An innovative model for management of cardiovascular disease risk factors in the low resource setting of Cambodia

Hernandez, Nazaneen Nikpour ; Ismail, Samiha; Hen, Heang ; van Pelt, Maurits ; Witham, Miles ; Davies, Justine

ABSTRACT

The author's institute in Cambodia utilises Peer Educators (PEs) to screen and manage diabetes and hypertension in the community; a revolving drug fund (RDF) is used to finance the programme. Clinical outcomes and retention in the program are necessary to know if implementation of this program is to be widespread. We analysed clinical outcomes and patient retention in the programme between 2007-2016 in Takeo, Cambodia. For all those enrolled in the programme, the average change in blood pressure (BP) and percentage with controlled hypertension (BP < 140 / < 90 mmHg) or diabetes (fasting blood glucose (BG) < 7mg/dl, post-prandial BG < 130mg/dl, or HBA1C < 7%) was calculated every 6 months from enrolment. Attrition rate in the nth year of enrolment was calculated; associations with loss to follow-up were explored using cox regression. 9139 patients enrolled between January 2007 and March 2016. For all hypertensives, mean change in systolic and diastolic BP within the first year was -15.1mmHg (SD 23.6, p <0.0001) and -8.6mmHg (SD 14.0, p <0.0001), respectively. BP control was 50.5% at year 1, peaking at 70.6% at 5.5 years. 41.3% of patients with diabetes achieved blood sugar control at 6 months and 44.4% at 6.5 years. An average of 2.3 years [SD 1.9] was spent in programme. Attrition rate within year 1 of enrolment ranged from 29.8% to 61.5% with average of 44.1% [SD 10.3] across 2008-2015. Patients with hypertension were more likely to leave the program compared to those with diabetes and males more likely than females. The programme shows a substantial and sustained rate of diabetes and hypertension control for those who remain in the program and could be a model for implementation in other low middle-income settings, however, further work is needed to improve patient retention.

INTRODUCTION:

The global aim of achieving Universal Health Coverage (UHC) requires innovative, wide-reaching interventions that improve access to care for vulnerable populations. Ageing populations, globalisation, reduction in physical activity, and changing diets have led to a rapid rise in non-communicable diseases (NCDs) against a backdrop of prevalent infectious diseases in many lower- and middle-income countries (LMICs). Cambodia, a LMIC in South East Asia, has a rapidly growing economy with aims to reach upper-middle income country status by 2030. Although poverty rates are falling, 4.5 million of the population of over 16 million remain in near poverty and are vulnerable (World Bank, 2020). Life expectancy at birth was 72.7 years and 66.8 years for females and males, respectively, in 2017; an increase of 20 years in the last two decades (IHME, 2017). As expected with rapid economic development, NCDs are becoming prevalent. NCDs accounted for 64% of all deaths in 2018, and in 2016 stroke was the leading cause of death with ischaemic heart disease ranked as fourth (WHO, 2018). Type-2 diabetes mellitus and hypertension - modifiable risk factors for these conditions – were found in 5.9% and 11.2% of the population, respectively, in 2016 (WHO, 2016; Sophal Oum, 2010), making them high-priority conditions to start tackling NCD morbidity and mortality. Despite this, in 2018, fewer than 25% of primary health centres reported to offer cardiovascular disease (CVD) risk factor stratification, guidelines for CVD prevention were not used in more than 50% of facilities, and only 30% of facilities reported medicines for treating NCDs were generally available (WHO, 2018). Data from countries in South East Asia has shown that fewer than 40% of the population with hypertension have been diagnosed and fewer than 10% have this controlled to target (Geldsetzer *et al.*, 2019). The figures are only slightly better for people with diabetes (Manne-Goehler *et al.*, 2019). In countries with underdeveloped health systems, such as Cambodia, community centred

models of care may provide solutions to ensure all healthcare needs of individuals are met (Schneider and Lehmann, 2016).

The delivery of chronic disease healthcare models has evolved in different ways across different settings. For example, in the United Kingdom (UK) primary care facilities are used in screening, initiating treatment, and monitoring. There is a strong focus on encouraging self-management for achieving disease control, and General Practitioners are incentivised with the Quality and Outcomes Framework (QOF) to screen patients (NHS Digital, 2020). However, in the UK, contact with the health services is frequent and people are offered health checks after the age of 40. In contrast, the United States of America (USA) provides the majority of management through secondary care facilities using national and private health insurance programs (Commonwealth Fund, 2016). In LMICs, strategies for dealing with NCDs are in their infancy, given the focus of healthcare provision has largely been on providing care for acute conditions. For screening, suggested approaches involve Community Healthcare Workers or similar cadre. However, these haven't been widely rolled out in real world settings (Munshi, Christofides and Eyles, 2019; Ndou *et al.*, 2013; Tang *et al.*, 2014). Many suggested approaches for treatment in LMICs developed in recent years include the diagonal approaches of integrating existing infectious disease services to manage long-term conditions. These services are largely run by non-governmental organisations and financed with out of pocket expenditure (Datta, Husain and Asma, 2019; Janssens *et al.*, 2007). Approaches specific to managing chronic diseases, via strengthened primary care infrastructures, have also begun to gain popularity, but are still often dependent on private funding grants rather than national revenue (Collins *et al.*, 2019; Laar *et al.*, 2019). Regardless of approach or setting, analyses have shown that large proportions of patients with diabetes or hypertension are lost at all stages of the cascade of care, from testing and diagnosis, to treatment, and ultimately control. In LMICs a large proportion are

lost in the first stage of the cascade (testing) (Manne-Goehler *et al.*, 2019; Pascal Geldsetzer, 2019). Therefore, there is a need for innovative new healthcare models that address the common barriers to accessing healthcare throughout the cascade of care, from disease recognition to adequate treatment, including high out of pocket expenses or reliable medication supply (Joshi *et al.*, 2008). Robust analyses of new programmes that aim to address the entire cascade are needed to inform the development of effective chronic disease management in LMICs.

The author's institute applies a unique healthcare model that utilises Peer Educators (PEs), patients with diabetes and/or hypertension themselves, to return to their local villages to screen and initiate management of fellow community members. Elsewhere, the role of PEs in diabetes and self-management has also been recognised in the last two decades (Brownson and Heisler, 2009) with increasingly robust data that shows impact (Debussche *et al.*, 2018) The Programme structure also uses a Revolving Drug Fund (RDF), which stabilises essential medicine provision and creates a sustainable income source (Cross *et al.*, 1986; van Olmen *et al.*, 2016; Murakami *et al.*, 2001). The PE roles have since been formalised into the existing national health infrastructure of two Operational Districts (ODs) in Cambodia, with a view to expand, whereas the RDF management remains under the organisation of The Programme. One previous study (Taniguchi *et al.*, 2017) has examined clinical effectiveness of The Programme between 2007 – 2013 in Takeo province, where it first started a rural network. Our paper expands on these clinical outcomes to include data until 2016 (a total of 8 years), and additionally to describe the long-term retention of patients, which is an important assessment of its long -term effectiveness

METHODS:

Target population:

The study population includes people aged over 18 years living in the largely rural Takeo province in Cambodia, who were screened and diagnosed with diabetes or hypertension. Takeo is sixth largest of the 25 provinces in Cambodia (population 899,485 [5.9%]) (National Institute of Statistics, 2019).

Programme description:

The Programme uses a community-centred approach to long-term care for diabetes and hypertension management. Peer Educators (PEs), patients selected for their motivation, are trained to screen and manage these conditions in their local village and health centre catchment area. PEs carry out screening of people aged 40 years and over and are given small payments for travel (US$0.04 per km), registering new patients (US$0.12 per patient), and more recently measuring blood glucose (US$0.62 per patient) and blood pressure (BP) (US$0.12 per patient). Local guidelines define presence of diabetes as fasting blood glucose (FBG) ≥ 126mg/dl or post-prandial blood glucose (PPBG) ≥ 180mg/dl, and hypertension as systolic ≥ 140mmHg and diastolic ≥ 90 mmHg. Only patients with blood glucose or pressure results above these thresholds are enrolled in the program, all other adults in the household are advised to contact the peer educator if they notice symptoms of diabetes. The role of PEs also includes arranging village health meetings to discuss lifestyle measures and diet. PEs are active in 21 of 100 Operational Districts (OD) of Cambodia and each OD is served by a referral hospital where physician-lead prescriptions are made. The Programme itself provides laboratory services and operates a RDF for vetted, reliable, and lower priced drugs supplied to contracted pharmacies. PEs act as an intermediary between the physician and less mobile patients to deliver and explain blood results, pick up prescriptions, and monitor

blood sugars and pressures. Early in its inception, in 2007, the program engaged at a national level to have PEs recognised as national healthcare workers; they were recognised in the National Strategic Plan for Prevention and Control of NCD 2013-2020 (Ministry of Health, 2012). The role of the PE has also been described in the 'National Standard Operating Procedures for Diabetes and Hypertension in Primary Care' (Ministry of Health, 2019). However, training of PEs is still undertaken by The Programme with a view to transitioning this to the care of national services in the coming five years.

Data:

Data from all patients enrolled in Takeo province from 1st February 2007 to 31st March 2016 were included in the study. Multiple electronic datasets containing enrolment data, laboratory results, doctors' follow-up, and PE follow-up were merged.

Variables captured at enrolment were: sex, age, whether prescription medication or traditional medicines were already being taken, smoking status, height and weight (using generic scales and a height measurement stick, and from which BMI was derived in kg/m2), fasting or post-prandial capillary blood glucose (mg/dl), and systolic and diastolic BP (mmHg). Capillary blood glucose variables were measured using 2007 Roche Accu-Chek**,** which was changed to ACON On Call Plus machine from 1st December 2009 onwards. HbA1c was measured in the laboratory using SIEMENS DCA. BP was measured using Automatic Citizen CH-432B machine in 2009, AS-35B in 2010, and in 2015 both ALP-K2 and Nissei SL 1902.

PEs classified patients with a fasting capillary blood glucose of ≥ 126mg/dl or post-prandial blood glucose of ≥ 180mg/dl as having diabetes. Patients with systolic BP ≥ 140mmHg and diastolic BP ≥ 90mmHg were classified as having hypertension. The clinical variables extracted from the follow up databases were systolic and diastolic BP (mmHg), capillary

glucose reading of fasting blood glucose (FBG) (mg/dl), post-prandial blood glucose (PPBG) (mg/dl), and/or HBA1C (%).

Study variables

Outcome measures

Our main outcomes were change in BP over time for patients enrolled into the program with hypertension.

Other outcomes were (1) The population in the program enrolled with hypertension or diabetes who were controlled over time (2) loss to follow up of participants enrolled in the program

Patients were defined as having either hypertension or diabetes based on the PE diagnosis. For hypertension, three disease groupings explored in the analyses were all people with *hypertension* (with or without diabetes), *diabetes and hypertension* (concurrent diabetes and hypertension), or *hypertension alone* (without diabetes). BP control at follow up was defined as systolic BP < 140mmHg and diastolic BP < 90mmHg (%). A separate analysis was done for patients with concurrent diabetes and hypertension, using a BP target of < 130mmHg systolic and < 80mmHg diastolic as per clinical guidelines for patients with diabetes.

For diabetes, all people with *diabetes* (with or without hypertension) were included. Blood sugar controlled to target at follow up was defined, as per local guidelines, as FBG of < 130mg/dl, PPBG < 180mg/dl or HBA1C < 7%. In patients who had more than one form of blood sugar measurement at a given follow up time, HbA1c was chosen as the preferred measure, PPBG was the second preferred, and FBG was the least preferred, based on our

latest understanding of the correlation of Point Of Care (POC) blood sugar testing with HbA1c levels (Ketema and Kibret, 2015) .

Time to follow up was calculated as date of follow up visit minus enrolment date, in years to the nearest 6 months. Patients were categorised as lost to follow up ("left the programme") if they had not reattended by one year after their last follow up date. Timepoint 0 represents the date of enrolment.

Explanatory variables

Overweight was classified as having a BMI of ≥ 23kg/m2 to reflect lower BMI average in Asia (WHO expert consultation, 2004), BMI of ≥ 25kg/m2 was also used to show comparison with global standards. BMI ≥ 30kg/m2 was defined as obese. Smoking was captured by self-report and taken to mean current smoker. Participants with no response to the question on smoking were classed as non-smokers.

Age-groups were categorised as aged under 60 or aged 60 and over. Whether on prescription or traditional medicine at baseline was captured as yes or no. In addition, the number of prescription medicines prescribed by the program to control BP or diabetes were captured as continuous variables at one-year post enrolment, as well as the maximum number of medications taken by each individual at any time point in the program.

Analyses

All data were analysed using open-source statistical program RStudio Inc – Version 1.0136 2016 under public license. For all analyses, a two-sided p value of <0.05 was taken as significant.

Entries with incomplete data – mostly missing follow up dates – or those with follow up dates that occurred before their enrolment day (incorrect data entry) were excluded from analyses. Outlier entries with systolic or diastolic BP < 20mmHg were also excluded. Data are described as n (%) for categorical and mean (SD) for normally distributed variables (after testing for normality of distribution).

For patients with hypertension, the systolic and diastolic BP (mmHg) change from baseline were computed using the follow up BP closest in time to each 6 monthly follow up time point. Where multiple BP recordings existed for a patient that were equally close to the follow-up year, the mean reading was used for analysis. The mean BP change from enrolment for all patients at each timepoint is displayed for each hypertension group and disaggregated by sex (male and female) and age-category (under 60 years and age 60 and over).

A paired samples t-test was carried out to test significance of the mean change from baseline in systolic and diastolic BP at each timepoint and an unpaired t-test was carried out to test significance between male and female sex.

Percentage of patients with systolic and diastolic BP within target range at each follow up time was displayed for each hypertension group. For all patients with hypertension, binary logistic regression was done using complete cases to assess the effects of explanatory variables; presence of diabetes, age group, sex, smoking status, BMI and number of medications for hypertension taken at the one-year time point, on whether hypertension was controlled to target.

For all participants with diabetes, the percentage of patients with controlled diabetes at each follow up time was calculated. To explore associations with diabetes controlled to target, binary logistic regression was done using complete cases, using the explanatory

variables; presence of hypertension, age group, sex, smoking status, BMI, and number of diabetes medications taken at the one-year time point.

Given attrition rates decline with increased duration in a program, attrition rates were calculated dependent on year of follow-up (n, the 'n'th year after enrolment) and the year (Y). Patients were defined as lost to follow up if they had not been seen in the year after their last visit, therefore, for any year, attrition rate, is the number of people enrolled in year 'Y-n', seen in year 'Y-1' and not seen in year 'Y', divided by the total number of people enrolled in year 'Y-n' who were seen in year 'Y-1'.

The formula used was as follows:

$$Attrition\ rate\ (n, Y) = \frac{Number\ of\ pariticpants\ enrolled\ in\ year\ (Y-n), followed\ up\ in\ year\ (Y-1)\ and\ missed\ follow\ up\ in\ year\ Y}{Number\ of\ people\ enrolled\ in\ year\ (Y-n)\ and\ followed\ up\ in\ year\ (Y-1)}$$

To explore the probability of any patients leaving the program at n years after enrolment, Cox regression analysis was done using complete cases with assumption of proportional hazards. Data were censored for those who remained in the program for the full duration of the data period. Explanatory variables included in the model were disease type (diabetes alone, hypertension alone, diabetes and hypertension), sex, age group, BMI, smoking status, and total number of medications taken at one year. Kaplan-Meier survival plots were plotted for disease groups.

This study is a retrospective exploratory analysis of real-world data and therefore no sample size calculation was carried out.

RESULTS:

9139 patients were enrolled in the programme between January 2007 and March 2016, of which 66.4% were female, mean age was 56.4 [SD 13.5], 80.3% had a diagnosis of

hypertension, and 47.6% had a diagnosis of diabetes (see appendix table 1.0 for characteristics of all patients enrolled). 6677 patients had data available for inclusion in analyses (see appendix table 2 for characteristics of excluded patients). Depending on analysis, not all 6677 patients had information available, 57 patients were excluded from analyses of blood pressure due to missing blood pressure measurements and 10 patients were excluded from analyses of diabetes due to missing blood sugar measurements (figure 1.0). Of the total 6677 patients included, 59.2% (3956) had diabetes, 74.7% (4987) had hypertension, 34.5% (2302) had diabetes and hypertension and 40.2% (2685) had hypertension alone (table 1.0). 67.1% patients included were female and the mean patient age was 55.7 years (SD 12.9). 15.7% patients were taking traditional medicines at enrolment and 5.4% reported smoking. 46.2% of all patients (48.5% of patients with diabetes) were overweight (BMI $\geq$ 23 kg/m^2). The mean (SD) number of medications taken for hypertension or diabetes at the one-year time point was 1.1 (1.2) and 0.8 (1.0), respectively. Mean (SD) maximum number of medications used to treat hypertension or diabetes in the program was 1.4 (1.3) and 1.0 (1.0), respectively (table 1.0).

From the time of enrolment to their last review date, patients had between 1 and 84 follow-up visits, with an average of 10.9 (SD 11.1) visits.

Blood pressure control:

For all patients with hypertension, change in BP (mmHg) from enrolment is shown in figure 2.0 (appendix table 3.0 shows the maximum and mean BPs for the 1174 patients who had measurements that were equidistant from the 6-month analysis timepoint). The mean change in systolic and diastolic BP from baseline within the first year was -15.1mmHg (SD 23.6, p <0.0001) and -8.6mmHg (SD 14.0, p <0.0001), respectively. The greatest fall in systolic blood pressure occurred at 2.5 years after enrolment, (-18.9 mmHg [SD 37.4, p

<0.0001]) and at 3.5 years for diastolic BP (-11.4mmHg [SD 24.5, p <0.0001], figure 2.0). For patients who had diabetes and hypertension, mean change in BP from baseline 1 year after enrolment was -10.9mmHg (SD 22.9, p < 0.0001) systolic and -7.1mmHg (SD 12.9, p < 0.0001) diastolic (appendix figure 1.0). For patients with hypertension alone, mean change in BP from baseline at 1.0 year was -20.0mmHg (SD 24.5, p < 0.0001) systolic and -8.5mmHg (SD 14.2, p< 0.0001) diastolic (appendix figure 1.1).

Considering all patients with hypertension, mean systolic or diastolic BP change from baseline was similar for males and females and for those older or younger than 60 years. (appendix figures 1.2 - 1.5).

Percentages of all people with hypertension with systolic and diastolic BP controlled to target at each follow up time are shown in figure 3.0. The proportion of patients with controlled BP climbs steadily to a peak of 70.6% at 5.5 years. Appendix figure 2.0 shows control for patients with concurrent diabetes and hypertension within the target of < 130/< 80 mmHg as per clinical guidelines. Binary logistic regression showed the presence of diabetes, being younger than 60 years old and smoking at enrolment were all significantly associated with having hypertension controlled at one year after enrolment. Whereas the number of antihypertensive medications taken, sex, and BMI were not significantly associated (appendix table 4.0).

Blood sugar control

The proportion of patients within blood sugar levels controlled remains stable throughout the study period (figure 3.0) at close to 40%. Binary logistic regression showed number of anti-glycaemic medications and BMI were significantly associated with blood sugar control at one year. Presence of hypertension, age group, sex and smoking status were not significantly associated (appendix table 5.0).

Attrition Rate

The average time spent in the program for all patients was 2.3 years [SD 1.9]. Average rate of attrition within the first year after enrolment, across the 7-year period (2008 – 2015) was 44.1% (SD 10.3, range 29.8% to 61.5%). Attrition in the 2nd year after enrolment ranged between 32.4% to 50.0% with a mean of 38.3% [SD 5.8] (figure 4.0). Cox Regression analyses results are shown in table 2.0. Those with hypertension alone were more likely to leave compared to those with diabetes alone. Age under 60 years was protective against leaving the programme as was those with higher BMI compared to those with BMI under 23 kg/m^2. Those who reported smoking were more likely to leave the programme as were those who took between 1 and 3 medications for diabetes or hypertension at one year.

figure 5.0 shows Kaplan-Meier plots of attrition for patients with hypertension, diabetes, or both hypertension and diabetes.

DISCUSSION:

The analyses show that a program using a revolving drug fund and peers to screen and follow up patients with hypertension and diabetes is effective at reducing BP and improving glycaemic control. However, retention in the program is low, with attrition being similar in each year after enrolment. The focus on healthcare provision in many LMICs has been on improving care for infectious diseases and reducing maternal and neonatal mortality and morbidity. However, with the Sustainable Development Goals, has come a focus also on reducing premature mortality from non-communicable diseases and provision of universal health coverage (UHC). Unfortunately, the reality is that coverage of diseases under UHC, even in countries where this exists, may not extend to non-communicable diseases (The Lancet, 2014), and looking towards other models of ensuring access to medicines for people with these conditions remains a valuable lesson. Thus, even though The Programme uses an

Out of Pocket payment system for ensuring medicines availability, our findings have important policy implications for other countries without UHC looking to scale up care for these diseases and suggest that although the model works in the short term, more needs to be done to encourage retention.

The most rapid reduction in systolic and diastolic BP was within the first year of enrolling with The Programme; the comparatively lower reduction in diastolic compared to systolic BP is in keeping with our understanding of the effect of common antihypertensive agents (Wu *et al.*, 2005). However, sustained BP reduction was observed throughout the study period. Although we did not formally assess changes in cardiovascular risk over time, the increasing proportion of patients with BP and diabetes controlled over time suggests that patients enrolled within The Programme will have lowered their cardiovascular risk (NICE, 2019).

Our findings, with more patients and longer duration of follow up were similar to those previously found (Taniguchi *et al.*, 2017). Whilst it is disappointing that results haven't improved over time, The Programme appears to achieve much higher levels of control compared to data analysed from the World Health Organizations (WHO) Study on Global Ageing and Adult Health (SAGE) where BP control ranged from 4.1% in Ghana to 14.1% in India (Lloyd-Sherlock *et al.*, 2014). BP and diabetes control was also higher in The Programme than has been shown in analyses of the cascade of care in other South East Asian or LMIC settings (Chow *et al.*, 2013; Geldsetzer *et al.*, 2019; Manne-Goehler *et al.*, 2019). Our relatively positive findings may be a particularity of the societal context or relatively developed setting of Cambodia. However, a Cambodian Médecins San Frontier (MSF) clinic for Diabetes from 2002 to 2008 (Raguenaud *et al.*, 2009) working in the same region as our programme, found only 24% patients achieved blood sugar control within one year. This suggests that the program itself had positive benefits, although whether these are

due to the use of peer educators or a revolving drug fund is not possible to tell from our study. The percentage control amongst The Programme is more comparable to those seen in a chronic care model implemented in Philippines called First-Line Diabetes Care (FiLDCare), which saw rates of control of 50.6% within six months. FiLDCare initiated self-management education in local health facilities using existing community health workers to encourage self-management at the community level. in contrast to the author's institute, The Philippines programme had the family physician being the primary contact for patients rather than the community health worker. The payments for medications in FiLDCare were also out of pocket although with a plan to become subsidised (Ku and Kegels, 2015). Experiences from settings where healthcare is free at the point of access suggest that cost of medications is not the only limiting factor to achieving diabetes control. For example, in the United Kingdom, where medications are either free or available for a small prescription charge rates of control were historically low; only 24% of people with diabetes had blood glucose measurements within target levels between 1998 and 2002 (Fox *et al.*, 2006). However, more recent data show control rates for type 2 diabetes as high as 66.8% in 2016-17 (NHS Digital, 2018). Potentially, multiple factors lie behind this increase, including health education – with an increase in awareness of diabetes and hypertension in the general public over time (Falaschetti *et al.*, 2014; Nazar *et al.*, 2015; Li *et al.*, 2010) and presence of pay for performance incentives for healthcare practitioners (Vaghela *et al.*, 2009). Although health literacy in general and specifically relating to cardiovascular diseases and its risk factors hasn't been formally assessed in The Programme, the use of PEs and the regular screening involved is likely to increase the knowledge of the general population. PEs are also paid on a per patient basis and this is likely to have a similar motivating effect to the UK pay for performance initiative.

That The Programme's outcomes compare favourably with those from other LMIC settings is encouraging. The focus of this paper was to illicit whether sustained reduction in clinical outcome measures were achieved in this real-world assessment of the programme and we are unable to comment on what aspects of it, e.g. peer educator or revolving drug fund, contribute to the favourable outcomes. Other analyses in LMIC provide evidence that PEs may contribute to improving glycaemic control, for example, a randomised control trial carried out in Mali where PEs delivered structured education programmes to promote self-management showed higher levels of diabetes control (Debussche *et al.*, 2018). The Programme's own PEs were implemented to specifically address the screening and diagnosis of patients as well as aiming to reduce barriers in accessing care and medications (van Olmen *et al.*, 2016). However, to what extent this influences clinical outcomes requires further research to ascertain, but this knowledge would enhance the applicability of elements of the chronic disease programme in other LMICs. Existing research supports the use of non-physician health workers, such as PEs, as a way of achieving key aspects of the WHO health system building blocks needed to deliver NCD care (Heller *et al.*, 2019). Peer groups have also been trialled in women's health programmes to improve maternal and child health (Lewycka *et al.*, 2013) and use of peers may improve care by reducing distances to accessing care, increasing patient knowledge and empowerment for improving behaviours to combat cardiovascular risk factors (Khetan *et al.*, 2017; Brownson and Heisler, 2009; Tang *et al.*, 2014).

Despite the short-term success of The Programme, the attrition rates are unacceptably high given that diabetes and hypertension are usually lifelong conditions. In some LMIC settings, the lack of recognition of diabetes or hypertension as chronic conditions by patients, combined with the costs of medications leads to high attrition rates (Rachlis *et al.*, 2016; Amira and Okubadejo, 2007; Buabeng, Matowe and Plange-Rhule, 2004). However, this isn't

always the case; one hypertension management programme in Vietnam found drop-out was as low as 14.3% over two years (Nguyen *et al.*, 2011) and the results from a diabetes management programme run in the same province of Takeo, by MSF, showed attrition over a 5-year period of 34% (Raguenaud *et al.*, 2009). The reasons for the high attrition rate in The Programme need to be explored. Given that we didn't have information about death of patients, and that a large proportion of those enrolled were over 60 years of age, it may be that the attrition rate could partly be explained by patient death, especially as the life expectancy in Cambodia is currently around 70 years. However, mortality is unlikely to be the only explanation and further qualitative research needs to be done to explore the reasons for leaving the programme and offer solutions. It is encouraging that over time we saw an overall decline in first-and second-year attrition for the programme. This may be related to The Programme's evolution and improved practise, with additional increased funding as it scaled up in 2010.

Study Limitations:

This real-world study used secondary data, and data capture was designed for clinical service rather than research studies. There were changes to the programme's data entry methodology over the period 2007 to 2016 linked with the set-up and expansion of The Programme, which led to gaps in data and some discrepancies with dating, which meant that large numbers of data entries had to be excluded between 2007 – 2009. The gaps in data and lack of information regarding reasons for leaving the program limits our ability to comment on causal factors for the results. The covariates included in our analyses were limited by the data that were available for the majority of patients. This limited, for example, our ability to reliably ascertain the influence of smoking status on attrition from

the programme. In addition, we have no information regarding the patients' use of alternative health services alongside The Programme, although our assumption is that it provided the majority of care for patients enrolled in the programme. There are low numbers of patients who were enrolled in the programme in the first few years of inception, which leads to low numbers of patients with data available for longer than six years. Some patients were already diagnosed with diabetes and/or hypertension, therefore our study can not assess the first two parts of the cascade (population prevalence to screened and screened to given diagnosis). However, assessing the latter parts of the cascade gives vital information about the ability of the health service to deliver good quality clinical care. In addition, for the diabetes group there were multiple methods for analysing blood sugar used by The Programme, therefore we were only able to look at diabetes outcomes as a binary variable (control or not control) compared to blood pressure analyses which allowed for change in BP analyses.

Death was not captured as an outcome, thus in our attrition analyses we were not able to distinguish between this and voluntarily leaving the program. Some of the improvements in outcomes seen may have been due to regression to the mean, however, given that this is an analysis of a real world program and treatments were given as they would be in clinical practice, we have not accounted for blood pressure at baseline in our analyses, as this would not be done in clinical practice to determine treatment success. Finally, it is also important to consider that in assessing the clinical effectiveness of novel chronic disease programmes, the possible adverse effects of overtreatment of both BP and blood sugar, which leads to hypotension and hypoglycaemia, need to be considered, especially amongst frail older persons (Monami *et al.*, 2013).

CONCLUSION:

This study shows that the innovative use of peer educators and a revolving drug fund as part of a community centred chronic disease programme results in substantial and sustained rates of diabetes and hypertension control for patients who remain in the program. The role of PEs at a village level reduces many barriers to accessing healthcare for the majority rural population in Cambodia. PEs bring point of care testing to village homes, act as a medium for long-term monitoring and drug prescription collection for less mobile patients, and share peer to peer health education at a local level. The Programme could prove to be a model for implementation in other low middle-income settings, however, further research is needed to determine reasons for the variable attrition rates.

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