Agenda item A66/8, Sixty-sixth World Health Assembly, 20–28 May 2013. Geneva: World Health Organization; 2013 http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_8-en.pdf?ua=1 |

# Thank you

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