

BMJ Open Study protocol for a cluster-randomised controlled trial of an NCD access to medicines initiative: evaluation of *Novartis Access* in Kenya

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ABSTRACT

Introduction: Novartis recently launched *Novartis Access*, an initiative to provide a basket of reduced price medicines for non-communicable diseases (NCDs) to be sold through the public and private non-profit sectors in programme countries. This study will evaluate the impact of *Novartis Access* on the availability and price of NCD medicines at health facilities and households in Kenya, the first country to receive the programme.

Methods and analysis: This study will be a cluster-randomised controlled trial. 8 counties in Kenya will be randomly assigned to the intervention or control group using a covariate constrained randomisation method to maximise balance on demographic and health characteristics. In intervention counties, public and private non-profit health facilities will be able to order *Novartis Access* NCD medicines from the Mission for Essential Drugs and Supplies (MEDS). Data will be collected from a random sample of 384 health facilities and 800 households at baseline, midline after 1-year of intervention, and end-line after 2 years. Quarterly surveillance data will also be collected from health facilities and a subsample of households through phone-based interviews. Households will be eligible if at least one resident has been previously diagnosed and prescribed a medicine for an NCD addressed by *Novartis Access*, including hypertension and diabetes. The primary outcomes will be availability and price of NCD medicines at health facilities, and availability, price, and expenditures on NCD medicines at households. Impacts will be estimated using intention-to-treat analysis.

Ethics and dissemination: This protocol was approved by the Institutional Review Boards at Strathmore University and at Boston University. Informed consent will be obtained from all participants at the start of the trial. The findings of the trial will be disseminated through peer-reviewed journals, international conferences, and meetings and events organised with local stakeholders.

Trial registration number: NCT02773095.

Strengths and limitations of this study

- To the best of our knowledge, this will be the first experimental evaluation of an industry-led access to medicines initiative in a developing country.
- This study will combine data from facility and household interviews conducted at baseline, midline, and end-line with quarterly surveillance data from phone-based interviews to estimate trends in access to medicines over time.
- The study will evaluate impacts on medicine availability and price and not on patient health outcomes.
- The results of this study will help inform the design and evaluation of access to medicines initiatives in the future.

INTRODUCTION

Over the last two decades, the prevalence of non-communicable diseases (NCDs) globally has increased significantly for a variety of reasons including population ageing and increased exposure to risk factors such as tobacco use, harmful consumption of alcohol, physical inactivity, and unhealthy diets.^{1 2} The NCD burden in low and middle income countries is growing particularly fast.³ In Kenya, NCDs account for 27% of deaths (about 370 000 per year) among people between 30 and 70 years old, and the probability of dying prematurely from NCDs is about 18%.^{4 5}

As in most low and middle income countries, medicines to treat NCDs are difficult to access or too expensive for many Kenyan households.^{6 7} According to a recent survey, only 33% of Kenyan patients prescribed NCD medicines have them in their home. Furthermore, 82% of NCD medicines purchased are paid for out-of-pocket.⁸ As a

result, NCD sequelae which are often avoidable with proper treatment account for more than half of hospital admissions in the country.⁹

Global stakeholders have signalled a commitment to confronting the growing burden of NCDs by including them in the Sustainable Development Goals.¹⁰ Increasing access to essential NCD medicines is a fundamental part of these efforts.¹¹ Against this backdrop, Novartis/Sandoz has recently launched *Novartis Access*, an initiative to provide a low-cost portfolio of NCD medicines in 30 low and middle income countries over the next 5 years.¹² The portfolio includes patented and generic medicines to treat diabetes, hypertension, heart failure, hyperlipidaemia, breast cancer and asthma. All medicines in the portfolio are included on the WHO's Model List of Essential Medicines.¹³ Novartis Access will be implemented in programme countries in close partnership with local governments and non-governmental organisations, with a focus on strengthening public sector systems.

In 2016, Kenya will be the first country to receive *Novartis Access* medicines. The portfolio of medicines will be distributed solely through the Mission for Essential Drugs and Supplies (MEDS), the main supplier for the large network of private (often faith-based) non-profit health facilities in the country, and also a key supplier for public facilities. In Kenya, NCD services are provided in the public and private non-profit sectors at dispensaries up through hospitals, and these facilities will be eligible to purchase *Novartis Access* medicines. Pricing policies for NCD medicines sold through the public sector in Kenya are determined at the county level, and substantial variation exists. The price paid by patients in the public sector is generally lower than in the private sector. For example, the median public sector price paid for glibenclamide, a common treatment for diabetes, is less than one-quarter of the price paid in the private for-profit sector.¹⁴ Private for-profit facilities and drug sellers will not be allowed to purchase *Novartis Access* medicines, and will continue to purchase standard Novartis products through existing mechanisms.

This study will be a cluster-randomised controlled trial evaluating the impact of *Novartis Access* on the availability and price of NCD medicines at health facilities and households in Kenya. Eight counties will be randomly assigned to the intervention or control group. In the intervention counties, public and non-profit health facilities will be allowed to order low-cost *Novartis Access* NCD medicines. The results of this evaluation will provide much needed rigorous evidence of the impact of a new large NCD medicine access programme, and will help inform the design and evaluation of similar initiatives in the future. It will also provide Novartis with valuable feedback that can be used to improve *Novartis Access* as it expands.

METHODS AND ANALYSIS

Participants, interventions, and outcomes

Eight counties have been non-randomly selected for inclusion in the study. Of the 47 total counties in Kenya,

17 counties were excluded because they do not purchase medicines from MEDS, and an additional 15 counties that had not purchased at least US\$100 000 worth of medicines through MEDS in the previous year were excluded. Three counties were excluded due to security concerns, and four additional counties were excluded to eliminate shared borders in the final sample, to minimise the risk of contamination between intervention and control counties. When considering counties with shared borders, those with the lower volume of MEDS purchases in the previous year were excluded.

Counties have on average: 5 public and private non-profit level five county referral hospitals; 3 public level four subcounty hospitals; 15 public and private non-profit level three health centers; and 85 public and private non-profit level two dispensaries (table 1). All 184 eligible level 3–5 facilities will be included in the study, and 200 level 2 dispensaries will be randomly selected for inclusion. For each facility included in the study, one private drug seller identified as the main alternative for that facility will be identified and included. Private drug sellers include registered pharmacies and drug stores, but not unregistered dispensing doctors or market sellers.

A total sample of 800 households will be randomly selected from the eight study counties (400 from *Novartis Access* counties; 400 from control counties) using a two-stage sampling procedure. In the first stage, 10 enumeration areas (EAs) will be selected in each county with probability proportional to size based on data from the most recent census. EAs have on average around 100 households and may be comprised of one or more villages. Then, in the second stage, 10 eligible households will be randomly selected in each EA and recruited into the study. All households in the EA will be listed in a random order, and enumerators will proceed down the list until 10 eligible households are identified. Households will be eligible if at least one member 18 years or older has been previously diagnosed and prescribed medicine for NCDs addressed by *Novartis Access*. All members of the household who fit that criterion will be recruited for the study. Based on the prevalence of the relevant NCD conditions in Kenya, we estimate that 20% of all households will meet the inclusion criterion.⁸

In the intervention counties, public and private non-profit health facilities will be allowed to purchase the portfolio of 15 low-cost *Novartis Access* NCD medicines

Table 1 Public and private non-profit health facilities per county

Type of facility (level)	Average number of facilities per county	
	Public	Private non-profit
Dispensaries (2)	50	35
Health centres (3)	10	5
Subcounty hospitals (4)	3	0
County referral hospitals (5)	3	2

Table 2 Novartis Access portfolio, generic equivalents, and therapeutic alternatives

Disease area	Novartis Access Medicines*	Generic Equivalents	Therapeutic alternatives
Hypertension and heart failure	Furosemide†	Furosemide†	Atenolol
	Amlodipine†	Amlodipine†	Captopril
	Bisoprolol	Bisoprolol	
	Valsartan	Valsartan	
	Ramipril	Ramipril	
Dyslipidaemia	Hydrochlorothiazide	Hydrochlorothiazide	
	Simvastatin	Simvastatin	
Diabetes type 2	Vildagliptin	Glimepiride	Glibenclamide
	Glimepiride	Metformin	
	Metformin		
Breast cancer	Letrozole	Letrozole	
	Anastrozole	Tamoxifen	
	Tamoxifen		
Asthma	Salbutamol	Salbutamol	

*The Novartis Access portfolio also includes amoxicillin for the treatment of child pneumonia. Medicines for other acute diseases will be surveyed as acute disease comparators.

†Treatment for hypertension only.

through MEDS (table 2). The medicines will be sold directly to MEDS at an average cost of US\$1 per monthly dose. Facility-level administrative data on NCD medicine purchases obtained from MEDS will be used to monitor the implementation of the intervention.

The primary outcomes of interest are medicine availability and price at health facilities, and medicine availability, price, and expenditures at patients' households. At facilities, availability will be measured for each disease area and defined as having at least one treatment medicine in stock, whether a Novartis Access medicine, a generic equivalent, or a therapeutic alternative (table 3).

At households, medicine availability will be measured in the same manner for each diagnosed disease. At facilities, price will similarly be measured for each disease area and defined as the lowest per unit price for a treatment medicine. At households, price will be measured for each diagnosed disease and defined as the per unit price paid for most recent treatment purchased. Household expenditures will be measured for each diagnosed disease and defined as total spending on treatment medicines in the previous 4 weeks. The price of medicines sold by registered private for-profit drug sellers is an important secondary outcome. Finally,

Table 3 Primary outcomes

Primary outcome	Level	Disease areas	Definition
Availability	Facility	Hypertension Heart failure Dyslipidaemia Diabetes type 2 Breast cancer Asthma	At least one treatment medicine in stock, whether Novartis Access, generic equivalent, or therapeutic alternative
	Household	Each diagnosed disease	At least one treatment medicine in the home, whether Novartis Access, generic equivalent, or therapeutic alternative
Price	Facility	Hypertension Heart failure Dyslipidaemia Diabetes type 2 Breast cancer Asthma	Lowest per unit price for a treatment medicine in stock
	Household	Each diagnosed disease	Per unit price paid for most recent treatment purchased
Expenditure	Household	Each diagnosed disease	Total spending on treatment medicines in the previous four weeks

patient and health worker perceptions of NCD medicine access will also be explored.

Data will be collected at facilities and households using a structured questionnaire at baseline prior to the implementation of *Novartis Access*, at midline after 1-year, and at end-line after 2 years (figure 1). Survey instruments will be adapted from tools previously developed for measuring medicine access by the WHO and Health Action International, which have been validated in several countries.^{15 16}

At each interview, a subsample of facilities and households will also be administered a qualitative interview. Additional surveillance data will be collected quarterly from facilities and a randomly selected subsample of households using a structured questionnaire administered over the phone.

The study is powered to detect a 10 percentage point increase in household availability of medicines due to *Novartis Access* at $\alpha=0.05$, assuming an intracluster correlation coefficient of 0.05, 10% loss to follow-up, and 33% availability in the control group.⁸ The study is also powered to detect a 10 percentage point increase in facility availability in the *Novartis Access* group at $\alpha=0.05$, assuming 50% availability in the control group.

Assignment of the intervention

The eight counties selected for inclusion in the trial will be randomised to the intervention or control group using a covariate constrained randomisation method to maximise balance on nine demographic and health variables: total population; population density; proportion of the population in urban areas; poverty rate; number of health facilities; physicians per capita; health spending per capita; overall value ordered through MEDS in previous year; and proportion of value ordered through MEDS in previous year by private non-profit versus public health facilities.¹⁷ Allocation will be masked from baseline data collectors. However, it will not be possible to mask the intervention from participants.

Data collection, management, and analysis

The health facility questionnaire has been adapted from an instrument developed by the WHO and Health Action International and previously used in Kenya, and captures information on medicine availability and medicine price.¹⁴ Facility data will be collected for *Novartis Access* NCD medicines, generic equivalents, and alternatives. Data will also be collected for a set of acute disease medicines to provide contextual information. The household questionnaire includes information on demographics, household assets, and key information on medicines, including whether prescribed NCD medicines are currently at the home, locations where medicines are most often purchased, prices paid, and overall household expenditures on medicines (and on other goods). The household questionnaire will be translated into local languages as appropriate.

A subsample of health facilities and subsample of households will also be administered a qualitative interview during baseline, midline, and end-line visits. A purposeful subsample of five level 2 dispensaries and five level 3–5 facilities will be selected in each county (80 facilities in total), and one staff member will be selected for the interview. A purposeful subsample of 10 households in each county (80 households in total) will be selected for qualitative interviews, which will be administered to one individual in the household who also completes the general household survey. Facilities and households will be selected for qualitative interviews to maximise variation in the viewpoints represented (eg, age, disease, wealth). The qualitative instrument has been designed to explore in depth key issues related to medicine access.

Surveillance data will be collected quarterly from all health facilities and a subsample of households. For health facility surveillance, a shortened version of the structured questionnaire with basic information on medicine availability and price will be administered over the phone each month to a rotating one-third sample of health facilities, such that all facilities are surveilled once per quarter. For household surveillance, a random sample of half of all study households with phones will be selected; half of study households will not be surveilled at all, to allow for an analysis of the potential effect of surveillance on household behaviour. Those households selected for surveillance will be administered a shortened version of the structured questionnaire with basic information on medicine availability and purchases over the phone. As with health facilities, a rotating one-third sample of households selected for surveillance will be surveyed by phone each month, such that all surveilled households are surveyed once per quarter. A 5% subsample of the surveilled health facilities and households will be visited in person to audit phone responses and confirm medicine price and availability through direct observation.

A local partner who specialises in the implementation of randomised controlled trials will manage fieldwork. Data will be collected electronically using Census and Survey Processing System (CSPro) software on tablets and managed using Microsoft Access software.

Data on baseline characteristics of health facilities and households will be compared across groups to assess balance. The impact of *Novartis Access* will be estimated using intention-to-treat analysis. Analysis of covariance (ANCOVA) methods will be used to control for potential baseline differences between groups.¹⁸ All impact analyses will be conducted using Stata statistical software (StataCorp. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP, 2015). Surveillance data will be explored to understand trends in outcomes over time. Finally, transcripts from qualitative interviews will be analysed using NVivo software (NVivo qualitative data analysis Software; QSR International Pty Ltd. Version 11, 2015). Responses will be coded based on overall

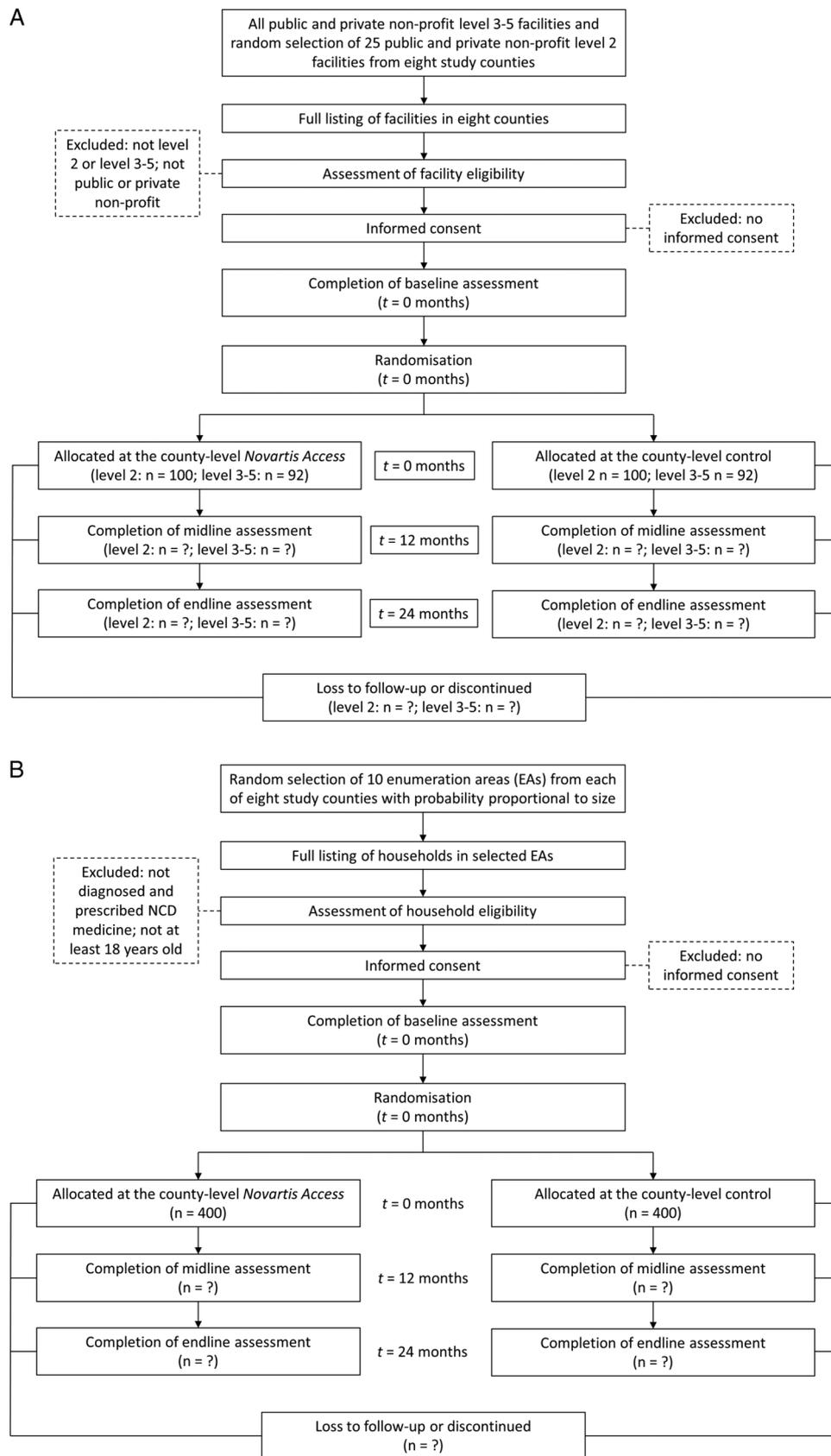


Figure 1 (A) Flow of facilities. (B) Flow of household participants. NCD, non-communicable disease.

perceptions of medicine availability, price, and quality, on perceptions of barriers to medicine access, and on perceptions of *Novartis Access* medicines compared with other medicines.

Limitations

There are important limitations to this work. First, household data on medicine prices will rely on participant reporting which may be subject to recall bias. In particular, if patients purchased multiple medicines at once, they may have difficulty recalling prices paid for individual medicines. Second, households without a mobile phone will be excluded from surveillance data collection, which may introduce bias. However, high mobile phone coverage is expected in the study population—according to the 2014 Demographic and Health Surveys, around 90% of households in Kenya have a mobile phone.¹⁹ A thorough analysis of this potential bias will be conducted using household baseline data. Finally, no health outcome data will be collected, and it will therefore not be possible to draw any conclusions as to the health impacts of *Novartis Access*. If the intervention is found to improve medicine price and availability, future studies should explore impacts on health outcomes.

DISSEMINATION

Informed consent will be obtained from all participants at the start of the trial. If a household member expresses interest in participating in the study, a study team member will explain the study in detail, verify eligibility, and obtain informed written consent where appropriate. Consent is not required prior to eligibility screening. As is standard in Kenya, all participants in the health facility and household surveys will be given compensation for their time. They will each receive 30 min of mobile phone airtime, a value of US\$0.53.

All identifying information collected from participants will be kept strictly confidential through the use of unique identifying numbers. An initial tracking file including participant names, study numbers, and address information, will be generated to allow for follow-up activities, but will be kept separate from all other data and will be password-protected, maintained on computers in locked offices, and only accessible to authorised study personnel. It will be destroyed within 6 months after the study is completed. All study results presented in written form will be aggregated, with no individual identifying information.

The findings of the trial will be disseminated through peer-reviewed journals, international conferences, and meetings and events organised with local and international stakeholders. The trial has been registered at Clinicaltrials.gov (NCT02773095). Finally, a website has been developed to serve as a repository for study information and documentation, and to establish a standard of transparency: sites.bu.edu/novartisaccessevaluation.

All study materials including quantitative and qualitative instruments are available on this website.

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Contributors RL is the principal investigator. PCR, VJW, TV, MAO and PGA are co-investigators. PCR, VJW, TV, MAO, PGA and RL designed the study. PCR wrote the initial draft of the manuscript. VJW, TV, MAO, PGA and RL contributed substantially to revising the manuscript. All authors give final approval of the version of the manuscript to be published.

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Disclaimer The funder will play no role in the design, management, analysis and reporting of the trial. The study team maintains all rights to the data generated by the trial and to the publication of results. Novartis has agreed to implement *Novartis Access* according to the randomised allocation procedure described in this paper to allow for a rigorous evaluation.

Competing interests RL was provided with travel and accommodation to present at two meetings held in Geneva, Switzerland about the evaluation of *Novartis Access* in May 2016.

Ethics approval This protocol was approved by the Institutional Review Boards at Strathmore University in Kenya and at Boston University in the USA. Additional approvals have been obtained from the Kenyan National Council for Science and Technology.

Provenance and peer review Not commissioned; externally peer reviewed.

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