Boston University Expert Review Meeting on the Evaluation of *Novartis Access*

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Boston University School of Public Health

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Overview of presentation

- Background: Access to Medicines Initiatives
- Evaluation of *Novartis Access*
  - Study design
  - Data collection & analysis
- Discussion of Methodological Issues
- Conclusion and Final Questions
- Instruments

BACKGROUND

Growing incentives for Pharma Industry to report on performance

- Since 2008 the Access-To-Medicine (ATM) Index is encouraging pharmaceutical companies to document their activities
  - Access to medicines is one dimension on which companies' performance is measured

  - Past reports indicate:

➡ Many 'Access Initiatives' are reported but they lack rigorous evaluation

Systematic review of pharma initiatives

In order to gain a better understanding of Pharmaceutical Industry led 'Access Initiatives' BU team carried out a systematic review:

1. What 'Access Initiatives' have been reported by pharma?
2. Which of these have published evaluation reports?
3. What methods were used to evaluate them?

Definition of Access Initiatives: interventions that aim to directly increase access to medicines through medicine donations, differential pricing, price subsidies, licensing agreements, or supply chain strengthening activities.

Review of IFPMA Health Partnerships and companies' annual reports

Sample: All companies listed in the ATM Index

Step #1: Classification of all IFPMA Health Partnerships and annual reports of non IFPMA members into 'Access Initiatives' focused on directly affecting availability and price of medicines

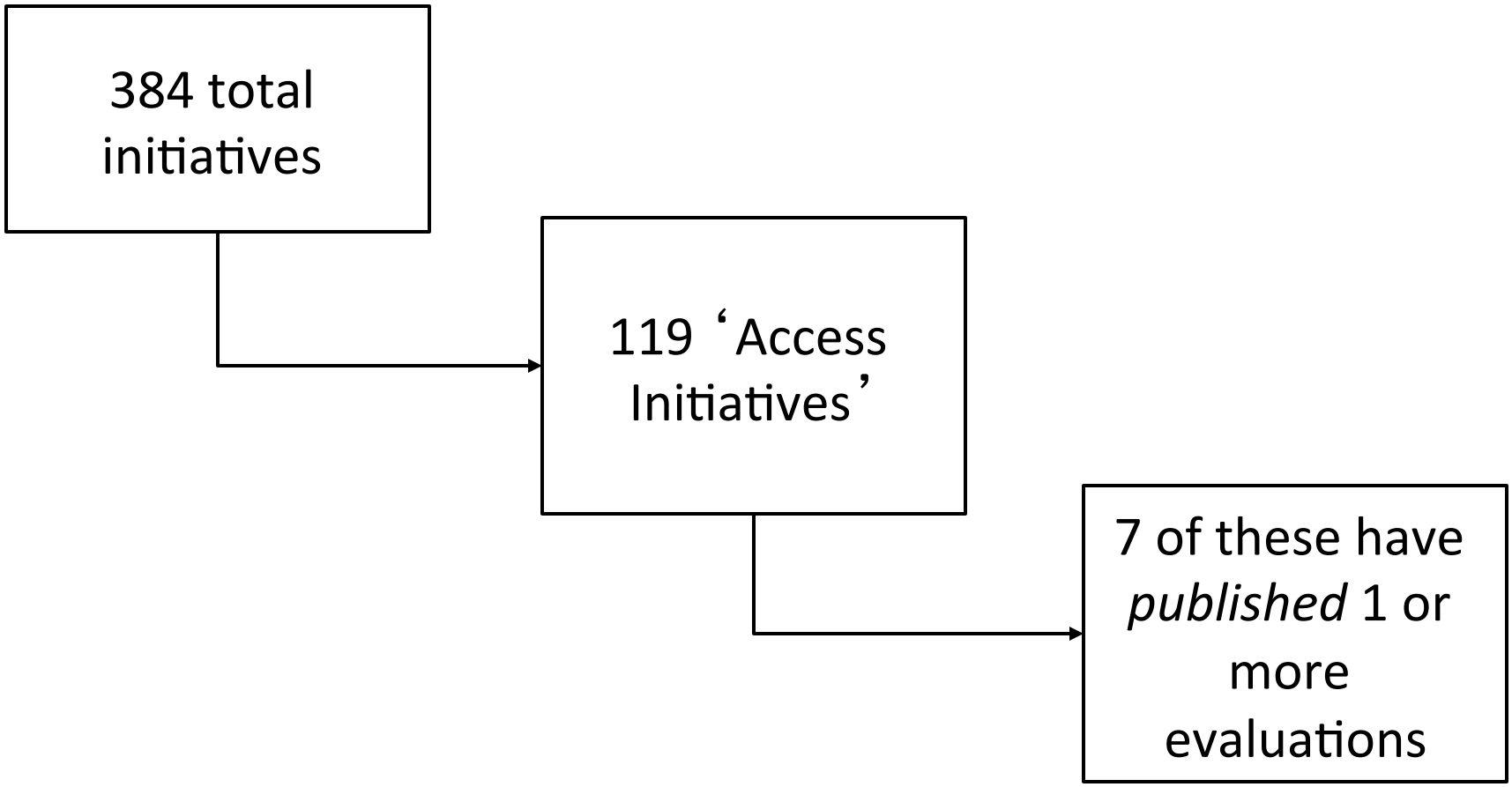
Step #2: Systematic search for all publications about identified initiatives via PubMed, Google, and initiative websites

Step #3: Classification of study methods used to evaluate initiatives

Graduate student team

(Left to right: Emeka Umeh, Preethi Swamy, Ela Fadli)

Overview of Industry-Led Initiatives



Company	Access initiatives	Reported impact	Initiatives with published evaluations	Number of publications identified
Abbott/AbbVie	8	6	0	0
Astellas	0	0	0	0
AstraZeneca	3	2	0	0
Bayer	3	1	0	0
Boehringer	5	2	0	0
Bristol-Myers Squibb	3	2	0	0
Celgene	0	0	0	0
Daiichi Sankyo	2	0	0	0
Eisai	4	0	0	0
Eli Lilly	2	0	0	0
Gilead	3	1	0	0
GlaxoSmithKline	7	1	0	0
Johnson & Johnson	5	1	0	0
Merck KGaA	5	5	0	0
Merck MSD	8	5	2	22
Novartis	14	8	3	9
Novo Nordisk	1	1	0	0
Pfizer	2	1	1	2
Roche	10	6	0	0
Sanofi	13	10	0	0
Takeda	1	1	0	0
Multi-Company Partnership	20	15	1	1
Total	**119**	**68**	**7**	**34**

Study Designs

Access initiative	Company	Published evaluations	RCT	ITS	Pre/post with control	Pre/post w/out control	Cohort	Post wit control	Post w/o control	Cost-effectiveness
GARDASIL Access Program	**Merck MSD**	**5**							5	
Mectizan Donation Program	**Merck MSD**	**17**		1	1	7	2	3	2	1
ACCESS (anti-malarial)	**Novartis**	**5**		2		2			1	
Oncology Access Programs	**Novartis**	**2**					1		1	
SMS for Life	**Novartis**	**2**		2						
International Trachoma Initiative	**Pfizer**	**2**				1	1			
Children Without Worms	**Multiple**	**1**							1	

*RCT = randomized controlled trial; ITS = interrupted time series

EVALUATION OF *NOVARTIS ACCESS*

What is special about this evaluation?

- Independent and autonomous evaluation
- Transparent process
- First rigorous evaluation of a NCD access initiative by a pharmacetical company in a LMIC
- Mixed methods
  - Quantitative – cluster-randomized controlled trial
  - Qualitative – In-depth interviews
  - Interrupted time series with data collection via phone
- Well documented methods which could be a standard for other evaluations

Study Aim

To evaluate the impact of *Novartis Access* on the availability and price of NCD medicines at health facilities and households in Kenya

Primary Objectives: Facility

To test the impact of *Novartis Access* on:

- **Availability** of *Novartis Access* medicines and equivalents at public and private non-profit facilities

- **Price** of *Novartis Access* medicines and equivalents at public and private non-profit facilities

- **Availability and price** of *Novartis Access* medicines and equivalents at alternative for-profit drug outlets to measure availability and price effects*

* Waning, B., Maddix, J., Tripodis, Y., Laing, R., Leufkens, H. G., & Gokhale, M. (2009). International Journal for Equity in Health. *International Journal for Equity in Health*, *8*, 43.

Primary Objectives: Household

To test the impact of *Novartis Access* on

- **Availability** of *Novartis Access* medicines and equivalents in households with NCD patients
- **Price** per unit for *Novartis Access* medicines and equivalents in households with NCD patients
- **Expenditure** on *Novartis Access* medicines and equivalents in households with NCD patients

Secondary Objectives

At the facility and household-level, to test the qualitative effect of *Novartis Access* on:

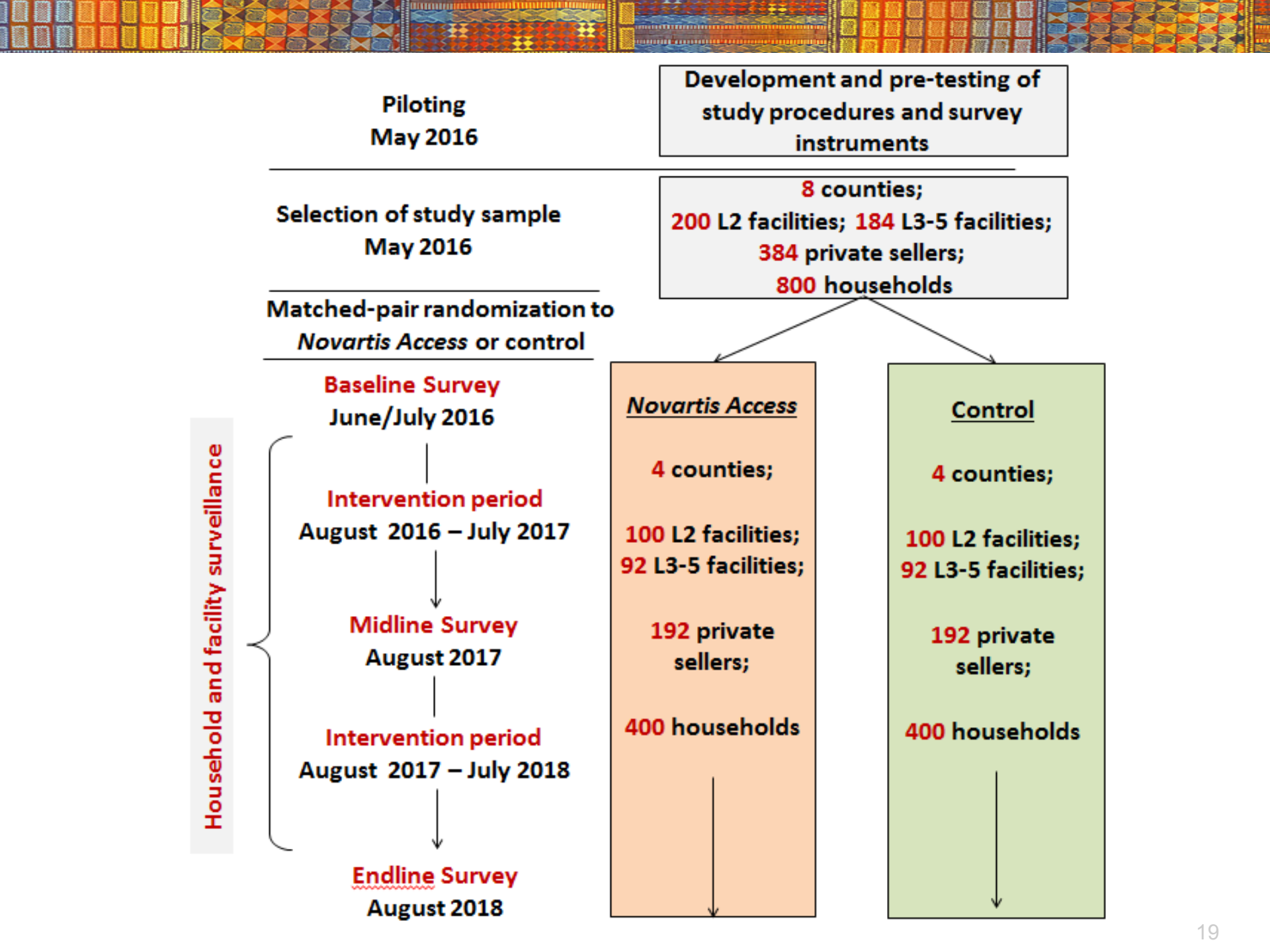
- **Awareness and preferences** both positive or negative for *Novartis Access* medicines and equivalents

STUDY DESIGN

Study design

- Cluster-randomized controlled trial
- Measurements at baseline, midline (after one year), and endline (after two years)

- Surveillance as part of the evaluation
  - Quarterly surveillance of all facilities in terms of stock. Monthly data will be available for ITS analysis.
  - 50% of households will receive calls quarterly
    - Data collected: products purchased in the previous three months.
    - Data will be collected and analyzed using interrupted time series analysis.
    - Incentives (airtime) provided for those who participate


Piloting
May 2016
Development and pre-testing of study procedures and survey instruments
Selection of study sample
May 2016
8 counties;
200 L2 facilities; 184 L3-5 facilities;
384 private sellers;
800 households
Matched-pair randomization to Novartis Access or control
Baseline Survey
June/July 2016
Intervention period
August 2016 – July 2017
Midline Survey
August 2017
Intervention period
August 2017 – July 2018
Endline Survey
August 2018
Household and facility surveillance
Novartis Access
4 counties;
100 L2 facilities;
92 L3-5 facilities;
192 private sellers;
400 households
Control
4 counties;
100 L2 facilities;
92 L3-5 facilities;
192 private sellers;
400 households

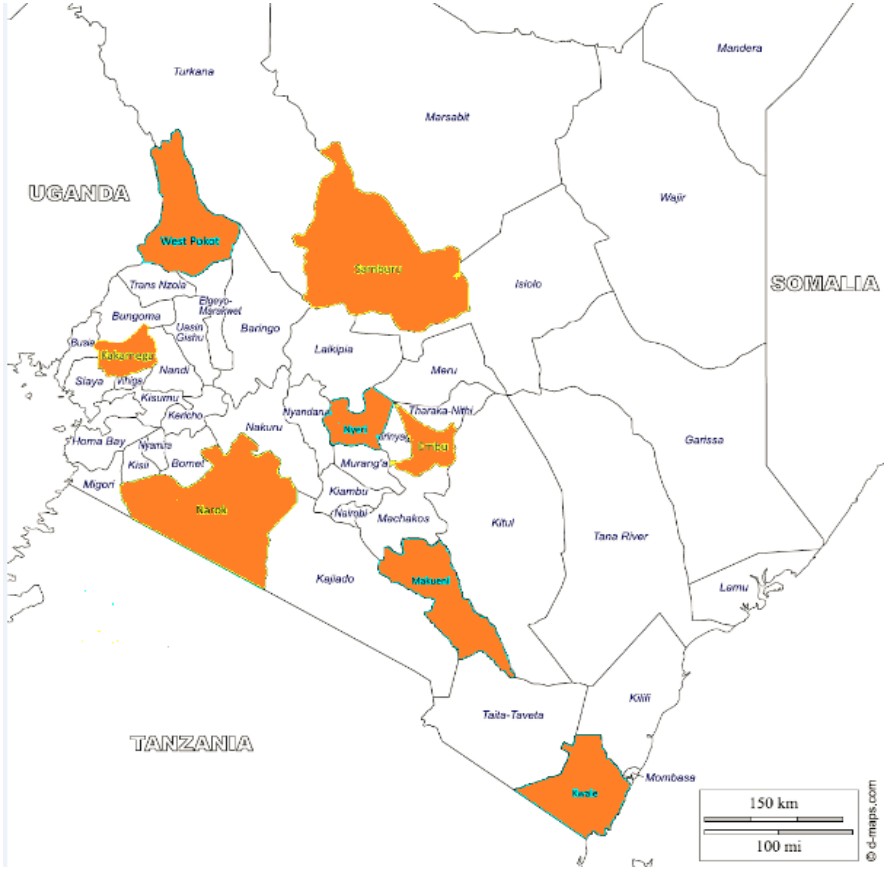
Medicines studied – focus on NCDs

Disease areas	Novartis Access Portfolio	Generic equivalents	Comparator products
Heart failure & hypertension	furosemide amlodipine bisoprolol valsartan ramipril hydrochlorothiazide	furosemide amlodipine bisoprolol valsartan ramipril hydrochlorothiazide	atenolol captopril
Dyslipidemia	simvastatin	simvastatin	
Diabetes Type 2	vildagliptin, glimepiride, metformin	glimepiride, metformin	glibenclamide, glimepiride
Breast Cancer	letrozole, anastrazole, tamoxifen	Letrozole, tamoxifen	
Symptoms relief for asthma and COPD	salbutamol	salbutamol	
Other key primary care medicines	amoxicillin	amoxicillin	ceftriaxone, ciprofloxacin, co-trimoxazole, diclofenac, paracetamol, diazepam amitriptyline, omeprazole

County selection

- 8 study counties selected using following criteria:
  - Established users of MEDS
  - Non-contiguous to minimize contamination
  - Excluded counties with security concerns

- Randomized to *Access* or control using covariate constrained randomization* to balance on:
  - Population density
  - Total population
  - Proportion of the population in urban areas
  - Poverty rate
  - Total number of health facilities
  - Physicians per capita
  - Health spending per capita
  - Overall value ordered through MEDS
  - Proportion of value ordered through MEDS by type of facility (mission versus public)



*Ivers *et al* Trials. 2012; 13: 120.

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Sampling of facilities

- Type of facilities
  - Public facilities
  - Private non-profit (faith-based)
  - Private for profit
- Level 3 - 5 health facilities (all):
    - **n=23 per county**
- Level 2 health facilities (random sample):
    - **n=25 per county**
- Private drug facilities (nearest to health facilities):
    - **n= 48 per county**

Household sampling

- **Total number: 800** (capable of detecting 10% increase in availability)
  - Intervention counties: 400 households
  - Control counties: 400 households

- **Two-stage cluster design**
  - Stage 1: 10 villages per county, probability proportionally to size
  - Stage 2: random selection of 10 eligible households per village

- **Eligibility criteria:**
  - At least 1 household member Dx and Rx hypertension; diabetes; asthma; , dyslipidaemia, heart failure or breast cancer
  - All members of the household that fit that criteria will be enrolled in the study
  - Estimated that 20% of households will meet these criteria which means that 5 times as many households will be screened

Power calculation

- Availability is (along with price) the primary study outcome.
  - Definition of outcome – facility level: the proportion of *Access* or equivalent NCD medicines that a facility has in stock.
  - Definition of outcome - household level: the proportion of prescribed *Access* or equivalent NCD medicines at the household.

- At the facility-level: assuming a proportion available in the control group of 50%, we will be powered to detect a 10 percentage point increase (from 50% to 60%) in availability in the Intervention group at $\alpha = 0.05$.

- At the household-level: assuming an attrition rate of 10%, an intracluster correlation coefficient of 0.05, and a proportion available in the control group of 33% (based on a recent survey in Kenya), we will be powered to detect a 10 percentage point increase (from 33% to 43%) in availability in the Intervention group at $\alpha = 0.05$.

DATA COLLECTION AND ANALYSIS

Data collection at facility and household

Facility

- **Availability** of medicines
- **Price** of medicines
- Facility data on services, including frequency of NCD diagnosis and prescribing

Household

- **Availability of medicines** in the household;
- **Prices paid** for medicines
- **Expenditures** on medicines (and on other goods);
- Locations where medicines were obtained;
- Perceptions and perceived barriers to management of NCDs.
- Other information: demographics & indicators of household wealth.

Surveillance of facilities and households

Facility

- **Stock received (Novartis Access and others)**

Household

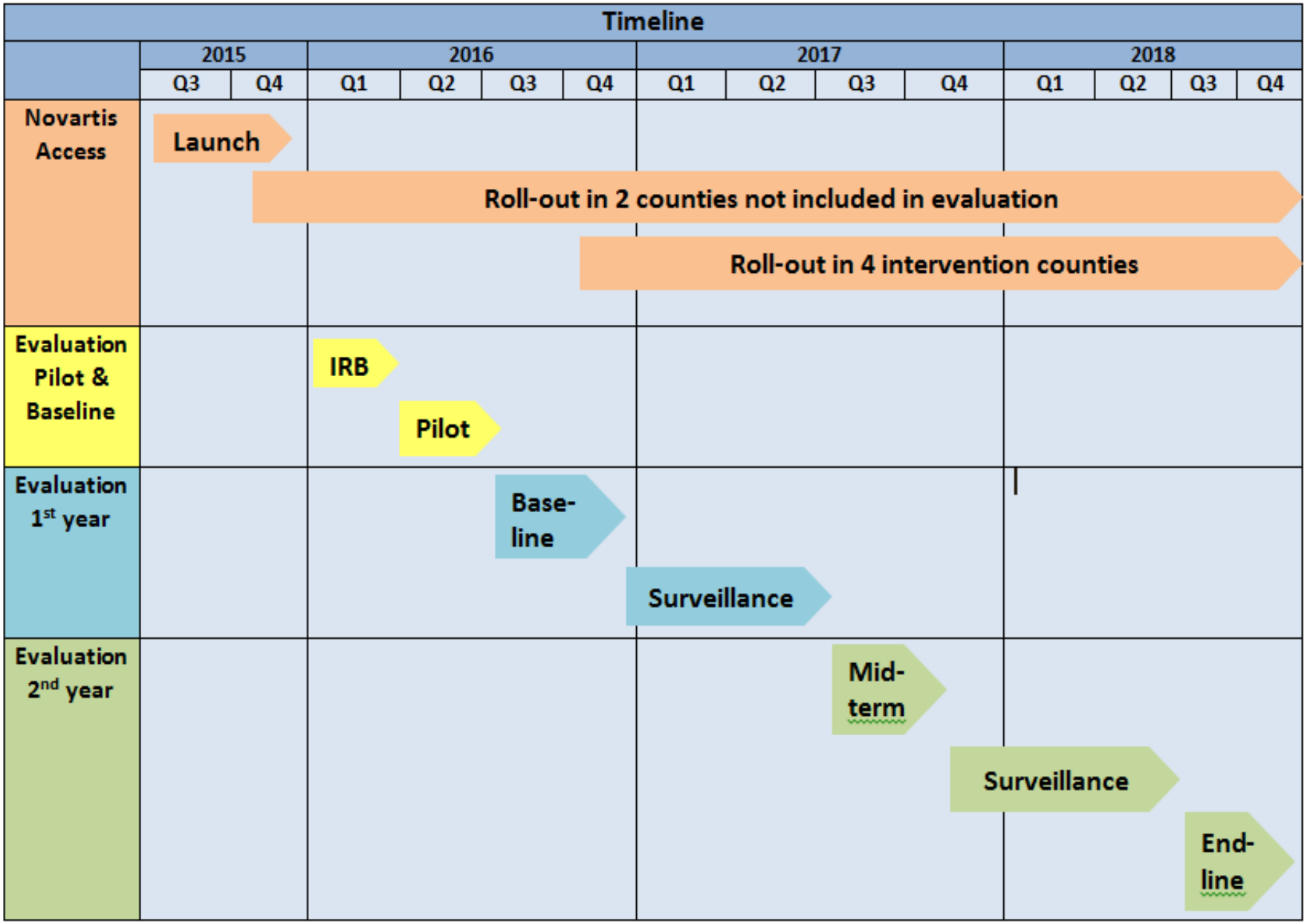
- **NCD medicines received in past three months;**
- **Prices paid** for the NCD medicines
- **Expenditures** on NCD medicines;
- Location where NCD medicines were obtained.

Data Analysis

- Estimate impact of *Novartis Access* by **comparing differences at midline and endline**, controlling for differences at baseline (difference-in-differences)
- **Time-series analysis** from surveillance at facility and household level
- Analysis to determine whether quarterly phone calls to households influence their behavior in terms of accessing NCD medicines
  - If not, phone surveillance would constitute a low cost strategy for future evaluations

Data analysis by subgroups

- Facilities by level of care and by type of provider
- Households by county, wealth measure, distance from facilities and type of NCDs


Timeline
2015
2016
2017
2018
Q3
Q4
Q1
Q2
Q3
Q4
Q1
Q2
Q3
Q4
Q1
Q2
Q3
Q4
Novartis Access
Launch
Roll-out in 2 counties not included in evaluation
Roll-out in 4 intervention counties
Evaluation Pilot & Baseline
IRB
Pilot
Evaluation 1st year
Base-line
Surveillance
Evaluation 2nd year
Mid-term
Surveillance
End-line

Methodological questions

- Please focus on methodology issues

DISCUSSION – OTHER ISSUES

Discussion of potential confounding factors

- Spill-over from intervention to control counties
- Interaction between *Novartis Access* and other access initiatives in Kenya (e.g. Familia Nawari, Astra Zeneca 'Healthy Heart', etc.)
- Challenge of identifying adequate numbers of breast cancer patients
- Revisions of portfolio of medicines
- Possible effect of political events
- Supply chain integrity
- External events such as new UHC initiatives
- Control counties may receive *Novartis Access* portfolio products depending on the results of the results at Year 1 with step wise analysis of outcomes

Conclusions

- We believe that it is possible to apply rigorous quasi-experimental methods to evaluate the true impact of Access Initiatives on price, access, and affordability of medicines.,
- Work in progress. We will learn as we go forward and from other evaluation initiatives
- Interested observers can follow our progress on our web site (see our project website):
  - Project agreements: http://sites.bu.edu/novartisaccessevaluation/agreements/
  - Protocol on Clinical Trials.gov (Article to follow)
  - Instruments
  - Data analysis including clean anonymized data sets
  - Results
- We are keen to receive feedback and suggestions
- We are open to assist others to undertake similar robust evaluations

THANK YOU

Contact us at:

Richard Laing (richardl@bu.edu): Principal investigator

Peter Rockers (prockers@bu.edu): Study design

Veronika Wirtz (vwirtz@bu.edu) Co Investigator

Taryn Vian (tvian@bu.edu): Development of qualitative instruments

Monica Onyango, (monyango@bu.edu): Data collection

Paul Ashigbie (gamelie@bu.edu): Development of instruments and manuals

Isabel Hirsch, (ihirsch@bu.edu): Program administrator

http://sites.bu.edu/novartisaccessevaluation/agreements/

QUESTIONS

- All Issues open for Discussion

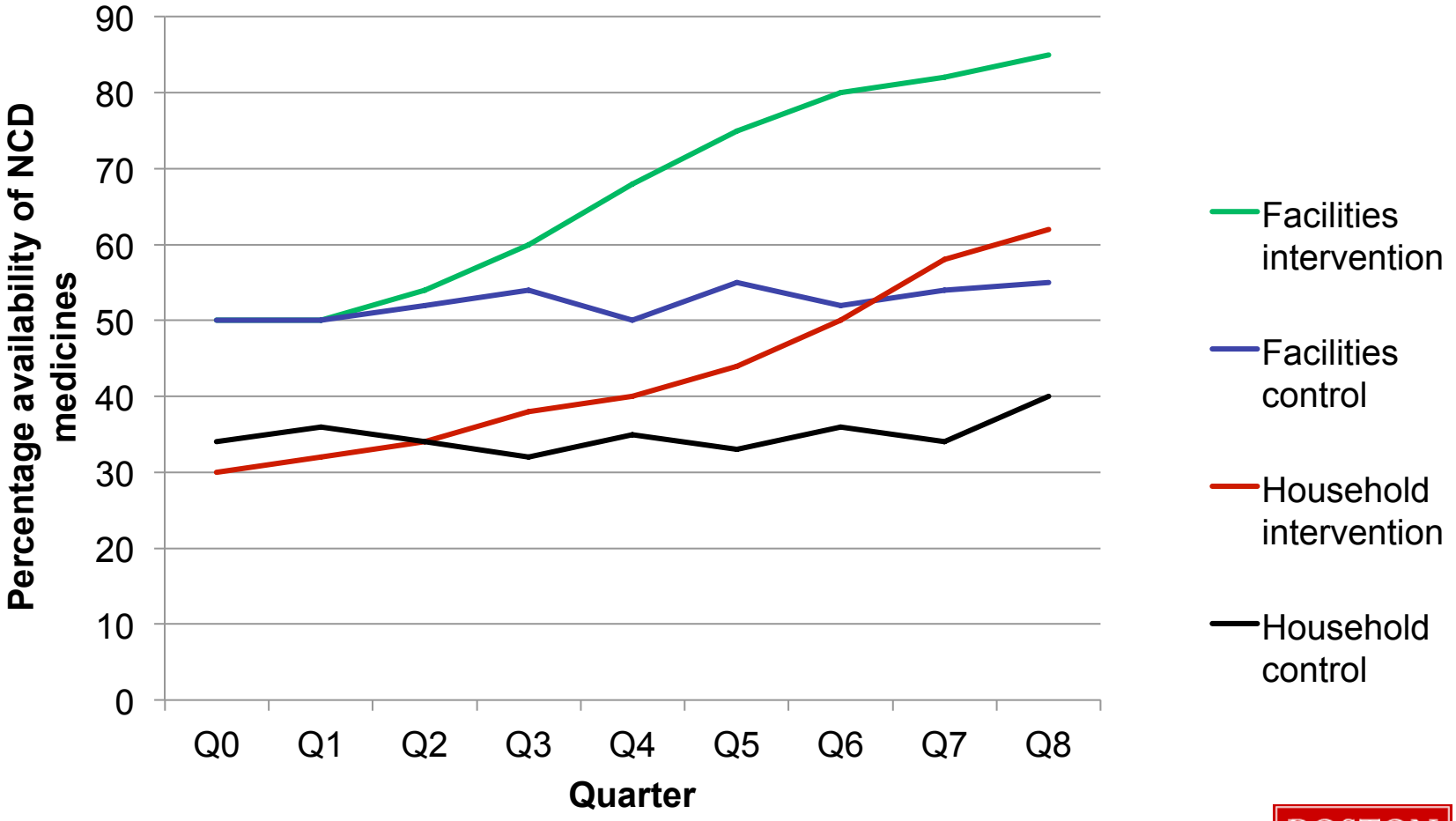
Example of a difference-in-difference analysis

- From Health Policy and Planning 2001
  Trapp, Todd, Moore and Laing

Table 4. Impact of supervision on adherence to standard treatment guidelines: intervention group vs. control and vs. comparison groups – difference in median change in scores and P value from Mann–Whitney U-test

Indicator condition	STG intervention compared to control (stock management intervention) Difference (%)	p value	STG intervention compared to comparison (no intervention) Difference (%)	p value
Diarrhoea without blood	**+31**	**0.017**	**+47**	**<0.001**
Acute respiratory infection	**+7**	**0.030**	**+17**	**0.001**
Urethal discharge	−1	0.6	**+32.5**	**0.042**
Genital ulcer disease	−3.5	0.9	+15.5	0.2
Overall score	+13.5	0.96	+29	0.34

Example of time-series: hypothetical



APPENDIX - INSTRUMENTS

Household screening tool - excerpt

PART 1

Household ID:	

PART 2

2.1 Has any member of this household been diagnosed with any of the following conditions:	Yes	No	Don't know
Asthma	1	2	3
Breast cancer	1	2	3
Diabetes	1	2	3
Hypertension	1	2	3
2.2. Has any member of your household who has been diagnosed of any of the above chronic diseases been told by a doctor or other health care provider that he/she should be taking medicines to treat this disease?	1	2	3
D4. If "No" in D3, why not?	Yes	No	
Asked to come back another time?	1	2	
- Asked to adopt lifestyle changes (e.g diet, exercise etc.)	1	2	
- Other – please specify	1	2	

Note: If there is a household member who has been diagnosed with at least one of these four diseases and has been asked by a health care provider to take medicines meant to treat at least one of these diseases, proceed in administering the full instrument. If not, the household is not eligible to participate in the survey.

Household survey - excerpt

SECTION C – HEALTH AND MEDICINES EXPENDITURE

Now I will be asking you a few questions about your household's expenditure on specific household needs.

C1. In the last four weeks, what did your household spend in total, including rent and other monthly expenses?	Amount (In local currency):
C2. In the last week, how much did your household spend on food? Include the value of any food produced and consumed by the household; exclude alcohol, tobacco, and restaurant meals	Amount (In local currency):
C3. In the last week, how much did your household spend on education?	Amount (In local currency):
C4. In the last week, how much did your household spend on transportation?	Amount (In local currency):
C5. In the last week, how much did your household spend on telephone communication?	Amount (In local currency):
C6. In the last week, how much did your household spend on health?	Amount (In local currency):
C7 In the last week, how much did your household spend on other expenditures?	Amount (In local currency):

Household key informants interview guide - excerpt

INSTRUMENT – H-KI:
Household Key Informant

SURVEY ID

Semi Structured Interview Guide: ***Interviewer:*** *"Now I'm going to ask you questions about your ideas and opinions on access to medicines. Let's start."*

Theme 1: Availability and Stockouts

1.1 Can you tell me about the availability of medicines at the public health facility closest to you? Are most medicines available? Tell me about which products are often in stock, and which products are not often in stock.

1.2 What do you do when products are not in stock?

Probe:

- Do staff tell you where else you can get the medicines? Where do they suggest you should go, and why? What are the advantages and disadvantages to going to this other place?
- Do health providers ever change the prescription or offer a different medicine that is in stock? Can you give me an example of this? Tell me more about what happened. What are the advantages and disadvantages of changing the medicine because the one you needed was not in stock?
- Sometimes health providers will purchase medicines themselves, then sell them to patients if there is a stockout at the facility. Does this sort of thing sometimes happen in the public health facility near you? What is your opinion about this? What do you think are the advantages and disadvantages?

Facility key informants interview guide - excerpt

INSTRUMENT – F-KI:
Facility Key Informant

SURVEY ID

Semi Structured Interview Guide: ***Interviewer:*** *"Now I'm going to ask you questions about your ideas and opinions on access to medicines. Let's start."*

Theme 1: Availability and Stockouts

1.1 Describe the situation in terms of availability of medicines in this facility? Are most medicines available? Tell me about which products are often in stock, and which products are not often in stock.

1.2 What do you or other staff do when products are not in stock? What do patients do?

Probe: Do you or other staff tell patients where else they can get the medicines? Where do you suggest they go, and why? What are the advantages and disadvantages?

Do you or other staff change the prescription or offer a different medicine that is in stock? Can you give me an example of this? What are the advantages and disadvantages?

Sometimes a staff will purchase medicines themselves, then sell them to patients if there is a stockout at the facility. Does this sort of thing sometimes happen here? If so, how do patients perceive this? What do you think are the advantages and disadvantages of this?

Facility level – data entry form (part I)

Medicine Price Data Collection Form

Use a separate form for each medicine outlet

Date : _____ Survey area number : _____

Name of town/village/district : _____

Name of medicine outlet (optional): _____

Medicine outlet unique survey ID (mandatory): _____

Distance in km from nearest town (population >50 000): _____

Type of medicine outlet :

- ☐ Public sector facility (specify level of care below):
  - ☐ Primary care facility
  - ☐ Secondary care facility
  - ☐ Tertiary care facility
- ☐ Private sector medicine outlet
- ☐ Other sector medicine outlet (please specify): _____

Type of price :

☐ Procurement price ☐ Price the patient pays

Type of data:

☐ Sample outlet ☐ back-up outlet ☐ validation visit

Name of manager of the medicine outlet: _____

Name of person(s) who provided information on medicine prices and availability (if different from manager):

Facility level – data entry form (part II)

A	B	C	D	E	F	G	H	I	J
Generic name, dosage form, strength	**Medicine Type**	**Brand or product name(s)**	**Manufacturer**	**Available yes/no**	**Pack size recommended**	**Pack size found**	**Price of pack found**	**Unit price (4 decimal places)**	**Comments**
Amitriptyline 25mg 25mg Tablet	Originator brand	.			100			per Tablet	
	Novartis Access Medicine				100			per Tablet	o Novartis Access Medicine
	Lowest-priced generic				100			per Tablet	
Amlodipine 10mg 10mg Tablet	Originator brand	.			90			per Tablet	
	Novartis Access Medicine				90			per Tablet	
	Lowest-priced generic				90			per Tablet	
Amlodipine 5mg 5mg Tablet	Originator brand	.			30			per Tablet	
	Novartis Access Medicine				30			per Tablet	
	Lowest-priced generic				30			per Tablet	
Amoxicillin 250mg 250mg dispersible tablet	Originator brand	.			20			per dispersible tablet	
	Novartis Access Medicine				20			per dispersible tablet	o Novartis Access Medicine
	Lowest-priced generic				20			per dispersible tablet	
Amoxicillin 500mg 500mg Tablet	Originator brand	.			21			per Tablet	
	Novartis Access Medicine				21			per Tablet	o Novartis Access Medicine
	Lowest-priced generic				21			per Tablet	
Anastrozole 1mg 1mg film-coated tablet	Originator brand	.			30			per film-coated tablet	
	Novartis Access Medicine				30			per film-coated tablet	o Novartis Access Medicine
	Lowest-priced generic				30			per film-coated tablet	