Salt substitution and community-wide reductions in blood pressure and hypertension incidence

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Declaration of interest

- I have nothing to declare

Conflicts of interests @jjaimemiranda

- This study
  - Funded by NHLBI-NIH
  - Global Alliance for Chronic Diseases (GACD) programme
  - NCT01960972
- Me
  - AHPSR/WHO, CONCYTEC, GCC, IDRC, MRC, NIH, SNF, Wellcome, WDF
  - No pharma funding

Hypertension a global health issue

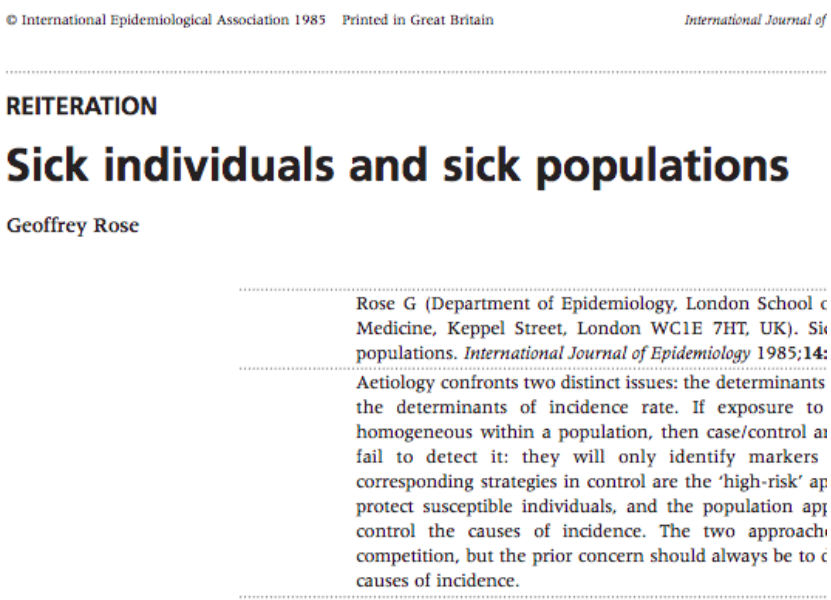
- Individuals, households, communities and societies
- Health systems
  - chronic care
  - human resources
  - task-shifting

Not enough cardiologists

- Forecasting imbalances in the global health labor market and devising policy responses
- The Supply and Demand of the Cardiovascular Workforce: Striking the Right Balance
- Urgent need for human resources to promote global cardiovascular health
- Trends and contexts in European cardiology practice for the next 15 years: the Madrid Declaration
- Too many patients, too few cardiologists to care?

Hum Resour Health 2018;16(1):5. | *J Am Coll Cardiol* 2016;68(15):1680-1689. | *Nat Rev Cardiol* 2011;8(2):114-7. | *Eur Heart J* 2007;28(5):634-7. | *Can J Cardiol* 2006; 22(11): 901–902.

Geoffrey Rose, 1985



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REITERATION

Sick individuals and sick populations

Geoffrey Rose

Rose G (Department of Epidemiology, London School c
Medicine, Keppel Street, London WC1E 7HT, UK). Si
populations. *International Journal of Epidemiology* 1985;14:

Aetiology confronts two distinct issues: the determinants
the determinants of incidence rate. If exposure to
homogeneous within a population, then case/control a
fail to detect it: they will only identify markers
corresponding strategies in control are the 'high-risk' ap
protect susceptible individuals, and the population apr
control the causes of incidence. The two approach
competition, but the prior concern should always be to c
causes of incidence.

"The corresponding strategies in control are the 'high-risk' approach, which seeks to protect susceptible individuals, and the population approach, which seeks to control the causes of incidence […] not usually in competition, but the prior concern should always be to discover and control the causes of incidence."

Rose G. Sick individuals and sick populations. *Int J Epidemiol* 1985; 14:32–38

The most important public health question

"'Why is hypertension absent in the Kenyans and common in London?'. The answer to that question has to do with the determinants of the population mean; for what distinguishes the two groups is nothing to do with the characteristics of individuals, it is rather a shift of the whole distribution —a mass influence acting on the population as a whole."

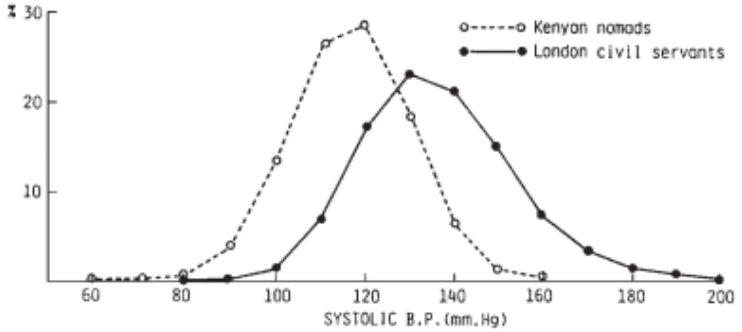


Figure 2 Distributions of systolic blood pressure in middle-aged men in two populations[2,3]

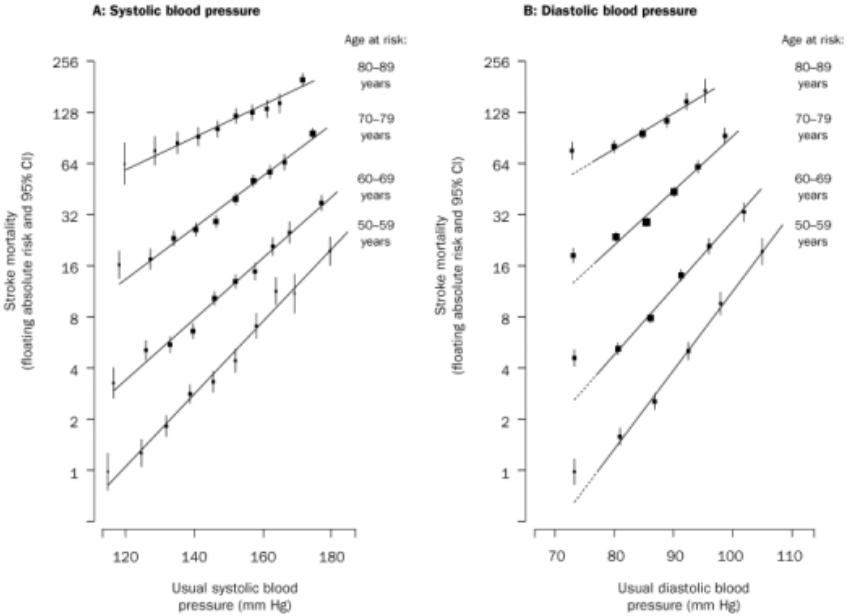
Rose G. Sick individuals and sick populations. *Int J Epidemiol* 1985; 14:32–38.

Blood pressure matters

"Even a 2 mm Hg lower usual SBP would involve about 10% lower stroke mortality and about 7% lower mortality from IHD or other vascular causes in middle age."

Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360(9349):1903-13.

Prospective Studies Collaboration



"So, for the general normotensive population, producing persistent reductions in average blood pressure of just a few mm Hg by some widely practicable methods […] should avoid large absolute numbers of premature deaths and disabling strokes."

Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360(9349):1903-13.

Salt and BP
↓sodium ↑potassium

Am J Clin Nutr. 2014 Dec;100(6):1448-54. doi: 10.3945/ajcn.114.089235. Epub 2014 Oct 15. Paperpile

Effects of salt substitutes on blood pressure: a meta-analysis of randomized controlled trials.

Peng YG[1], Li W[1], Wen XX[1], Li Y[1], Hu JH[1], Zhao LC[1].

Heart. 2019 Jun;105(12):953-960. doi: 10.1136/heartjnl-2018-314036. Epub 2019 Jan 19. Paperpile

Effect of low-sodium salt substitutes on blood pressure, detected hypertension, stroke and mortality.

Hernandez AV[1,2], Emonds EE[1], Chen BA[1], Zavala-Loayza AJ[3], Thota P[4], Pasupuleti V[5], Roman YM[1], Bernabe-Ortiz A[3,6], Miranda JJ[3].

Cochrane Database Syst Rev. 2006 Jul 19;(3):CD004641. Paperpile

Potassium supplementation for the management of primary hypertension in adults.

Dickinson HO, Nicolson DJ, Campbell F, Beyer FR, Mason J.

Telling people to reduce salt…

Hooper L, Bartlett C, Davey Smith G, Ebrahim S. Systematic review of long term effects of advice to reduce dietary salt in adults. *BMJ* 2002;325(7365):628.

- Aim: To assess the long term effects of advice to restrict dietary sodium in adults with and without hypertension.
- Conclusion: Intensive interventions, unsuited to primary care or population prevention programmes, provide only small reductions in blood pressure and sodium excretion, and effects on deaths and cardiovascular events are unclear.
- 2014 Cochrane review update: conclusions unchanged

Study protocol: NCT01960972

Bernabe-Ortiz *et al. Trials* 2014, **15**:93
http://www.trialsjournal.com/content/15/1/93

TRIALS

STUDY PROTOCOL **Open Access**

Launching a salt substitute to reduce blood pressure at the population level: a cluster randomized stepped wedge trial in Peru

Antonio Bernabe-Ortiz[1,2], Francisco Diez-Canseco[1], Robert H Gilman[3,4], María K Cárdenas[1], Katherine A Sacksteder[3] and J Jaime Miranda[1,5*]

Study objective and design

- To assess the efficacy of a **pragmatic** intervention using a **salt substitution** strategy to reduce blood pressure, as well as its impact on the incidence of hypertension, at the population level using a **stepped wedge cluster trial** in **Peru**.

Tumbes, Peru

Department: Tumbes

Population: ~200,000

Poverty level: ~25.0%

Hypertension: 27%
(≥35 years, in 2010)

Regular salt, 100% NaCl

Participants

- All adults ≥18yo
  - 2376/2605 (91.2%) enrolled
- 6 semi-rural villages
  - Agriculture or fishing
- Excluded
  - chronic kidney disease
  - heart disease, digoxin tx

Intervention

- To guarantee the full replacement of salt in the entire village
  - What? Salt substitute
  - How? Free of charge but in exchange of regular salt (*)
  - Where? Households, small shops, bakeries and community kitchens, food vendors including street vendors and restaurants.
  - When? 2014-2017

(*) 1 Kg of regular salt ~US$ 0.20-0.30

Outcomes

Primary

- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
  - BP measured every 5 months
  - 7 rounds of measurements

Secondary

- Incidence of hypertension
  - SBP ≥140 mm Hg or DBP ≥90 mm Hg
- Changes in levels of sodium and potassium excretion in 24-hour urine.
  - random sub-sample of participants
- SBP and DBP
  - by HT status
  - by age groups

Formative Research

- Identify optimal flavor
  - Triangle taste test
  - 75% NaCl & 25% KCl
- Identify target audience
  - Interviews + focus groups
  - Women & community
- Develop product identity
  - Short questionnaire
  - 60 participants, 10 per village

Product Identity

- **Name**: Liz
- **Character**: Local women
- **Packaging**: Transparent plastic bags, red and orange colors, including product information, 1 Kg
- **Salt container**: Plastic, screw cap, 1 Kg. capacity

Social Marketing Campaign

4Ps

Product | Salt Liz

Price | Exchange

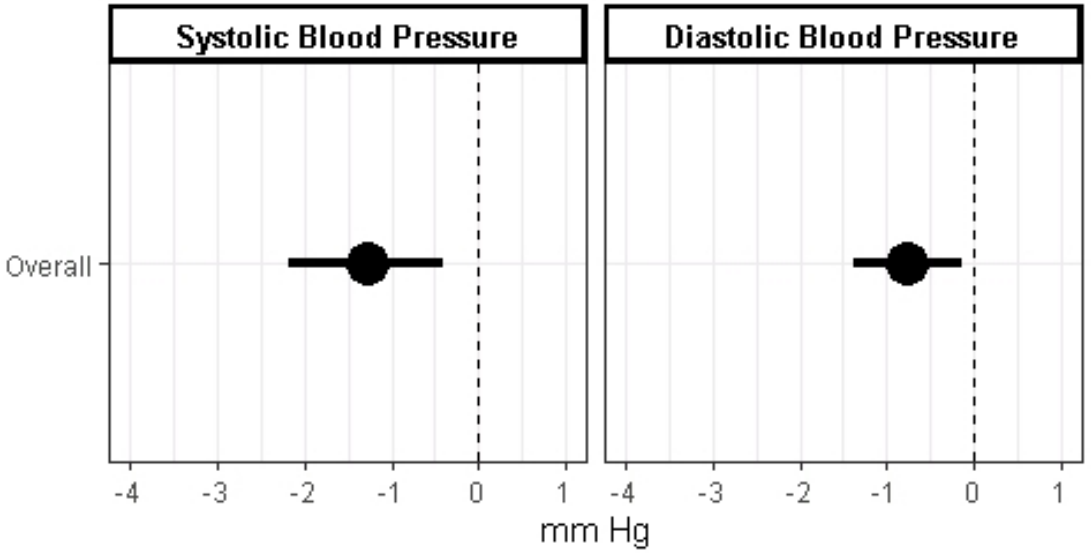
Place | Door-to-door + network

Promotion | Campaign

Table 1: Baseline characteristics

	Baseline N=2376	Time in Control (person-years)	Time in Intervention (person-years)
Sex			
Female	1197 (50.4%)	1335.2	1768.4
Male	1179 (49.6%)	1212.0	1836.9
Age			
Mean (SD)	43.3 (17.2)		
18-29 years	633 (26.6%)	595.6	703.0
30-44 years	780 (32.8%)	880.2	1226.9
45-64 years	656 (27.6%)	715.3	1129.2
≥65 years	307 (12.9%)	356.1	546.3
Wealth Index			
Bottom	689 (29.6%)	629.4	1137.8
Middle	785 (33.7%)	866.5	1180.6
Top	855 (36.7%)	1001.1	1232.5
Education			
<7 years	836 (35.2%)	909.0	1281.0
7-11 years	1090 (45.9%)	1185.3	1636.6
≥12 years	450 (18.9%)	452.9	687.6

	Baseline N=2376	Time in Control (person-years)	Time in Intervention (person-years)
Study Site (village)			
A	536 (22.6%)	1.7	1366.1
B	447 (18.8%)	286.9	883.1
C	329 (13.9%)	329.0	518.3
D	414 (17.4%)	542.1	460.2
E	328 (13.8%)	637.0	256.3
F	322 (13.6%)	750.6	121.3
BMI			
Mean (SD)	27.2 (4.6)		
Normal Weight	758 (32.7%)	762.3	1160.1
Overweight	985 (42.5%)	1093.0	1492.2
Obese	573 (24.7%)	629.1	887.0
Blood Pressure			
SBP [mean (SD)]	113.1 (17.0)		
DBP [mean (SD)]	72 (10.1)		
Hypertension			
No	1911 (81.7%)	2088.0	2825.6
Yes	428 (18.3%)	476.1	646.2



Overall reductions in SBP and DBP

SBP -1.23 mm Hg [95% CI -0.38; -2.07], p = 0.004

DBP -0.72 mm Hg [95% CI -0.10; -1.34], p = 0.022

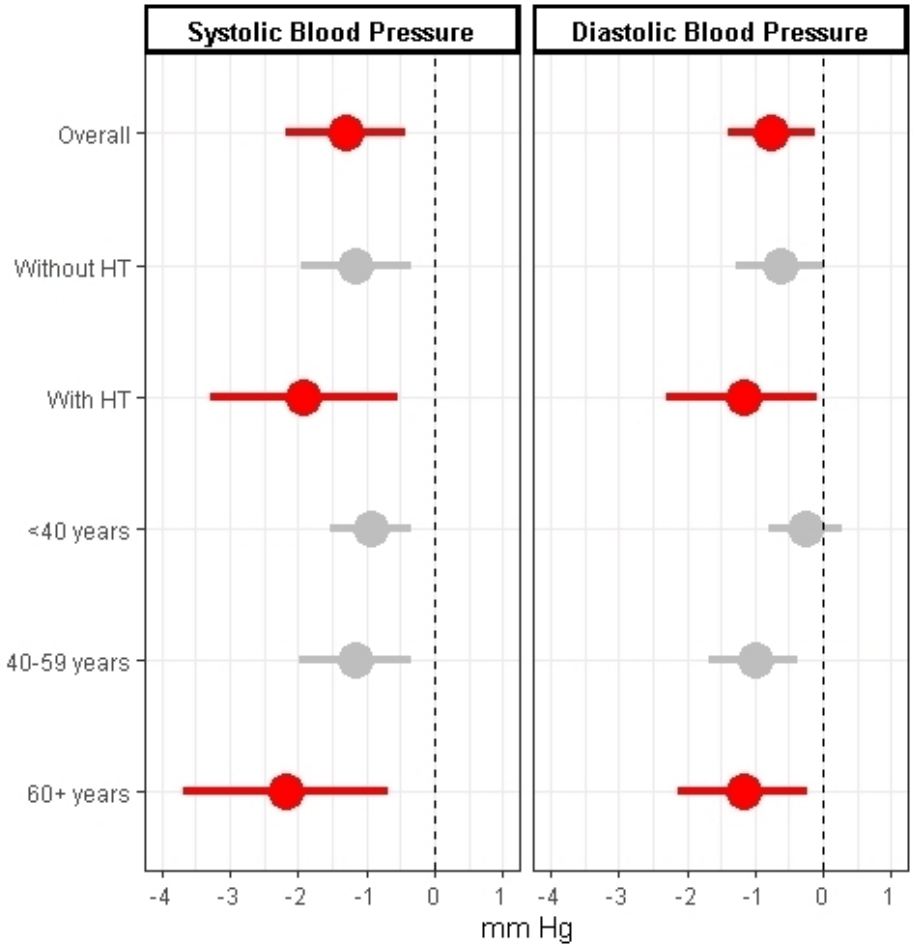
Reductions in SBP and DBP

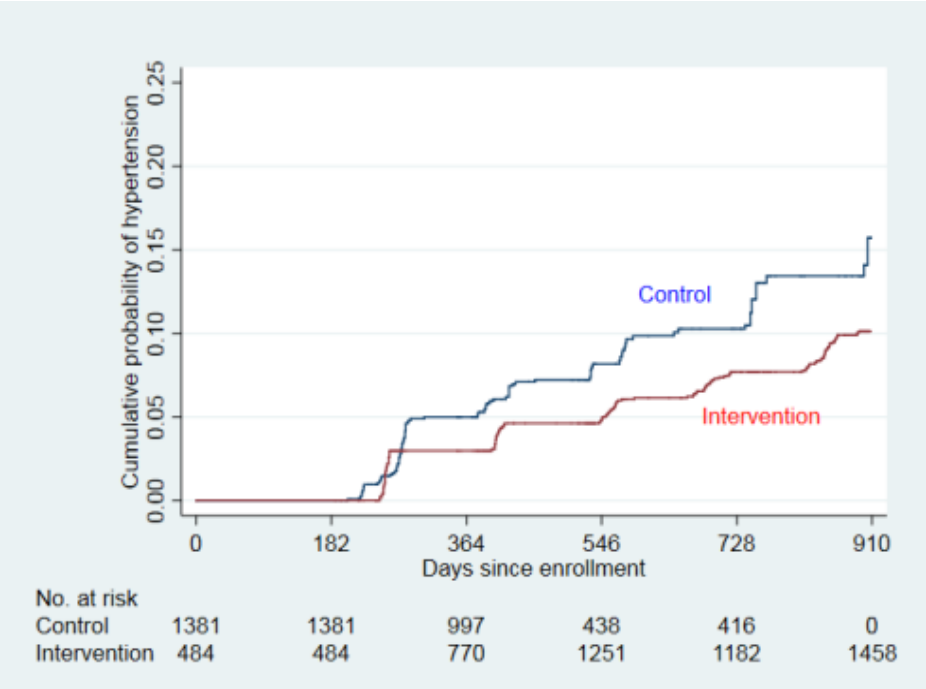
People with hypertension

SBP -1.92 mm Hg [95% CI -3.29; -0.54]

Subjects ≥60 yo

SBP -2.17 mm Hg [95% CI -3.67; -0.68]





Cumulative probability of developing hypertension

Fully-adjusted model: HR 0.45 [95% CI 0.66 – 0.31], p0.001>

24-hour urine samples

Random sub-sample of 600 participants

Sodium

- Baseline 3.94g ± SD 1.86
- End 3.95g ± SD 1.83

p = 0.93

Potassium

- Baseline 1.97g ± SD 1.20
- End 2.60g ± SD 1.20

p < 0.001

Pragmatic intervention

Blood pressure matters

"Even a 2 mm Hg lower usual SBP would involve about 10% lower stroke mortality and about 7% lower mortality from IHD or other vascular causes in middle age."

Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360(9349):1903-13.

Conclusions

- Our project established an effective pragmatic population-wide salt substitute strategy
  - Reductions in the whole population's blood pressure
  - Higher reductions in high-risk groups
    - Individuals with hypertension, ≥60 years old
  - 55% reduction in hypertension incidence (HR 0.45)

Key messages

- Hypertension rates and non-adherence to medication are global concerns, and non-pharmacological interventions at the population level to improve blood pressure control are required
- Our social marketing intervention demonstrated population-wide benefits
  - Public health gains through shifting the population distribution
  - Clinical and health systems impacts by halving hypertension incidence
- Switching to low-sodium high-potassium salts is feasible and it is effective in reducing blood pressure

The future

- Salt substitutes into daily life
  - Adaptation → further changes in Na, K
  - Think about K, not only about Na
- Potentially better results
  - 27% were 18-29 years-old
  - Baseline level of SBP was 113 mm Hg

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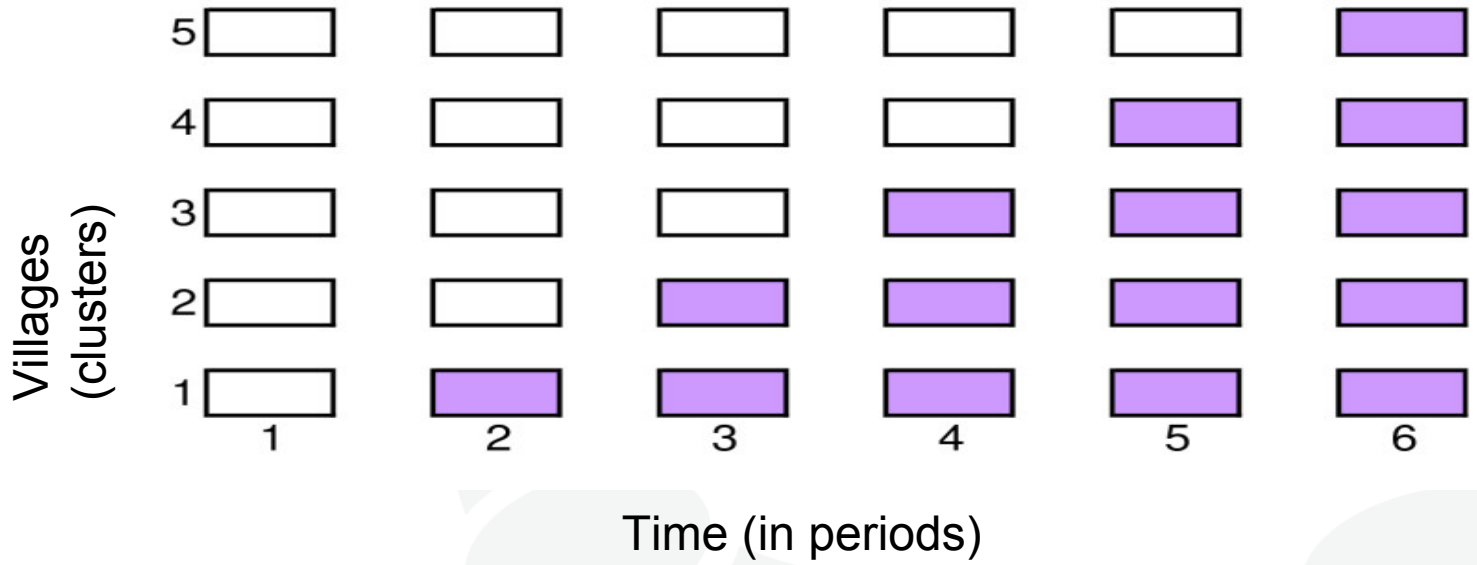
Design: stepped wedge trial



Source: Brown CA, Lilford RJ. *BMC Med Res Methodol* 2006;6:54

Adverse events

None