Now it's been made, will it be used? Exploring the pathway from the lab to the community through effectiveness and equity

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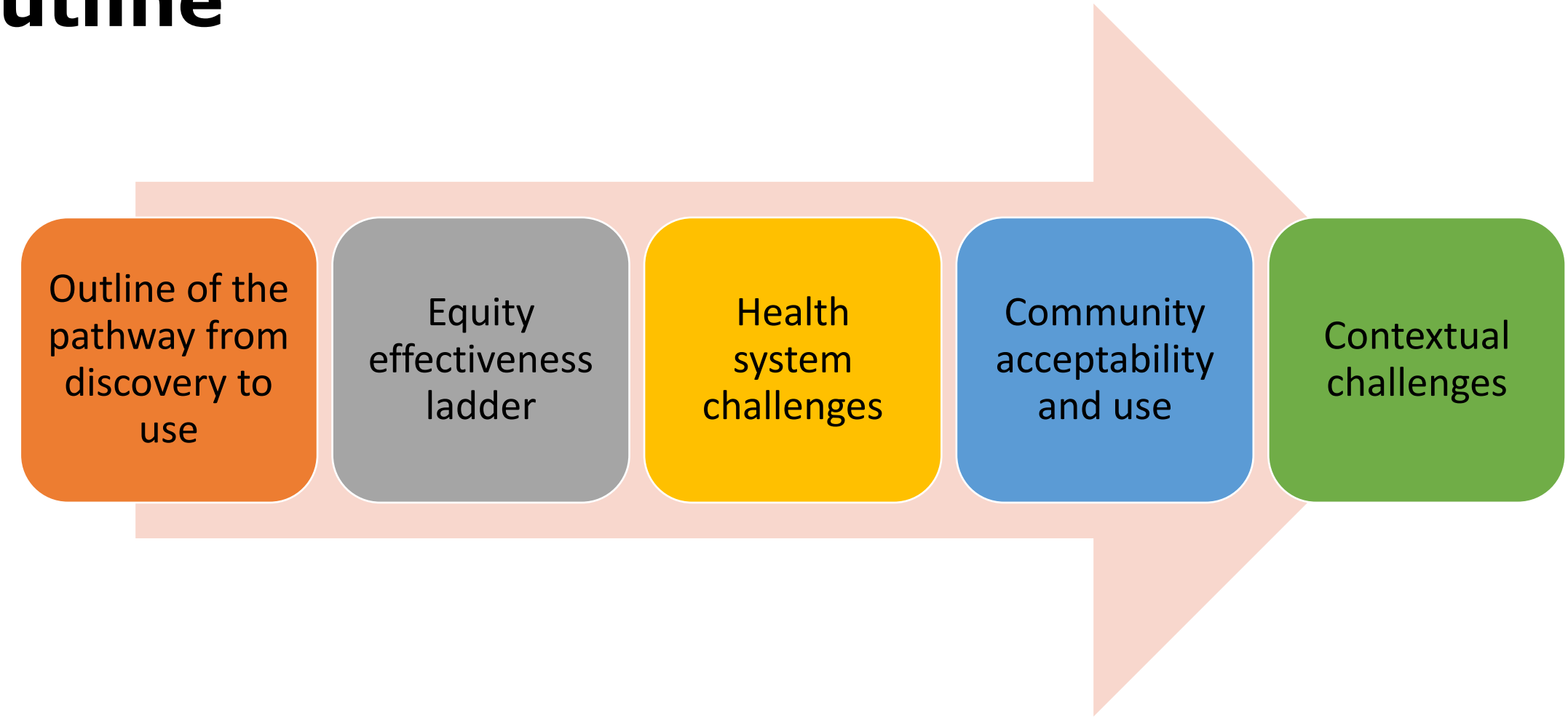
Outline


Outline of the pathway from discovery to use
Equity effectiveness ladder
Health system challenges
Community acceptability and use
Contextual challenges

My aim

To introduce some of the challenges to equity and effectiveness faced in the rollout and use of medical products, and;

To illustrate opportunities to consider the end user during development stage

Neglected Tropical Diseases and Malaria

NTDs

- 20 infectious diseases and conditions identified in the current WHO roster
- Affects 1.7 billion people globally
- Preventable and treatable
- Ancient diseases
- Affect the most poor and vulnerable people in the world
- Low mortality and high morbidity
- High degree of co-endemicity
- Impact inhibits development
- "NTDs promote poverty and poverty promotes NTDS"*
- Very little drug development – RoI unlikely'

Malaria

- In 2021, 247 million cases globally, with 619,000 deaths^
- WHO African Region bears the greatest burden of malaria in the world – with 95% of cases, 96% deaths^
- Approach to control and eliminate malaria includes vector control, bed nets, case management, preventive chemotherapy and vaccines
- Since Oct 2021, WHO recommends the RTS,S/AS01 malaria vaccine for children living in moderate – high transmission

(*Hotez et al 2007; *Fenwick 2012; ^WHO https://www.who.int/news-room/fact-sheets/detail/malaria; 'Walker M et al (2021) Clin Infect Dis.15;73(6)
)

PC-NTDs

- Neglected tropical diseases (NTDs) that use preventive chemotherapy for elimination as a public health problem
- Lymphatic filariasis, schistosomiasis, onchocerciasis, soil-transmitted helminths, trachoma
- Annual or biannual mass drug administration (MDA) to all eligible individuals living in endemic communities
- No diagnosis prior to treatment
- Delivery largely through volunteers, teachers
- Successful elimination requires consistent and high levels of participation in communities over time

Source: BBC News

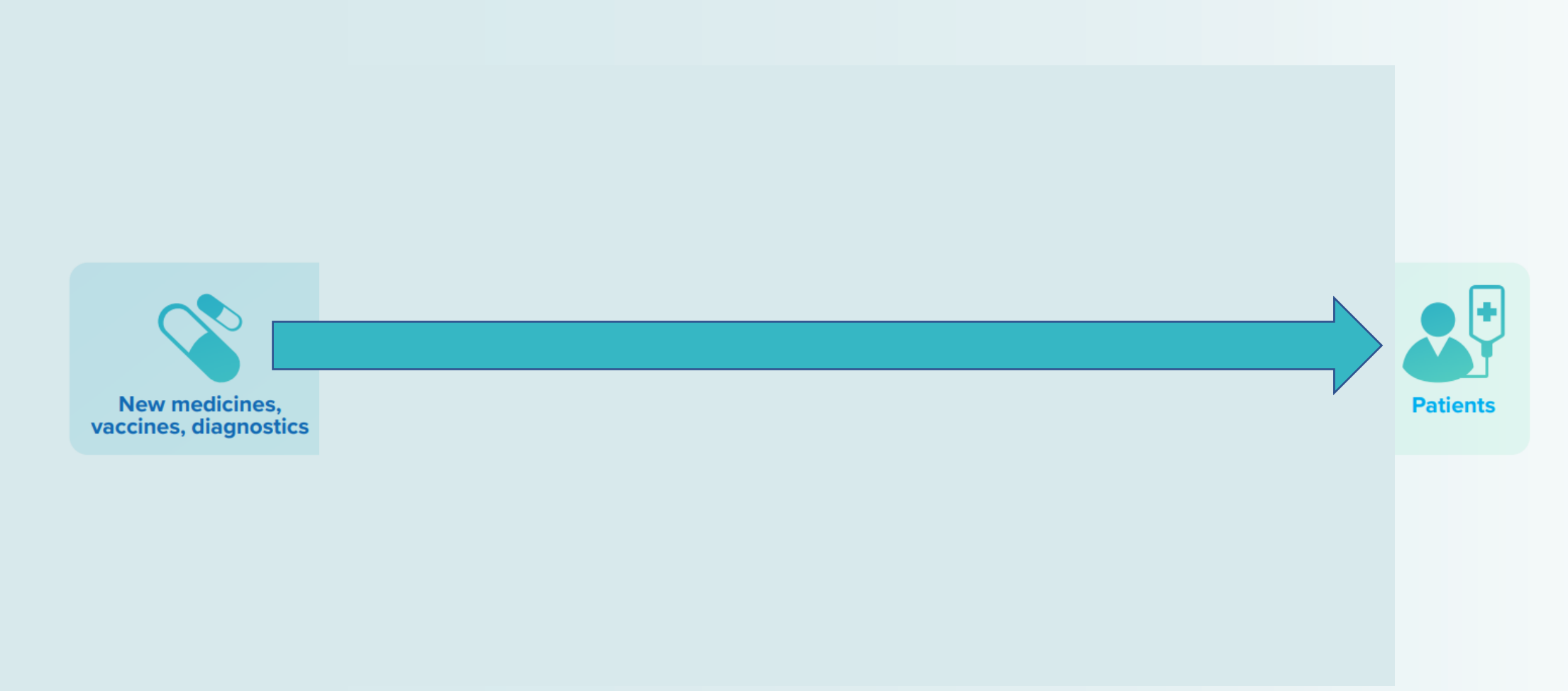


Figure: Access and Delivery Partnership

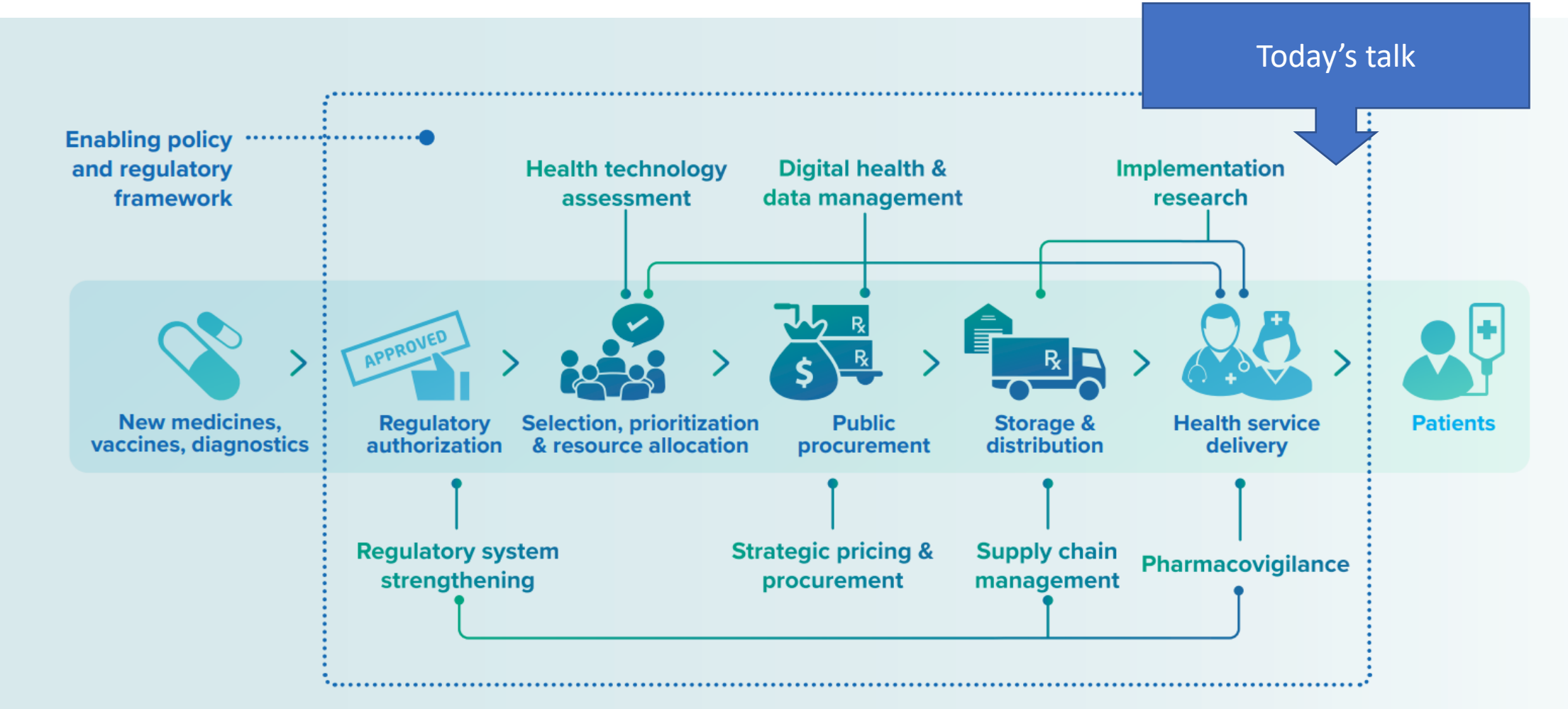
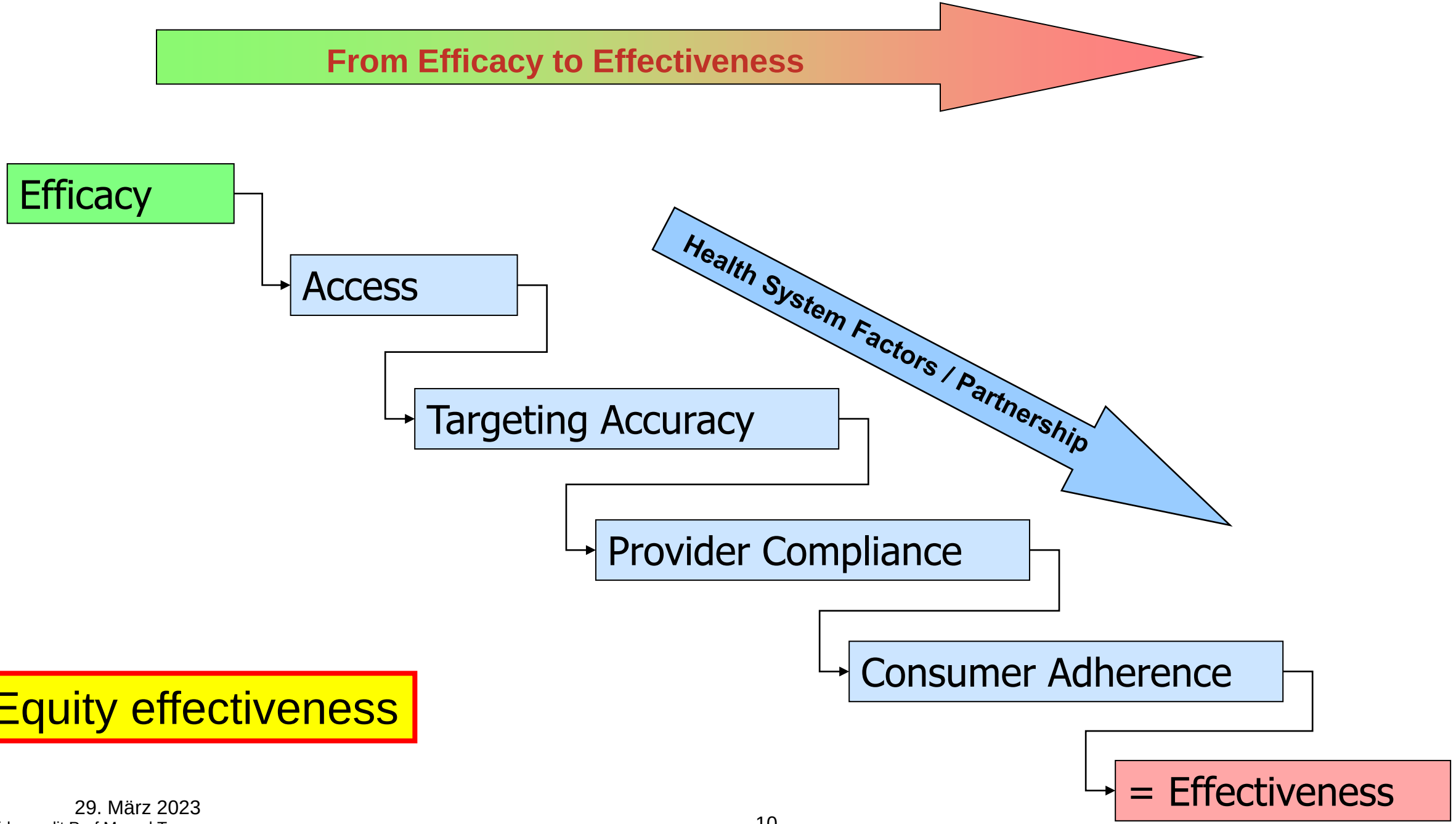
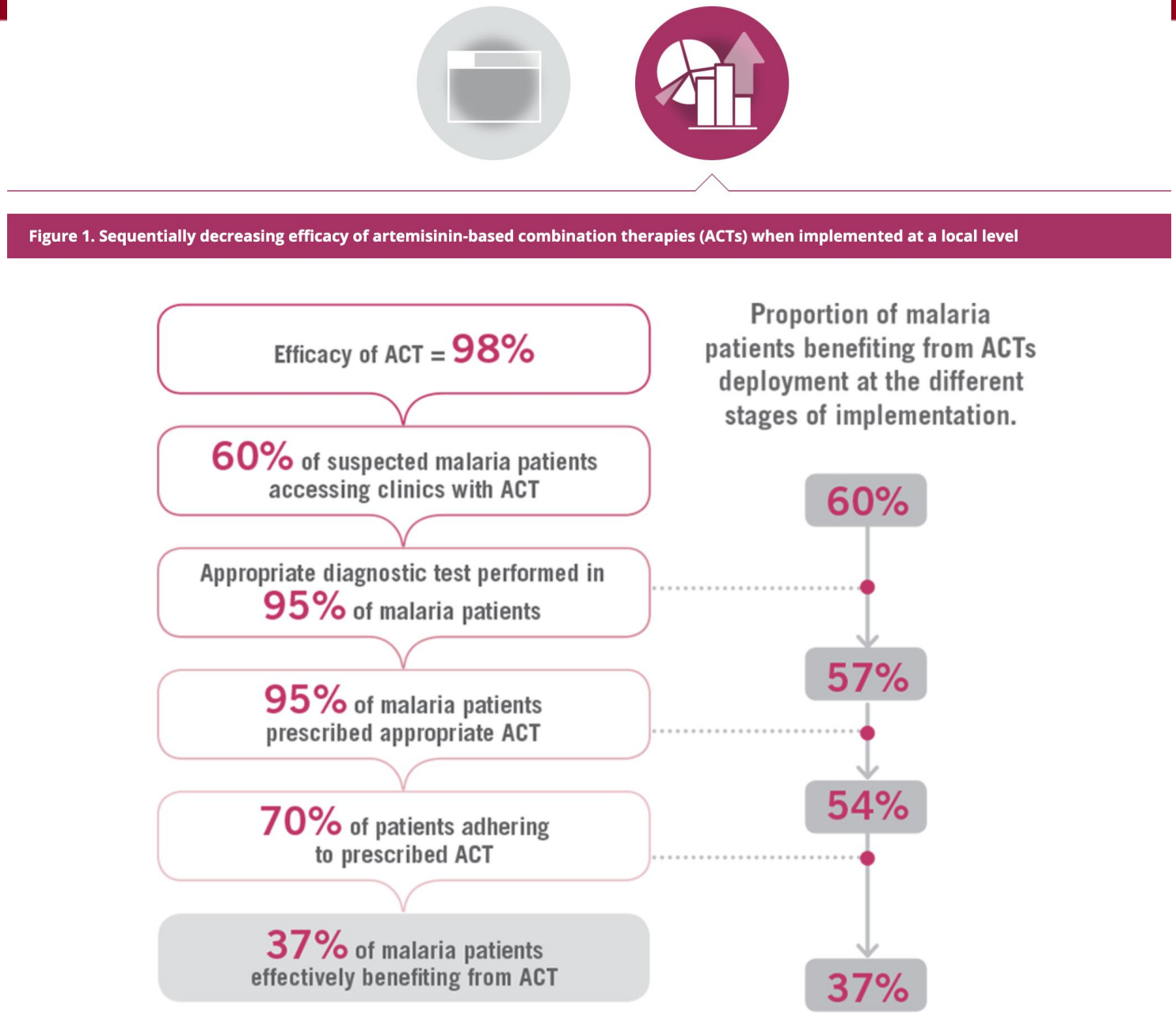


Figure: Access and Delivery Partnership

What happens when a product (drug, diagnostic, vaccine) enters the delivery system?

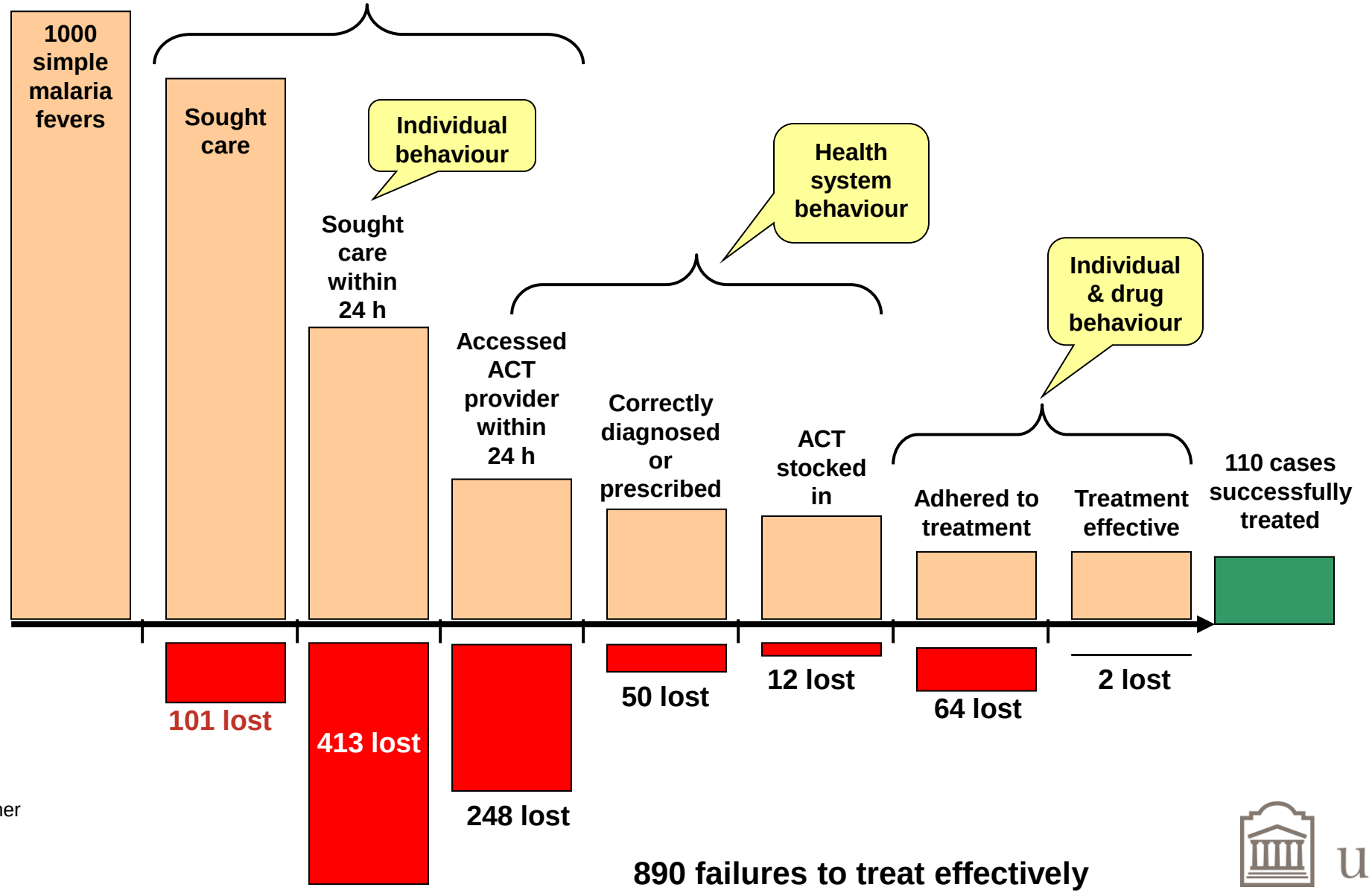

From Efficacy to Effectiveness
Efficacy
Access
Targeting Accuracy
Provider Compliance
Consumer Adherence
= Effectiveness
Health System Factors / Partnership
Equity effectiveness

Artemisinin-based combination therapy (ACT) for treatment of malaria



Source: Understanding implementation research (adphealth.org)

System effectiveness of ALU in Rufiji Tanzania



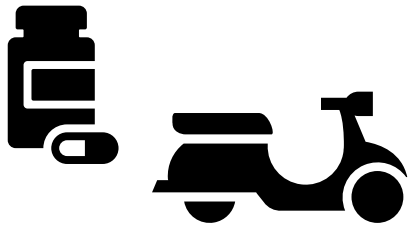
Slide credit Prof Marcel Tanner

890 failures to treat effectively

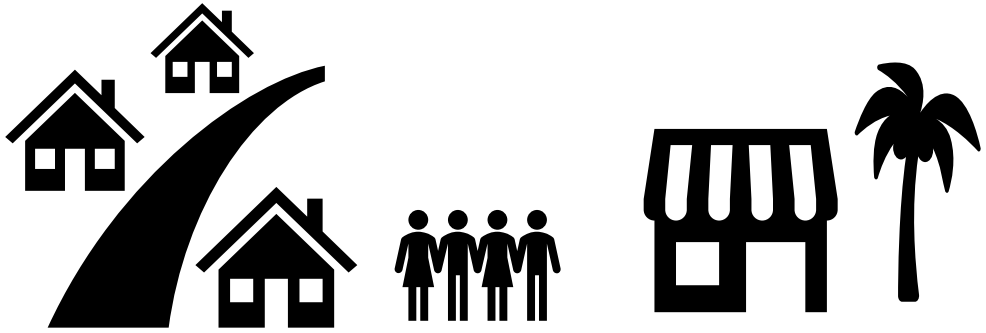
Equity effectiveness related to MDA

Mass drug administration (MDA) for lymphatic filariasis (LF)

Volunteers, CHWs trained to deliver safe and free tablets = community drug distributors (CDD)



CDDs bring tablets to their catchment areas (~5 days work)

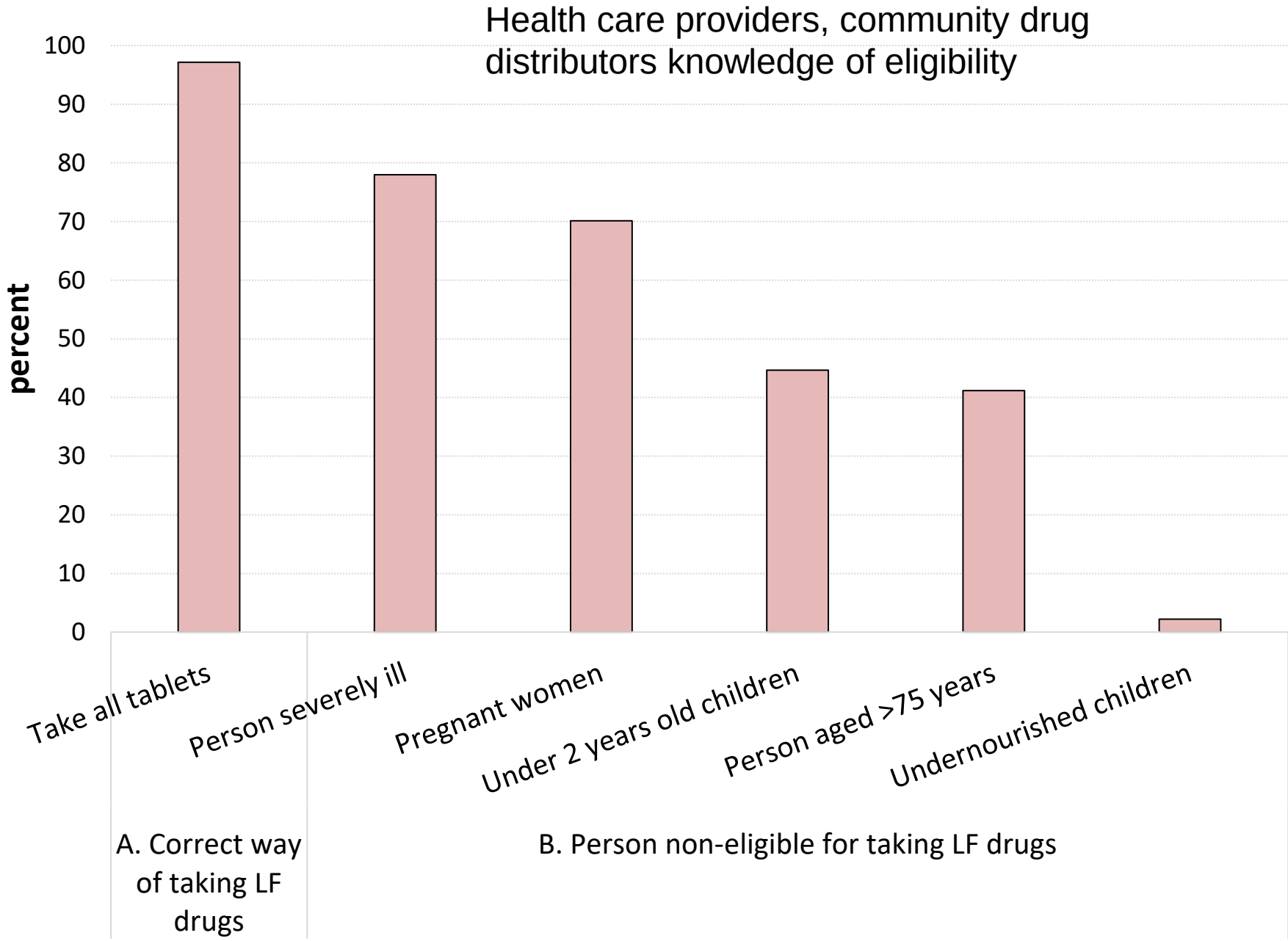


- Deliver tablets - House to house or distribution posts
- Target to treat 65% of total population living in endemic area for 4-6 years for elimination;
- No individual diagnosis; if person is infected, risk of adverse events

Access to treatment

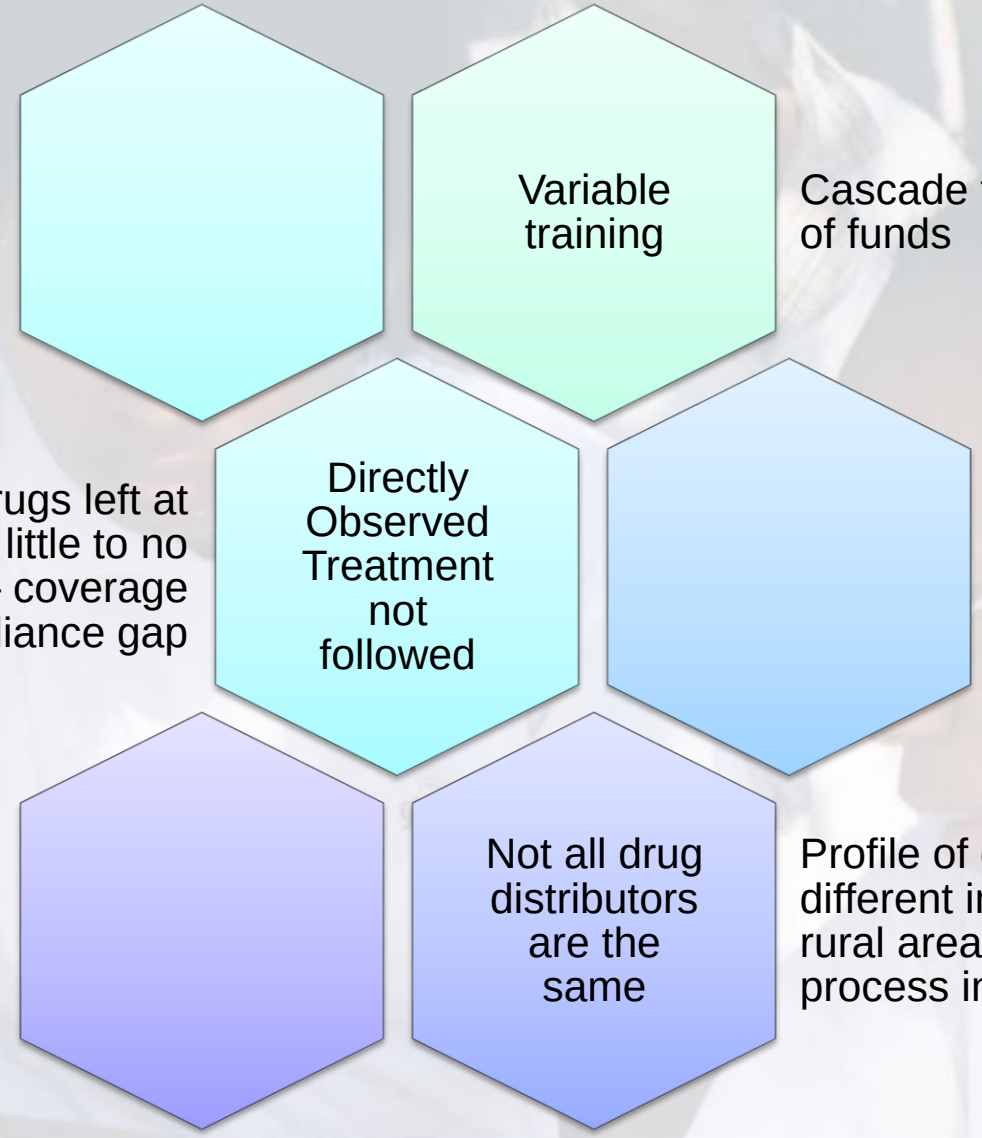
Targeting accuracy: Eligibility criteria for LF MDA

Agam District and Depok City
Indonesia
N=318



Titaley et al. *Parasites Vectors* **11**, 315 (2018)

Provider compliance



Coverage – compliance gap

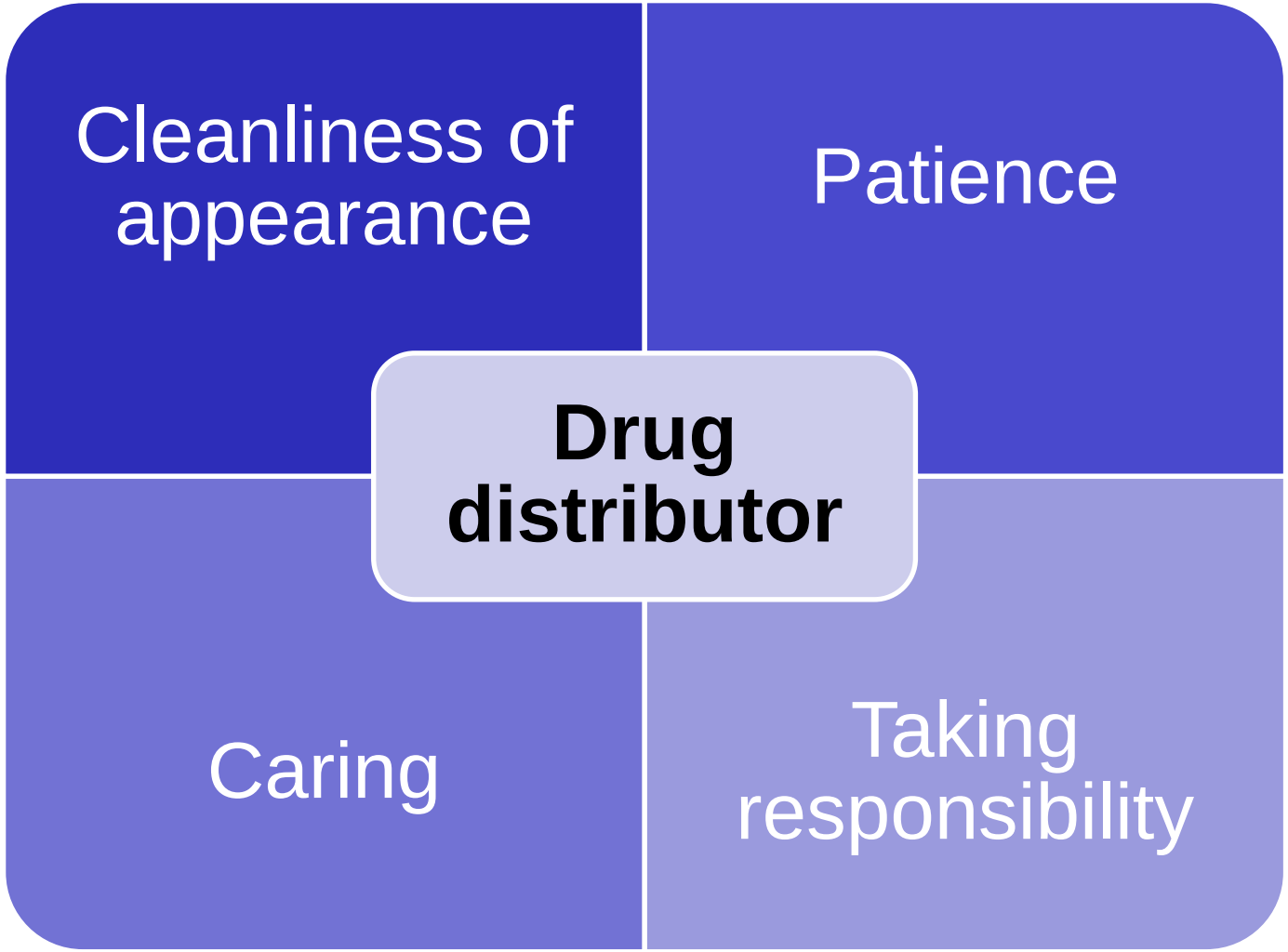
	Agam District		Depok City		Total	
	Baseline	Endline	Baseline	Endline	Baseline	Endline
N = total sample						
Have ever received the LF drug during MDA	80.6%	100%*	76.3%	76.9%	78.4%	88%*
N = individuals who had ever received LF drugs during MDA						
Received LF drug during last MDA	68.7%	90.8%*	69.7%	73.8%	69.2%	82%*
Took the LF drug in the last MDA	66.6%	84.1%*	48.2%	67.3%*	57.3%	77%*
Knew someone in the house that had taken LF drugs	75%	84.6%*	69.4%	81.9%*	72.3%	83.5%*
LF drugs perceived as safe	73%	71.9%	62%	66.9%	67.62%	69.79%
Reported to have swallowed all of the LF drugs at once	71.6%	82.1%*	53%	66.7%*	62.5%	75.4%*

*Change in percentage where p<0.05

doi:10.1371/journal.pntd.0005027.t003

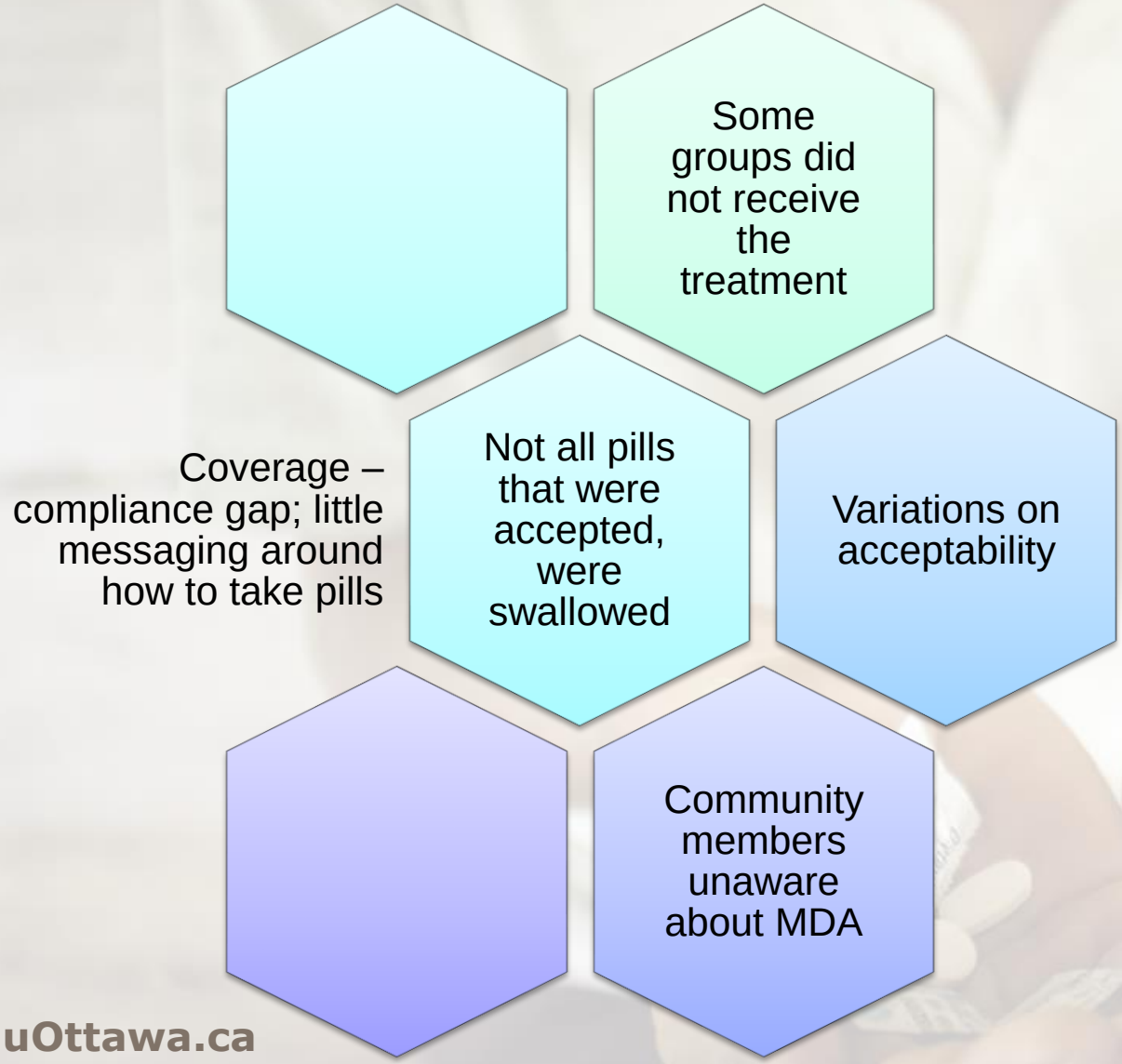
Krentel et al (2016) . PLOS NTD 10(11)

Professionalism



Krentel et al (2021) PLoS Negl Trop Dis 15(3)

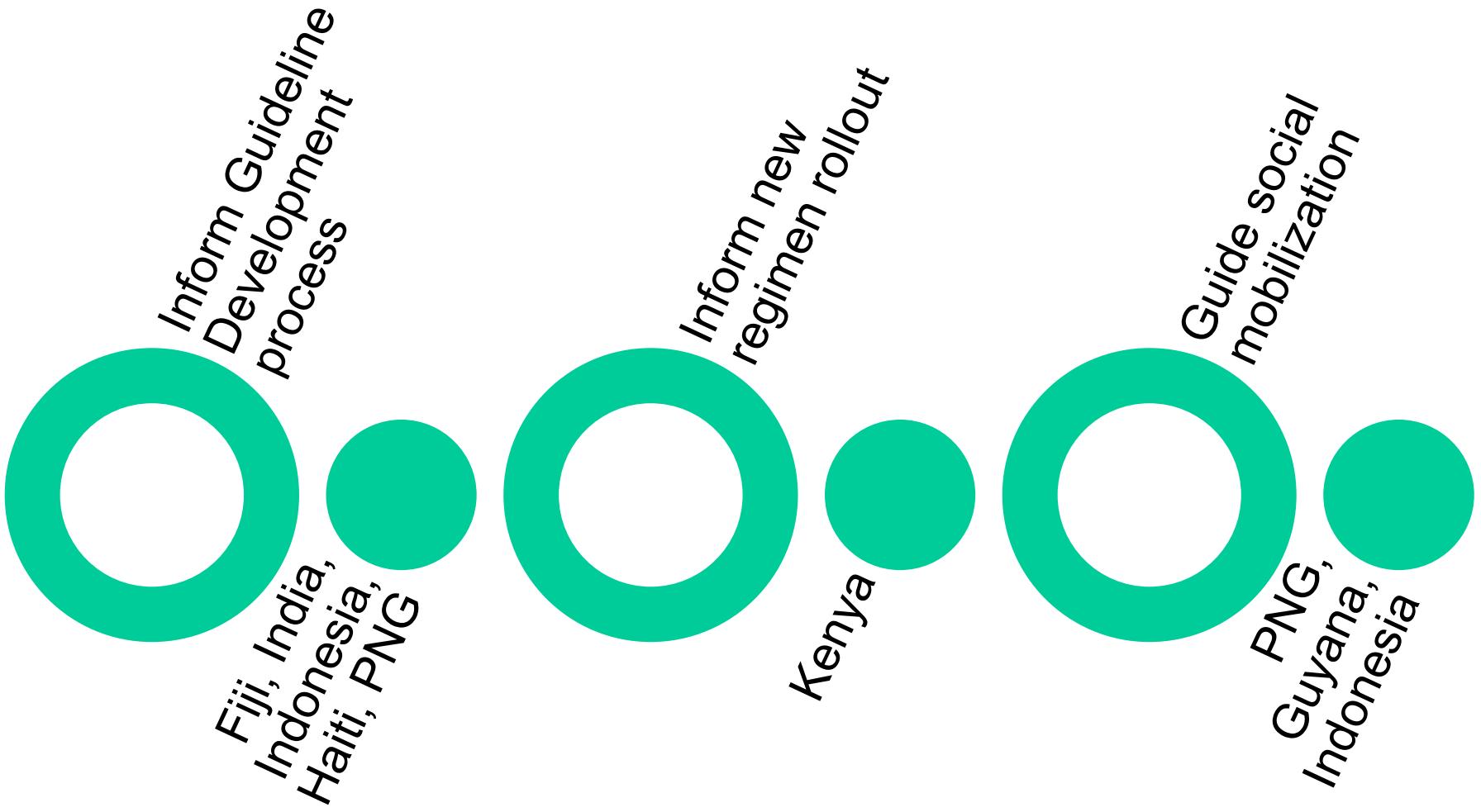
Patient adherence



Characteristics of acceptability

Working definition by Sekhon, Cartwright, & Francis (2017)

Acceptability research in LF MDA IDA*



*Triple Drug regimen: Ivermectin, DEC, Albendazole

Acceptability of new triple drug regimen (IDA)

- 5 countries
- No difference in acceptability between standard and new treatment regimen
- Number of pills was not a major factor
- Reassured eligible national programs about the use of a new treatment regimen
- Guided community social mobilization
- Informed a better understanding of adverse events

Krentel et al (2021) PLoS Negl Trop Dis 15(3); King et al (2022) Am J Trop Med Hyg. 15;106(5_Suppl)

Adverse events with triple drug regimen (IDA) for LF

Variable	Males		Females		Total		
Felt better after treatment							
Yes	101	**10.1%**	47	5.1%	148	7.7%	p < 0.0001
No	903	89.9%	868	94.9%	1771	92.3%	
Self-reported experiencing AE							
Yes	279	27.8%	321	**35.1%**	600	31.3%	p = 0.001
No	725	72.2%	594	64.9%	1319	68.7%	

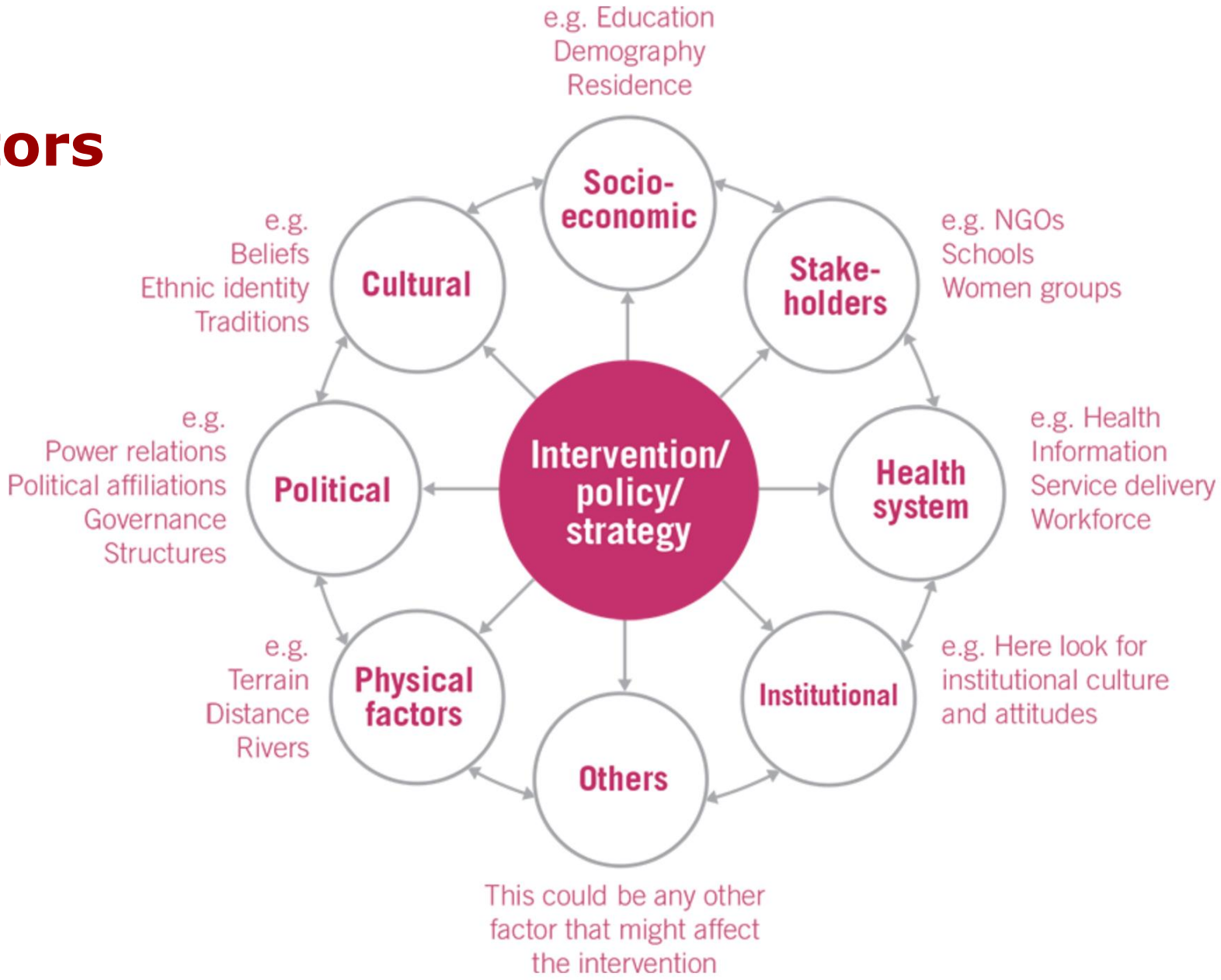
In safety trial data, men have less clinical AE than women do; 12% assess with clinical AE, 10.9% Grade 1*

Krentel et al (2021) PLoS Negl Trop Dis 15(3); *Weil et al (2019) PLoS Med. Jun 24;16(6)

Treatment and adverse events

- Number of pills can be important factor; but not if well-explained
- Education about *how* to take pills is not always prioritized
- Adverse events remain a common reason why people don't participate in MDA
- Variation between males and females

Contextual factors



https://adphealth.org/irtoolkit/

Contextual factors: Community ownership

- Takes time which is not always budgeted for
- Timing of the distribution is not ideal (season, time of day)
- Social mobilization – timing and budget
- Urban ownership is more challenging

*Gyapong JO et al 2018

Contextual factors: other health priorities

- As countries move closer to elimination, they no longer see cases of people with lymphedema
- Risk becomes harder to communicate
- PC-NTDs focus on preventive chemotherapy, not vector control

Contextual factors: Cultural and social norms

- Gender dynamics in the household
- How information is passed within the community and household
- Urban versus rural differences

Contextual factors: complex situations

- Movement of peoples has made access challenging:
  - Economic migration
  - Nomadism or seasonal migration
  - Internally displaced persons
- Health services for migrants may be absent or inadequate[1]
- Conflict, insecurity
- Climatic events
- Misinformation, disinformation

Source: gettyimages.dk

[1]Aagaard-Hansen J and Chaignat CL (2010)

Conclusion

- Context of implementation is complex
- Once products enter the distribution system, challenges arise which lower their equity effectiveness
- At development stage,
  - Consider the size, shape, taste, storage of the product for the user (especially in a low-resource setting)
  - Leverage opportunities to add acceptability and feasibility research to the development process

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PNG Institute for Medical Research, Papua New Guinea
RECONSTRA, Indonesia
Task Force for Global Health, USA
Washington University at St. Louis, USA
University of Health and Allied Sciences, Ghana
Universitas Indonesia

Thank you!

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