Effect of Novartis Access on availability and price of non-communicable disease medicines in Kenya: a cluster-randomised controlled trial

Peter C Rockers, Richard O Laing, Paul G Ashigbie, Monica A Onyango, Carol K Mukiira, Veronika J Wirtz

Summary

Background Novartis Access is a Novartis programme that offers a portfolio of non-communicable disease medicines at a wholesale price of US$1 per treatment per month in low-income and middle-income countries. We evaluated the effect of Novartis Access in Kenya, the first country to receive the programme.

Methods We did a cluster-randomised controlled trial in eight counties in Kenya. Counties (clusters) were randomly assigned to the intervention or the control group with a covariate-constrained randomisation procedure that maximised balance on a set of demographic and health variables. In intervention counties, public and non-profit health facilities were allowed to purchase Novartis Access medicines from the Mission for Essential Drugs and Supplies (MEDS). Data were collected from all facilities served by MEDS and a sample of households in study counties. Households were eligible if they had at least one adult patient who had been diagnosed and prescribed medicines for one of the non-communicable diseases targeted by the programme: hypertension, heart failure, dyslipidaemia, type 2 diabetes, asthma, or breast cancer. Primary outcomes were availability and price of portfolio medicines at health facilities, irrespective of brand; and availability of medicines at patient households. Impacts were estimated with intention-to-treat analysis. This trial is registered with ClinicalTrials.gov (NCT02773095).

Findings On March 8, 2016, we randomly assigned eight clusters to intervention (four clusters; 74 health facilities; 342 patients) or control (four clusters; 63 health facilities; 297 patients). 69 intervention and 58 control health facilities, and 306 intervention and 265 control patients were evaluated after a 15 month intervention period (last visit February 28, 2018). Novartis Access significantly increased the availability of amlodipine (adjusted odds ratio [aOR] 2·84, 95% CI 1·10 to 7·37; p=0·031) and metformin (aOR 4·78, 95% CI 1·44 to 15·86; p=0·011) at health facilities, but did not affect the availability of portfolio medicines overall (adjusted β [aβ] 0·05, 95% CI –0·01 to 0·10; p=0·096) or their price (aβ 0·48, 95% CI –1·12 to 0·72; p=0·500). The programme did not affect medicine availability at patient households (aOR 0·83, 95% CI 0·44 to 1·57; p=0·569).

Interpretation Novartis Access had little effect in its first year in Kenya. Access programmes operate within complex health systems and reducing the wholesale price of medicines might not always or immediately translate to improved patient access. The evidence generated by this study will inform Novartis's efforts to improve their programme going forward. The study also contributes to the public evidence base on strategies for improving access to medicines globally.

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Introduction

The burden of non-communicable diseases is growing in low-income and middle-income countries, straining national health systems and compounding economic hardship.[1] In Kenya, non-communicable diseases account for 27% of deaths among people between 30 years of age and 70 years of age, most due to causes related to hypertension and diabetes.[2] To address this burden, patients need to have reliable access to essential medicines to manage their conditions, among other strategies.[3] In Kenya, patients with non-communicable disease face several barriers to access, often related to affordability and availability.[4] Most of these patients in the country pay out of pocket for their medicines, and stockouts at public health facilities are frequent.[5,6] These barriers disproportionately affect the poorest patients, exacerbating health inequities.[7]

The Sustainable Development Goals include a target to reduce premature mortality from non-communicable diseases by a third by 2030.[8] The UN has recognised private sector engagement as crucial to achieving the Sustainable Development Goals, following on from the explicit mention of the role of pharmaceutical companies in making essential medicines more affordable in developing countries in Target 8E of the Millennium Development Goals.[9] The *Lancet* Commission on Essential Medicines for

Research in context

Evidence before this study

In 2016, we conducted a systematic review to identify published evaluations of pharmaceutical industry-led access programmes in low-income and middle-income countries and to assess the quality of the available evidence on the effect of these programmes. First, we developed a list of industry-led access programmes by reviewing the Health Partnerships Directory of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). Information from the directory was supplemented with information from reports published by the Access to Medicine Index and annual and corporate social responsibility reports for non-IFPMA companies. On May 1, 2016, we searched PubMed, Google Web, and Google Scholar for published evaluations of identified access programmes, using as search terms the name of the programme, the name of the company, the focus disease, and the focus countries. We did not set restrictions on the publication date of evaluations.
We identified 120 access programmes that fit our criteria, seven of which had at least one published evaluation. We reviewed all of the published evaluations and assessed their quality using the GRADE system. None of the evaluations were rated as high quality and three were rated as moderate quality. We found no previous evaluations that used a randomised controlled trial design. None of the published evaluations provided clear evidence on the effect of a price reduction programme similar to Novartis Access.

Added value of this study

To our knowledge, this study is the first randomised controlled trial assessing the effect of a pharmaceutical industry-led access to medicines programme. We found that Novartis Access, a programme offering a portfolio of non-communicable disease medicines at a wholesale price of US$1 per treatment per month in Kenya, had little effect during its first year on the availability of medicines at facilities. Although the programme significantly increased the availability of amlodipine and metformin at health facilities, there was no effect on medicine prices or on availability at patient households. The study contributes to the public evidence base on strategies for improving access to non-communicable diseases medicines in low-income and middle-income countries. The study also contributes to ongoing discussions on the role of measurement and transparency in establishing accountability for private sector social programmes.

Implications of all the available evidence

Novartis Access is one of a growing number of pharmaceutical industry-led access programmes. Few of these programmes have been rigorously evaluated, and little is known about their effect or which strategies work best to improve access. This study suggests that offering a portfolio of medicines at a reduced price might not lead to immediate improvements in patient access. In order to build a more robust evidence base on this important topic and ensure accountability, rigorous measurement and transparent reporting should be adopted as a standard for pharmaceutical industry efforts to improve access to medicines globally. This study demonstrates that pharmaceutical companies can use robust, high-quality methods to evaluate their access programmes.

Universal Health Coverage[10] once again highlighted the role and responsibility of pharmaceutical companies in contributing to efforts to make medicines affordable globally. Within this context, Novartis has launched Novartis Access, a programme that provides low-cost medicines for non-communicable diseases in low-income and middle-income countries.[11] Kenya was the first country to receive Novartis Access after an initial announcement in 2015. As part of the programme, a portfolio of medicines for treatment of hypertension, heart failure, dyslipidaemia, type 2 diabetes, asthma, and breast cancer was made available for purchase by the Mission for Essential Drugs and Supplies (MEDS), a main distributor to public and non-profit health facilities in Kenya, at a wholesale price of US$1 per treatment per month.

For the **Mission for Essential Drugs and Supplies** see http://www.meds.or.ke

We did a cluster-randomised controlled trial to test the effect of Novartis Access on availability and price of non-communicable disease medicines in eight counties in Kenya. Public and non-profit health facilities in counties randomised to receive the programme were allowed to purchase Novartis Access medicines from MEDS. Data were collected from health facilities and a sample of households in study counties at baseline and again after a 15 month intervention period.

Methods

Study design and participants

The study was a cluster-randomised controlled trial implemented in eight counties in Kenya. Study counties were selected from 47 total counties in Kenya through a three-stage process. First, three counties were excluded due to security concerns. Second, 32 counties were excluded because they did not purchase a substantial volume (at least $100 000) of medicines from MEDS in the previous year and had little potential exposure to the programme. Third, four additional counties were excluded to eliminate shared borders in the final sample, to minimise the risk of contamination between intervention and control counties. The eight counties included in the study were Embu, Kakamega, Kwale, Makueni, Narok, Nyeri, Samburu, and West Pokot.

All public and non-profit health facilities within the eight study counties served by MEDS were enrolled in the study. In Kenya, public sector medicine purchasing is managed at the county level, and in counties served by MEDS nearly all public health facilities from local dispensaries through county referral hospitals can purchase from MEDS. MEDS is also the main medicine supplier for the large network of non-profit health

facilities in Kenya, and therefore nearly all non-profit facilities in study counties were enrolled. The final list of eligible facilities was confirmed by MEDS before the start of the study.

Households were randomly selected in two stages of sampling. In the first stage, 80 census enumeration areas (ten in each county) were randomly selected with probability proportional to population size on the basis of data from the most recent census. In the second stage, ten starting points were randomly chosen from within each enumeration area with Global Positioning System information on area boundaries from the most recent census.[12] For each random starting point, the nearest household was visited and screened for eligibility. If found to be ineligible, the next nearest household to the left was visited and screened for eligibility. This process continued until an eligible household was found for each random starting point. In counties with a low prevalence of diagnosed non-communicable diseases, a small number of enumeration areas did not have ten eligible households. Additional enumeration areas were randomly selected in these counties with probability proportional to population size and the same household sampling procedure was followed. The aim was to enrol 100 households in each county and 800 households in total at baseline. Eligible households were provided with study information as part of the informed consent procedure and decided whether to enrol at that time.

To be eligible for the study, a household had to have at least one permanent resident 18 years or older who had been diagnosed and prescribed medicines for one of the following non-communicable diseases: hypertension, heart failure, dyslipidaemia, type 2 diabetes, asthma, or breast cancer. The Novartis Access portfolio includes medicines to treat these diseases. Eligibility criteria were assessed through self-report at the time of recruitment. All who were eligible were recruited from households with multiple residents who met these criteria. Participants provided informed consent before study initiation. The study was approved by Institutional Review Boards at Strathmore University in Kenya (protocol number 0042/16) and at Boston University in the United States (protocol number H-348730) before enrolment of participants.

Randomisation and masking

Counties (clusters) were randomised by the study team before baseline enrolment to either the intervention or the control group with a covariate-constrained randomisation procedure[13] that maximised balance on a set of demographic and health variables: total population, population density, proportion of the population in urban areas, poverty rate, number of health facilities, physicians per person, health spending per person, 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. Group assignment was masked from data collectors. Participants were not told which group they were assigned to, although complete masking of participants was not possible.

	Medicine
Hypertension and heart failure	Furosemide* Amlodipine* Bisoprolol Valsartan Ramipril Hydrochlorothiazide
Dyslipidaemia	Simvastatin
Type 2 diabetes	Vildagliptin Glimepiride Metformin
Asthma	Salbutamol
Breast cancer	Letrozole Anastrozole Tamoxifen

The Novartis Access portfolio also includes one medicine not used for non-communicable diseases (amoxicillin, 250 mg dispersible), which was not analysed. *Treatment for hypertension only.

Table 1: **Medicines included in the Novartis Access portfolio**

Procedures

After baseline enrolment, Novartis Access was rolled out in intervention counties where public and non-profit health facilities were allowed to purchase programme medicines from MEDS. Table 1 presents the 14 non-communicable disease medicines included in the Novartis Access portfolio. These medicines were packaged with programme-specific branding. Generic or originator forms of the same medicines produced by various manufacturers are available for purchase throughout Kenya. Novartis Access medicines were offered exclusively to MEDS throughout the study period, although conversations with the government purchaser (the Kenya Medical Supplies Authority [KEMSA]) about their inclusion in the programme were ongoing during this time. Private sector outlets were not allowed to purchase Novartis Access medicines during the study period. All groups maintained their ability to purchase standard Novartis and Sandoz products through previously established channels.

For the **Kenya Medical Supplies Authority** see http://www.kemsa.co.ke

MEDS and KEMSA are the primary medicine suppliers for public and non-profit health facilities in Kenya, although facilities can purchase medicines not available through MEDS or KEMSA from other suppliers. For public facilities, medicine purchases are usually made through county health management teams[14] while non-profit facilities purchase medicines directly from suppliers. Data on the relative market shares of MEDS and KEMSA are not publicly available. However, MEDS estimates that they supply roughly 40% of medicines by volume to public and non-profit facilities, with KEMSA accounting for most of the remaining supply (Mariana Mutwiri, personal communication, Oct 29, 2018).

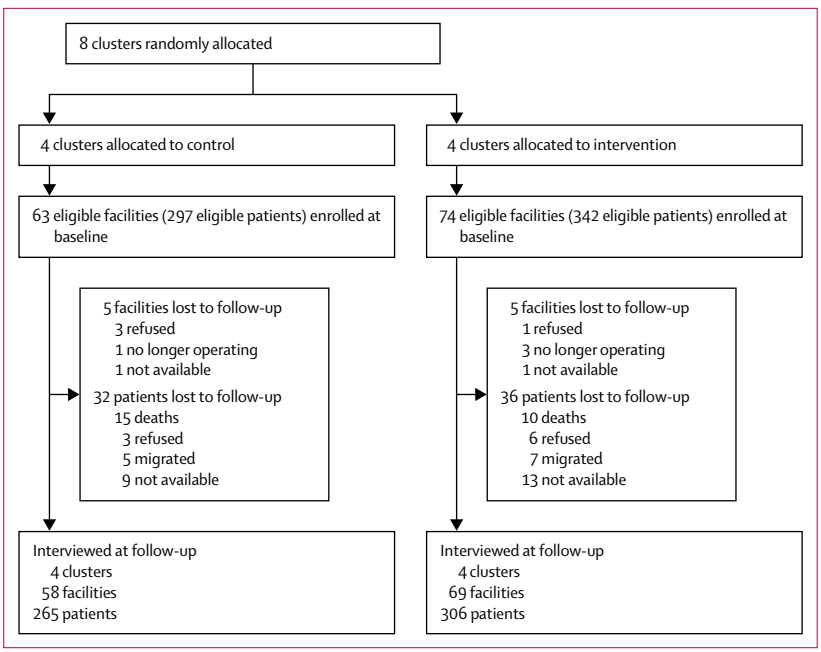

Figure 1: **Trial profile**

For **currency conversion** see http://xe.com

For more on the **inflation adjustment** see www.usinflationcalculator.com/inflation/historical-inflation-rates/

Surveys were administered at health facilities and households at baseline before implementation of Novartis Access (Sept 5–Oct 13, 2016) and after a 15 month intervention period (Jan 22–Feb 23, 2018). Surveillance data on stock of Novartis Access-branded medicines were collected by assessors by calling the cell phone of a staff member at each health facility monthly from Dec 6, 2016, until Dec 19, 2017. Additionally, qualitative interviews were done at follow-up with staff at a randomly selected subsample of 27 facilities to better understand medicine procurement decisions and general awareness of the Novartis Access programme. Finally, Novartis provided information on the date of regulatory approval and the date of first importation for each Novartis Access medicine in Kenya.

Outcomes

The primary outcomes were medicine availability and price at health facilities, and medicine availability at households. Availability and price at health facilities were assessed for the 14 medicines included in the Novartis Access portfolio, and were measured for all branded and generic versions of those medicines. When a facility had more than one version of a medicine, the lowest price was used. Data on medicine stock and prices were collected during an unannounced visit by study assessors who interviewed dispensing staff and confirmed responses through direct observation of stock shelves. Availability was defined as having a medicine in stock on the day of the assessment, irrespective of whether the medicine was Novartis Access brand or how many units were available. Availability was analysed for individual medicines, and for a composite measure defined as the proportion of the 14 medicines available. Medicine prices were converted to median price ratios (MPRs) by dividing the observed price at the facility by the median supplier price reported in the 2015 International Medical Products Price Guide.[15] Medicine prices were analysed for individual medicines and as a composite measure defined as the average value of the MPR for the medicines (of the 14) that were in stock on the day of the assessment. Medicine prices were captured in Kenyan shillings, while the most recent International Medical Products Price Guide median supplier prices are available in 2015 US$; before calculating MPRs, International Medical Products Price Guide prices were converted to Kenyan shillings and inflation adjusted to correspond to the first day of data collection for each survey round. This method was developed by WHO and Health Action International and has previously been validated in several low-income and middle-income countries.[16]

Household medicine availability was measured during unannounced home visits. Respondents were asked whether they had medicines in the home for treatment of their non-communicable disease, and those who indicated that they did were asked to show the medicines to the assessor for confirmation. For each confirmed medicine, assessors collected information on name, pack size, and dosage form, as well as price paid per pack. Medicine names were confirmed as non-communicable disease treatments during data cleaning. Participants with at least one confirmed medicine for treatment of their non-communicable disease were defined as having medicines available, irrespective of whether the medicine was Novartis Access brand or part of the programme portfolio. The study protocol identified household medicine prices and expenditures as primary outcomes. However, some respondents had difficulty recalling this information which led to substantial amounts of missing data. As a result, the study was underpowered on these outcomes and for this reason they were excluded from the analysis.

The household sample size was determined to provide statistical power to detect a ten percentage point increase in the probability of having a non-communicable disease medicine at home with α equal to 0·05, assuming eight clusters of equal size, 10% loss to follow-up, and an intracluster correlation coefficient of 0·05. The intracluster correlation assumption was similar to the one used in the ongoing LARK hypertension trial in Kenya[17] and aligns with published estimates from recent studies among rural populations in the USA and Canada.[18,19]

Statistical analysis

First, we compared baseline characteristics of health facilities and household respondents in the intervention and control groups, and characterised attrition by treatment group. We then estimated the effect of the intervention on the primary outcomes of interest at

	Control			Novartis Access		
	All enrolled (n=63)	Remaining at follow-up (n=58)	Lost to follow-up (n=5)	All enrolled (n=74)	Remaining at follow-up (n=69)	Lost to follow-up (n=5)
Level						
Dispensary	40 (63%)	37 (64%)	3 (60%)	39 (53%)	38 (55%)	1 (20%)
Health centre	9 (14%)	8 (14%)	1 (20%)	17 (23%)	15 (22%)	2 (40%)
District hospital	13 (21%)	12 (21%)	1 (20%)	14 (19%)	12 (17%)	2 (40%)
County hospital	1 (2%)	1 (2%)	0	4 (5%)	4 (6%)	0
Public ownership	22 (35%)	22 (38%)	0	37 (50%)	36 (52%)	1 (20%)
Proportion of NCD medicines available*	0·14 (0·13)	0·14 (0·12)	0·10 (0·19)	0·20 (0·12)	0·19 (0·09)	0·34 (0·28)
Amlodipine	16 (25%)	15 (26%)	1 (20%)	22 (30%)	19 (28%)	3 (60%)
Furosemide	34 (54%)	33 (57%)	1 (20%)	62 (84%)	58 (84%)	4 (80%)
Hydrocholorothiazide	12 (19%)	11 (19%)	1 (20%)	16 (22%)	13 (19%)	3 (60%)
Metformin	30 (48%)	29 (50%)	1 (20%)	56 (76%)	52 (75%)	4 (80%)
Salbutamol	24 (38%)	23 (40%)	1 (20%)	35 (47%)	32 (46%)	3 (60%)
Average MPR†	2·94 (1·57)	2·82 (1·51)	5·20 (0·71)	2·78 (1·44)	2·65 (1·35)	4·11 (1·90)

Data are n (%) or mean (SD). NCD=non-communicable disease. There were too few observations in facilities lost to follow-up to estimate median price ratios (MPR). *Proportion of the following medicines in stock: amlodipine, anastrozole, bisoprolol, furosemide, glimepiride, hydrochlorothiazide, letrozole, metformin, ramipril, salbutamol, simvastatin, tamoxifen, valsartan, and vildagliptin. †Average MPR for amlodipine, anastrozole, bisoprolol, furosemide, glimepiride, hydrochlorothiazide, letrozole, metformin, salbutamol, simvastatin, and tamoxifen. Ramipril (available at two facilities), valsartan (available at two facilities), and vildagliptin (available at one facility) were excluded because they did not have a published median reference price.

Table 2: **Baseline characteristics of study facilities**

	Control			Novartis Access		
	All enrolled (n=297)	Remaining at follow-up (n=265)	Lost to follow-up (n=32)	All enrolled (n=342)	Remaining at follow-up (n=306)	Lost to follow-up (n=36)
Age (months), mean (SD)	57·9 (15·9)	58·1 (15·8)	55·0 (16·4)	58·9 (17·3)	59·2 (16·9)	57·1 (20·7)
Sex						
Female	212 (71%)	190 (72%)	22 (69%)	228 (67%)	209 (68%)	19 (53%)
Male	85 (29%)	75 (28%)	10 (31%)	114 (33%)	97 (32%)	17 (47%)
Married	202 (68%)	180 (68%)	22 (69%)	244 (71%)	220 (72%)	24 (67%)
Completed primary school	140 (47%)	126 (48%)	14 (44%)	165 (48%)	145 (47%)	20 (56%)
Household wealth quintile, mean (SD)	3·0 (1·4)	3·0 (1·4)	2·7 (1·5)	3·0 (1·4)	3·0 (1·4)	3·0 (1·6)
NCD diagnosis						
Hypertension	203 (68%)	184 (69%)	19 (59%)	242 (71%)	217 (71%)	25 (69%)
Diabetes	68 (23%)	57 (22%)	11 (34%)	74 (22%)	63 (21%)	11 (31%)
Asthma	57 (19%)	51 (19%)	6 (19%)	72 (21%)	66 (22%)	6 (17%)
Heart failure	10 (3%)	8 (3%)	2 (6%)	14 (4%)	11 (4%)	3 (8%)
Dyslipidaemia	0	0	0	2 (1%)	2 (1%)	0
Had medicine at home	196 (66%)	179 (68%)	17 (53%)	221 (65%)	199 (65%)	22 (61%)

NCD=non-communicable disease.

Table 3: **Baseline characteristics of study patients**

health facilities and households using an intention-to-treat approach. For continuous outcome variables, hierarchical linear regression models with cluster random effects were fit using STATA's *xtreg* package to estimate unadjusted and adjusted effects (β). For dichotomous outcome variables, we fitted hierarchical logistic regression models with cluster random effects using STATA's *melogit* package to estimate unadjusted and adjusted odds ratios. Regression models were not fitted for individual medicines found at less than 5% of facilities at follow-up. Data on availability of these medicines at baseline and follow-up are presented in the appendix, along with p values from Fisher's exact tests comparing availability at follow-up.

See Online for appendix

All unadjusted models included controls for the outcome variable measured at baseline. For the health facility

	Control (n=58)	Novartis Access (n=69)	ICC	Unadjusted†		Adjusted‡	
				OR (95% CI)	p value	OR (95% CI)	p value
Amlodipine	18 (31%)	33 (48%)	0·06	2·45 (1·04–5·76)	0·041	2·84 (1·10–7·37)	0·031
Furosemide	42 (72%)	60 (87%)	0·11	1·51 (0·34–6·63)	0·588	1·74 (0·39–7·75)	0·468
Hydrocholorothiazide	40 (69%)	59 (86%)	0·21	2·28 (0·44–11·87)	0·327	2·72 (0·49–14·98)	0·251
Metformin	30 (52%)	56 (81%)	0·17	3·02 (1·08–8·48)	0·036	4·78 (1·44–15·86)	0·011
Salbutamol	30 (52%)	39 (57%)	0·01	1·12 (0·50–2·53)	0·785	1·12 (0·51–2·50)	0·772

Data are n (%) unless otherwise stated. All regression models include random effects for study clusters (ie, counties). ICC=intracluster correlation coefficient. OR=odds ratio. *Anastrozole, bisoprolol, glimepiride, letrozole, ramipril, simvastatin, tamoxifen, valsartan, and vildagliptin were found at three or fewer facilities at follow-up and were not analysed for impact. A summary of availability for those medicines is provided in the appendix. †Controlling for baseline value of the outcome. ‡Controlling for baseline value of the outcome, facility level, and public ownership.

Table 4: **Effect of Novartis Access on number of facilities with medicines available***

	Control (n=265)	Novartis Access (n=306)	ICC	Unadjusted*		Adjusted†	
				β (95% CI)	p value	β (95% CI)	p value
Proportion of NCD medicines available‡	20% (13%)	27% (11%)	0·17	0·04 (–0·04 to 0·12)	0·294	0·05 (–0·01 to 0·10)	0·096
MPR							
Average for NCD medicines§	2·78 (1·41)	2·85 (1·68)	0·02	0·27 (–0·78 to 1·32)	0·614	0·48 (–0·92 to 1·88)	0·500
Amlodipine	2·64 (1·76)	2·36 (1·30)	0·05	–0·75 (–2·71 to 1·22)	0·457	–0·20 (–1·12 to 0·72)	0·670
Furosemide	3·59 (2·28)	3·54 (2·32)	0·15	–0·25 (–2·30 to 1·80)	0·812	0·27 (–1·92 to 2·46)	0·812
Hydrochlorothiazide	4·61 (3·02)	4·50 (3·02)	0·17	–0·40 (–3·22 to 2·42)	0·780	0·15 (–2·24 to 2·55)	0·899
Metformin	2·69 (1·57)	2·76 (2·20)	0·13	0·42 (–0·96 to 1·81)	0·548	0·53 (–0·39 to 1·46)	0·260
Salbutamol	1·31 (0·44)	1·17 (0·32)	0·19	–0·20 (–0·59 to 0·20)	0·330	–0·12 (–0·39 to 0·15)	0·371

Data are mean (SD) unless otherwise stated. All regression models include random effects for study clusters (ie, counties). ICC=intracluster correlation coefficient. NCD=non-communicable disease. MPR=median price ratio. *Controlling for baseline value of the outcome. †Controlling for baseline value of the outcome, facility level, and public ownership. ‡Proportion of the following medicines in stock: amlodipine, anastrozole, bisoprolol, furosemide, glimepiride, hydrochlorothiazide, letrozole, metformin, ramipril, salbutamol, simvastatin, tamoxifen, valsartan, and vildagliptin. §Average MPR for amlodipine, anastrozole, bisoprolol, furosemide, glimepiride, hydrochlorothiazide, letrozole, metformin, salbutamol, simvastatin, and tamoxifen. Ramipril (available at two facilities), valsartan (available at two facilities), and vildagliptin (available at one facility) were excluded because they do not have a published median reference price.

Table 5: **Effect of Novartis Access on probability of availability and price of medicines at facilities**

analysis, adjusted models included the level of the health facility and whether it was public or non-profit as controls. For the household analysis, adjusted models included a set of baseline demographic variables: age, sex, marital status, education level, household size, and household wealth.

The main results are intention-to-treat estimates. As a robustness check, we did an as-treated analysis using county-level variation in the average number of Novartis Access medicine offerings per facility. Offerings were defined as the number of unique Novartis Access medicines available at a facility at the 15 month follow-up visit. As a second robustness check, we re-estimated household-level effect in the full study population with sampling weights and a finite population correction. Finally, we re-estimated household-level effects using linear probability models with cluster random effects to complement interpretation of the main results. All analyses were done with STATA version 14.

This trial was registered on ClinicalTrials.gov before baseline data collection (NCT02773095). The full study protocol was published before the start of baseline data collection.[20]

For the **funding agreement** see http://sites.bu.edu/evaluatingaccess-novartisaccess/agreements/

Role of the funding source

The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The funding agreement is publicly available. The corresponding author had full access to all of the data in the study and had final responsibility for the decision to submit for publication.

Results

Eight counties were randomly assigned to intervention (Kwale, Makueni, Nyeri, and West Pokot counties; 74 facilities, 342 patients) or control (Embu, Kakamega, Narok, and Samburu counties; 63 facilities, 297 patients). Across the full study area, 7870 households were visited at baseline and screened for eligibility. At the 15 month follow-up (last visit Feb 28, 2018), 69 (93%) facilities and 306 (89%) patients were retained in the intervention

	Control	Novartis Access	ICC	Unadjusted*		Adjusted†	
				OR (95% CI)	p value	OR (95% CI)	p value
Full sample (n=571)	208/265 (78%)	227/306 (74%)	0·10	0·85 (0·36–2·04)	0·721	0·83 (0·44–1·57)	0·569
Patients with hypertension (n=401)	155/184 (84%)	176/217 (81%)	0·10	0·84 (0·35–2·00)	0·692	0·94 (0·57–1·55)	0·831
Patients with diabetes (n=120)	48/57 (84%)	50/63 (79%)	0·13	0·91 (0·12–7·02)	0·926	1·08 (0·09–13·35)	0·951
Patients with asthma (n=117)	34/51 (67%)	43/66 (65%)	0·16	0·98 (0·25–3·82)	0·977	0·98 (0·25–3·90)	0·975

Data are n/N (%) unless otherwise stated. All regression models include random effects for study clusters (ie, counties). ICC=intracluster correlation coefficient. OR=odds ratio. *Controlling for baseline value of the outcome. †Controlling for baseline value of the outcome and a set of baseline demographics: age, sex, marital status, education, household size, and household wealth.

Table 6: **Effect of Novartis Access on number of patients with medicines at home**

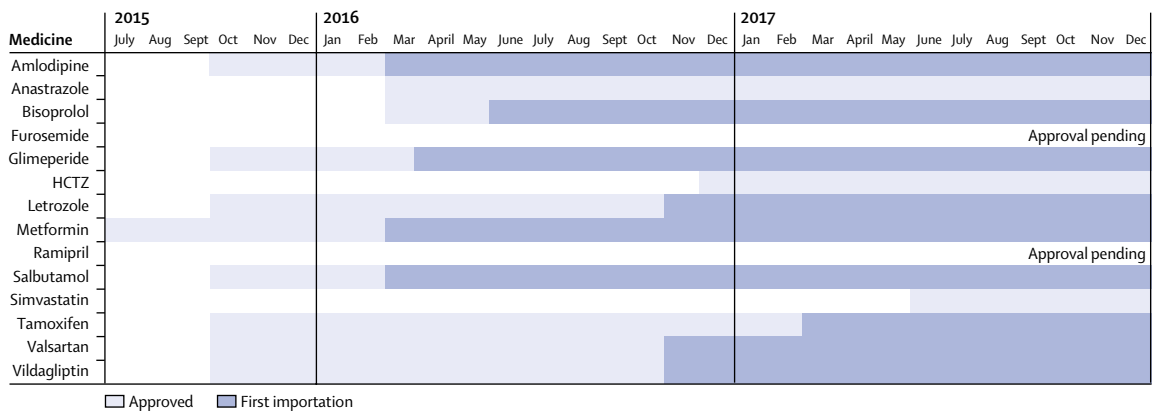

Figure 2: **Regulatory approval and first importation of Novartis Access medicines**
HCTZ=hydrochlorothiazide.

group, and 58 (92%) facilities and 265 (89%) patients were retained in the control group (figure 1).

More than half of study facilities were dispensaries, while five were county hospitals (table 2). There was a near-even split between public and non-profit facilities. On average, less than 20% of the medicines were available at facilities at baseline, and the average MPR was around 3. Overall, intervention and control facilities had similar baseline stocks of medicines for non-communicable diseases included in the Novartis Access portfolio, although intervention facilities were more likely to have furosemide and metformin than were control facilities.

Study patients were 58 years old on average and 69% were women (table 3). More than two-thirds had hypertension, while 23% had type 2 diabetes and 19% had asthma. No patients with breast cancer were identified. Around 65% of patients had medicines to treat their disease in their home at baseline. Characteristics of patients were similar in the intervention and control groups.

Controlling for baseline value of the outcome, facility level, and public ownership, Novartis Access significantly increased the availability of amlodipine (adjusted odds ratio [aOR] 2·84, 95% CI 1·10 to 7·37; p=0·031) and metformin (aOR 4·78, 95% CI 1·44 to 15·86; p=0·011) at health facilities (table 4). There were no significant effects on the availability of other medicines at facilities (table 4) or on the mean probability of availability for all medicines in the Novartis Access portfolio (adjusted β [aβ] 0·05, 95% CI –0·01 to 0·10; p=0·096; table 5). Similarly, there was no effect on the mean MPR of those medicines (aβ 0·48, 95% CI –1·12 to 0·72; p=0·500). Impact estimates from adjusted linear probability models (appendix) showed that Novartis Access significantly increased the probability that facilities had metformin (aβ 0·17, 95% CI 0·05 to 0·29; p=0·006). The effect on the probability that facilities had amlodipine was not statistically significant (aβ 0·16, 95% CI –0·09 to 0·42; p=0·200).

Controlling for baseline value of the outcome, age, sex, marital status, education, household size, and household wealth, Novartis Access had no effect on the odds that patients had non-communicable disease medicines at home (aOR 0·83, 95% CI 0·44–1·57; p=0·569; table 6). Estimates from a model with sampling weights and a finite population correction were not meaningfully different (appendix). There was no effect when stratifying by hypertension (aOR 0·94, 95% CI 0·57–1·55; p=0·831), diabetes (aOR 1·08, 95% CI 0·09–13·35; p=0·951), and asthma (aOR 0·98, 95% CI 0·25–3·90; p=0·975). Impact estimates from adjusted linear probability models were consistent with the main results and showed no effect of Novartis Access on the probability that patients had non-communicable disease medicines at home (appendix).

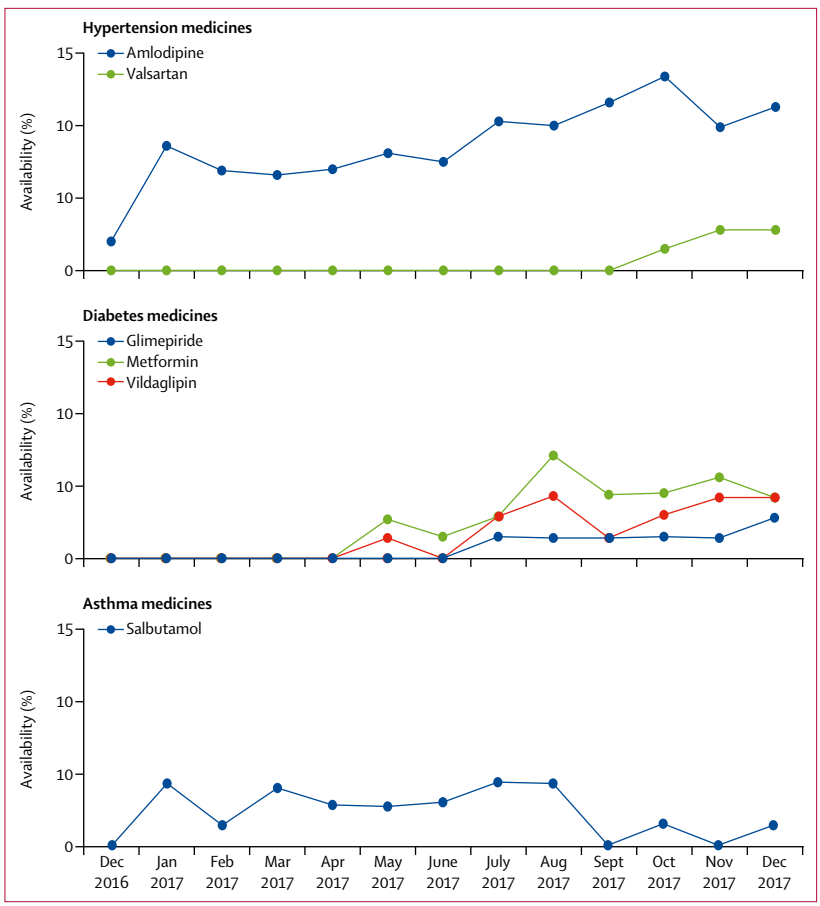

Figure 3: **Surveillance of Novartis Access medicine availability in intervention counties**

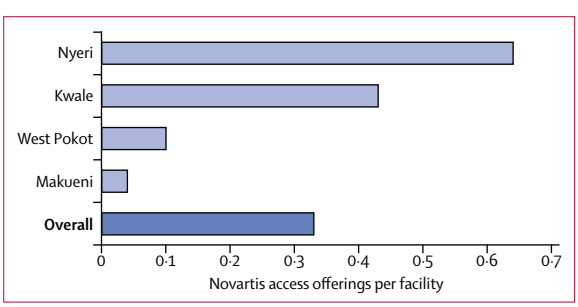

Figure 4: **County-level uptake of Novartis Access medicines**

The intracluster correlation for the full sample of patients was 0·10.

Figure 2 describes the timeline of regulatory approval and first importation of Novartis Access-branded medicines into Kenya. Metformin was the first medicine to be approved in July, 2015, and imported in March, 2016. Several other medicines were approved in October, 2015, and of these amlodipine and salbutamol were the first to be imported in March, 2016, followed by glimepiride in April, 2016. Several additional medicines were approved and imported in late 2016 and early 2017. At the time of the 15 month follow-up in early 2018, two medicines—furosemide and ramipril—had not yet received regulatory approval.

Surveillance data on stock of Novartis Access-branded medicines show that amlodipine was the first medicine available at health facilities in intervention counties, in December, 2016, followed by salbutamol in January, 2017 (figure 3). Novartis Access-branded metformin and vildagliptin were first available in May, 2017, followed by glimepiride in July, 2017. Finally, valsartan was first available in October, 2017. The other medicines in the Novartis Access portfolio were not found at health facilities during the study period. By the time of the 15 month follow-up, amlodipine was found at around 12% of intervention facilities, while the other medicines were found at 3–5% of facilities.

There was county-level variation in uptake of Novartis Access-branded medicines at health facilities (figure 4). Nyeri had the greatest uptake, with an average of 0·64 offerings per facility. Kwale had more than 0·43 offerings per facility, while West Pokot and Makueni had less (0·10 and 0·04 offerings per facility, respectively). At follow-up, two facilities in one control county were found to have one Novartis Access-branded medicine each, suggesting minor contamination in the study design. Using county-level variation in uptake of Novartis Access-branded medicines to estimate as-treated effects (table 7), we found that greater uptake was not significantly associated with household availability.

During qualitative interviews, fewer than 5% of health facility staff indicated that they had heard of Novartis Access from at least one source outside of the study. Sources that were mentioned included conversations with local medicine suppliers, printed brochures, and professional workshops.

Discussion

We investigated the effect of Novartis Access on availability and price of medicines for non-communicable diseases at health facilities and homes in eight counties in Kenya. After 15 months, the programme had a positive effect on availability of amlodipine and metformin at facilities, but had no effect on availability of the other medicines in the Novartis Access portfolio. The effect estimates for amlodipine and metformin are consistent with stock levels of Novartis Access-branded versions of those medicines found at intervention facilities at follow-up. We found no effect on the price of medicines at health facilities, or on the availability of medicines at households. To our knowledge, this trial is the first randomised assessment of the impact of a pharmaceutical industry-led access to medicines programme.[21] This study also contributes to ongoing discussions on the role of measurement and transparency in establishing accountability for private sector social programmes.[22,23]

Aspects of the market for medicines for non-communicable diseases in Kenya could have limited

uptake of Novartis Access-branded medicines by health facilities and patients. First, the Novartis Access brand was new in the country and there was probably little awareness of the programme. During qualitative interviews conducted with facility staff at follow-up, less than 5% indicated having heard about Novartis Access from sources outside of the study. Second, the timing of regulatory approval and importation probably contributed to the programme's modest effect. The medicines found to have increased availability due to the programme—amlodipine and metformin—were the first to be imported into Kenya following regulatory approval. Novartis Access-branded versions of these medicines were found at facilities at follow-up. Amlodipine and metformin are used to treat hypertension and diabetes, respectively, the two most prevalent non-communicable diseases in the study population. Development of awareness of the programme among facility staff and patients requires time, and that process could not truly begin until the medicines were approved and in the country. It is possible that greater uptake of Novartis Access-branded medicines at facilities and larger overall effects would be found over a longer study period. Third, the medicines included in the programme portfolio were not necessarily the most in-demand medicines used to treat the diseases being targeted. For example, at baseline a large proportion of hypertension patients reported using nifedipine to treat their condition, a medicine which is not included in the portfolio, and few reported using amlodipine, which is included.[24] Similarly, beclometasone is the recommended treatment for most asthma cases but is not included in the programme portfolio. Several of the medicines (eg, bisoprolol, ramipril, valsartan, and simvastatin) were not available even at well stocked hospital pharmacies. County-level variation in medicine procurement and distribution practices, and patient disease burden and demand for treatment, might have contributed to observed variation in facility-level availability of programme medicines.[25] Fourth, while Novartis Access aimed to provide medicines at a reduced price, $1 per treatment per month is not necessarily a bargain for some of the included medicines. For some of the medicines in the portfolio, $1 per treatment per month is well above the international median reference price.[15] Fifth, the decision to distribute Novartis Access medicines solely through MEDS to public and non-profit facilities could have inhibited household uptake, as previously published evidence from the baseline survey shows that most participants regularly purchase their medicines at private sector outlets.[26]

Contradictions between the essential medicines list (EML) and the standard treatment guidelines (STGs) in Kenya might have inhibited uptake of Novartis Access, and contributed to low availability of non-communicable disease medicines included in the programme portfolio and overall.[27] The Kenya National EML states that most non-communicable disease medicines should only be available at subdistrict hospitals and higher level facilities[28] while local STGs do not restrict the management of common non-communicable diseases to specific levels of care.[29–31] County procurement processes are largely guided by the EML, which might have contributed to low availability at lower-level facilities where many patients reported purchasing non-communicable disease medicines. Furthermore, some medicines in the Novartis Access portfolio—bisoprolol, glimepiride, ramipril, valsartan, and vildagliptin—are not included in the Kenya National EML, which could have limited purchasing by counties. Availability of essential medicines in Kenya is higher at private sector outlets than at public and non-profit outlets.[32]

There were important limitations to this work. First, given the regulatory complexity of the programme and the newness of the Novartis Access brand in Kenya, the 15 month study period was probably insufficient to observe the full effect of the programme. A year 2 follow-up assessment is planned, although Novartis Access will be altered in the second year and there will not be an opportunity to evaluate the programme in its current design over a longer time period. Second, our household sample was restricted to patients who had been diagnosed and were prescribed medicines for their non-communicable disease, and as a result our measure of household availability did not account for those who might have had a non-communicable disease and needed medicines but who were undiagnosed. As a result, our measure of availability should not be interpreted as an overall measure of access. Third, counties in Kenya that purchased less than $100 000 worth of medicines from MEDS in the year before baseline were excluded from the study. This factor might limit the generalisability of our findings. Counties that purchase greater volumes of medicines from MEDS as compared to KEMSA might have larger networks of faith-based health facilities and outlets, which could modify the effect of the programme. Fourth, the estimated intracluster correlation for the primary household outcome (0·10) was higher than we assumed in the initial power calculation (0·05). In addition, we were not able to enrol the target sample size due to low prevalence of diagnosed non-communicable diseases in three

	Unadjusted*		Adjusted†	
	OR (95% CI)	p value	OR (95% CI)	p value
Full sample (n=571)	1·05 (0·97–1·13)	0·243	1·03 (0·97–1·10)	0·326
Patients with hypertension (n=401)	1·02 (0·94–1·11)	0·600	1·00 (0·93–1·08)	0·936
Patients with diabetes (n=120)	1·13 (0·96–1·33)	0·139	1·93 (0·87–4·29)	0·105
Patients with asthma (n=117)	1·19 (0·91–1·55)	0·197	1·19 (0·86–1·66)	0·286

The independent variable is the number of Novartis Access offerings in the county. All regression models include random effects for study clusters (ie, counties). OR=odds ratio. *Controlling for baseline value of the outcome. †Controlling for baseline value of the outcome and a set of baseline demographics: age, sex, marital status, education, household size, and household wealth.

Table 7: **As-treated analysis of household availability at 15 month follow-up**

counties. Both of these factors contributed to lower statistical power than anticipated. Fifth, we estimated facility-level effect across all 14 medicines included in the Novartis Access portfolio, and when considered together the number of tests has an increased potential for at least one false-positive result. It might be appropriate to apply the Bonferroni correction and consider the critical p value threshold for these tests to be 0·003, in which case all facility-level effect estimates are non-significant. Sixth, the nature of Novartis Access necessitated county-level randomisation which limited the number of clusters that could be feasibly included in the study. While the baseline balance shown in table 1 suggests that the study groups were quite comparable, we are not able to describe historical trends which would further confirm the internal validity of the study. The baseline imbalance in availability of metformin at facilities, although controlled for in the main regression analysis, could indicate different historical trends across groups which could be a source of bias. Finally, a substantial number of respondents could not accurately recall medicine prices or expenditures, and these outcomes were excluded from the analysis due to missing data. Asking respondents at baseline to obtain and keep receipts for all medicine purchases during the study period could be an alternative approach that yields better data in future studies.

This paper is, to our knowledge, the first to present experimental evidence on the effect of an industry-led access-to-medicines programme.[21] The UN has recognised the key role that the pharmaceutical industry should play in the effort to achieve universal health coverage globally.[8] While we found that Novartis Access had little effect in its first year in Kenya, Novartis's commitment to rigorous measurement and transparent reporting should serve as a standard for other industry efforts in this area.[22,23] Access programmes operate within complex health systems and reducing the wholesale price of medicines might not always or immediately translate to improved patient access. Programme planners should adopt a health systems perspective and consider implementation challenges from project inception. Our findings underscore the need for more evaluation of industry-led access programmes. The evidence generated by this study will inform Novartis's efforts to improve their programme going forward. The study also contributes to the public evidence base on strategies for improving access to medicines globally.

Contributors

PCR, ROL, PGA, MAO, and VJW contributed to the conception of the study, study design, and data interpretation. CKM contributed to data collection and data interpretation. PCR conducted the data analysis and drafted the initial manuscript. All authors critically revised the manuscript and approved the final version.

Declaration of interests

PCR, ROL, PGA, MAO, and VJW report research grants from Sandoz International, a subsidiary of Novartis International, for the conduct of this study. PCR, ROL, and VJW report additional grants from the International Federation of Pharmaceutical Manufacturers and Associations outside the submitted work. ROL was provided with travel and accommodation by Novartis International to present on the protocol for this study at two meetings held in Geneva, Switzerland, in May, 2016. CKM has no competing interests.

Data sharing

Data for the baseline and 15 month follow-up are available upon request from Boston University (http://sites.bu.edu/evaluatingaccess-novartisaccess/kenya/data).

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