S1 File. The protocol of the study

S2 File. Ethics approval for this study

S3 Table. Sensitivity analysis: effects of individualized, evidence-based counseling on use of antihypertensive drugs when different cutoff values (days) were employed to define the outcome

S4 Table. Sensitivity analyses: effects of individualized, evidence-based counseling on good adherence to treatment when different cutoff values were employed to define the outcome

Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

Title:

Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.

Introduction:

In recent years, cardiovascular diseases (CVDs) have become one of the major causes of disease burden in China, accounting for approximately 40% of all deaths.(1, 2) Hypertension is an important modifiable risk factor of CVDs. In a systematic review, antihypertensive therapy has been proven to decrease the risk of stroke and coronary heart disease by 46% and 21%, respectively.(3) The continuous, gradual and smooth increase of absolute CVD risk with blood pressure, makes determining the threshold for initiating antihypertensive therapy a complicated issue. Evidence, people's value and preferences, and resources currently available, are the three major factors taken into account.(4, 5) Given the individualized feature of the other two influencing factors,(6-8) it would be difficult to have a consistent cutoff of CVD risk probability for initiating antihypertensive therapy for every hypertensive patient. Thus, the decision to initiate antihypertensive therapy ought to be based on two-way communication between physicians and patients.(5, 9)

To facilitate shared decision making, patients need to be prepared with knowledge specific to their own disease situations, for instance, absolute risk of CVDs, and benefits and harms of antihypertensive therapy.(10-14) In studies evaluating the efficacy of information communication for patients at risk of CVDs carried out in western countries, patients experienced decreased decisional conflicts,(11-14) had improved knowledge on their disease conditions,(12, 13) and participated more in their decision-making,(10) after obtaining individualized risk information. Moreover, patients were more willing and more compliant to reduce their CVDs risk,(10, 15) compared to their counterparts. Communication on patients' risk information has already been recommended by guidelines in the UK.(4)

However, it remains far less than routine in China, neither recommended by the guideline,(16) nor practiced by physicians.(17) Physician-centered communication and decision making based on their obsolete knowledge still predominates in prescription of antihypertensive therapy and individualized medical information remains far out of patients' reach. (17, 18)

Given the different cultural and social background in China and other foreign countries, it is difficult to predict the benefits of the information communication in the Chinese population. Whether the individualized antihypertensive information will influence patients' medication use in China remains unknown, as is how such information will change patients' medicine-taking behaviors. These are key questions to be answered for potential guideline modifications in the near future. We are going

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to explore the influence of individualized antihypertensive information on patients' medication use in an exploratory randomized controlled trial.

Aims:

As a primary objective, this study aims to explore the effects of individualized antihypertensive information on medication use (treatment rate and rate of good adherence) in hypertensive patients in China. As a secondary objective, this study aims to assess the roles of this information in the life style and the willingness to take medicines among the hypertensive patients.

Hypothesis:

Our null hypothesis is that the individualized antihypertensive information will have no effects on the rate of treatment or the rate of good adherence in hypertensive patients in China. The alternative hypothesis is that this information will increase both rates.

Methods:

1. Design overview:

A two-site, randomized controlled trial is going to be conducted to compare the individualized antihypertensive information on the basis of life style suggestions and usual care with life style suggestions and usual care solely in hypertensive patients. Eligible patients will be randomly allocated to two paralleled study groups with a ratio of 1:1. Patients will know their groupings, but they will be blind to the hypothesis of this study. Doctors will be blind to patients' grouping status.

2. Settings and patients:

Sequential clinic patients who are eligible and agree to participate will be enrolled in two primary care centers in Longgang District, Shenzhen, Guangdong Province. Inclusion criteria of the study subjects are as follows:

(1) Patients with primary hypertension;
(2) Age range: 35-65 years old;
(3) BP lower than 160/100mmHg at diagnosis, or systolic blood pressure lower than 145mmHg for patients already on antihypertensive medications measured in clinic at recruitment;
(4) Patients have at least graduated from primary school;
(5) No deafness, blindness, or dementia, have no difficulty in understanding the antihypertensive information and information in the questionnaire;
(6) Residents in Shenzhen, patients have no plan to move to other cities or countries in the following 6 months;
(7) Informed consents have been signed.

Patients with any one of the following conditions will be excluded from this study:

(1) Patients with hypertensive emergencies and urgencies, which are judged by

physicians in the primary care centers;

(2) Patients with drug-induced hypertension, drugs include sympathomimetic agents, non-steroidal anti-inflammatory drugs (NSAIDs) and cycloxoygenase 2 (COX-2) inhibitors, corticosteroids, central nervous system (CNS) stimulants, estrogens and progesterone, dietary supplements, serotonin-norepinephrine reuptake inhibitors (SNRIs), immunosuppressants; (19)

(3) Patients with histories of coronary heart diseases, cerebrovascular diseases, chronic heart failure, chronic renal diseases, or diabetes mellitus, etc.

(4) Patients' risk of cardiovascular diseases over 20% in the future ten years;

(5) Patients who did not get total cholesterol (TC) measured within 2 years before the study, or those whose TC values cannot be found in the medical record;

(6) Women in pregnancy or lactation;

(7) Patients possibly with low compliance to follow-up.

3. Intervention:

Patients in the experimental group will receive individualized antihypertensive information, life style education and care as usual. Patients in the control group only get life style education and usual medical care. The individualized information includes the following contents and an example of intervention with a baseline risk of 20% assumed is attached at the end of this protocol.

(1) Estimated baseline risk of cardiovascular diseases in the future ten years, estimated by Fuwai equation;

$$P_{men} = 1 - 0.9835^{exp\{0.3277(age_i - 46)/5 + 0.6711(SBP_i - 120)/20 + 0.1367(TC_i - 4.6) + 0.1360(BMI_i - 22)/3 + 0.6894(Smoke_i - 0.73) + 0.1195(Diabetes_i - 0.02)\}}$$

$$P_{women} = 1 - 0.9948^{exp\{0.4641(age_i - 45)/5 + 0.6090(SBP_i - 119)/20 + 0.1479(TC_i - 4.6) + 0.1593(BMI_i - 22)/3 + 0.4457(Smoke_i - 0.17) + 0.9946(Diabetes_i - 0.02)\}}$$

In patients already on antihypertensive or lipid-lowering medications, treatment effects are adjusted by the following equations:

a. Antihypertensive medications (20):
   BP prior treatment = BP measured + 15mmHg;

b. Lipid-lowering medications (4):
   TC prior treatment
   = 1.283*TC after treatment – 1.123 + 0.384*Ln(dose of simvastatin)
   = 1.419*TC after treatment – 2.205 + 0.475*Ln(dose of atrovastatin)

The values of TC measured after the lipid-lowering therapy are going to be obtained from patients' medical record, which were measured within 2 years before the study initiates. Reduction of 26% (3) in baseline risk probabilities by lipid-lowering medications is also taken into consideration in the corresponding

patients.

Since the CVD events estimated by Fuwai equation are mainly the ischemic ones, the estimated probabilities are adjusted based on the ratio of incidences of coronary heart diseases and cerebrovascular diseases (21), as well as that of incidences of ischemic and hemorrhagic cerebrovascular diseases (22) in the Chinese population.

(2) Estimated absolute risk reduction by antihypertensive drug therapy, calculated as follow:

Absolute risk reduction (ARR) = Baseline risk × Relative risk reduction (RRR)

RRR: from a systematic review published within 5 years before this study (3);

(3) Medicinal side effects and the estimated probabilities;

(4) Estimated monetary costs of antihypertensive medicines each year;

(5) Qualitative description of opportunistic costs of not initiating pharmaceutical therapy.

4. Outcomes of interest:

*** Primary outcomes:**

(1) Rate of treatment:

$$\textbf{Treatment rate} = \frac{\textbf{Patients currently on antihypertensive medication}}{\textbf{Total number of patients}} \times \mathbf{100}\%$$

Patients currently on antihypertensive medication are defined as those who took antihypertensive medicines in the past two weeks.

(2) Rate of good adherence:

$$\textbf{Rate of good adherence} = \frac{\textbf{Patients with good adherence}}{\textbf{Total number of patients}} \times \mathbf{100}\%$$

Patients with good adherence are defined as those with percentage of tablets taken as prescribed over 80% in the past week.

*** Secondary outcomes:**

(1) Changes of willingness to take antihypertensive medicines, obtained at the end of the intervention;

(2) Life style information by self-report, in the past two weeks before the time points of follow-up:

a. Amount of cigarette smoked per week;

b. Amount of alcohol consumed per week;

c. Amount of physical exercises per week in considering of duration and intensity;

d. Change of amount of salt intake;

e. Change of amount of fat intake.

5. Implementation of the study:

*** Baseline survey and measurement:**

Research assistance will conduct the baseline survey, and extract the values of total cholesterol and prescription information from the medical records. Nurses or doctors will participate to measure the blood pressure, height, and body weight.

(1) Demographic characteristics: gender, age, occupation, education level, medical insurance status;

(2) Life style information: smoking, alcohol drink, salt and fat intake, and physical exercises;

(3) Data used in risk estimation in Fuwai equation: (23)

Systolic blood pressure (SBP): SBPs will be measured at the visit of recruitment. Patients will be asked to rest in sitting position for at least five minutes and avoid drinking coffee, tea, or smoking within thirty minutes before blood pressure taken. Three consecutive blood pressures will be taken with calibrated mercury sphygmomanometer. Record the average SBPs. (23) Doctors or nurses who have been trained to follow the aforementioned standards will take SBPs.

Total cholesterol (TC):

Use the recorded values of TC within in 2 years before the study initiates, taken from medical records.

Smoking status: It is classified as current and non-current smokers. Current smokers are defined as smoking at least one cigarette per day for at least the past 12 months. The definition and classification are consistent with those in the Fuwai Equation. (24-26)

Body mass index (BMI): Weight and height will be measured by the nurses with patients wearing light indoor clothes and no shoes. BMI is calculated as follow:

$$BMI\ (kg/m^2) = weight\ (kg)/\ (height\ (m))^{\ 2}$$

(4) Medication use and prescription information:

Medication use: Record whether patients are currently taking antihypertensive medicines or not. (27) For those on treatment, take detailed information, including doses taken for each time, times of medicine taking per day, days per week in the past week.

Prescription information: Record names of all the prescribed antihypertensive drugs, doses and frequency of medicine taking, as well as doses of lipid-lowering drugs from patients' medical records.

(5) Knowledge and attitudes on hypertension:

a. The risk probability of CVD in the future 10 years estimated by the patient, whether the patient perceives it as high or low, acceptable risk probability of CVDs in the future 10 years;
b. Benefits of antihypertensive drugs in reducing the CVD risk probability

estimated by the patient, whether the patient perceives it as prominent enough or not;

c. The perceived severity of CVDs by the patient;
d. Perceived barriers of taking antihypertensive drugs (adverse effects, costs);
e. Reasons for taking or not taking antihypertensive drugs.

(6) **Contact information:** home address, at least two telephone numbers to ensure the connection with each patient.

*** Randomization and allocation:**

Random numbers (100 evens and 100 odd numbers) are generated by the software of Stata 10.0. Each random number will be enclosed in an opaque and sealed envelope, and kept in a locked drawer. A specific nurse is centrally in charge of patient allocation in both center and she does not participate in any other parts of the study. Patients will be allocated based on the number they get- evens for the intervention group, and odds for the control group.

*** Giving intervention:**

Formulas for estimating CVD risk in the future 10 years, ARR by antihypertensive treatments have been edited in the software of excel 2007. The corresponding risk probabilities can be simply obtained by imputing the values of the risk factors, such as age, gender, systolic blood pressure, total cholesterol, and BMI. Health educators will fill the information sheet, based on the calculated values, and then give the intervention by reading the individualized information on the sheet. The intervention will be given for twice by face-to-face and by telephone, respectively, with a gap of one week.

Health educators will be well trained before the study on (i) the explicit meaning of CVD risk and ARR by antihypertensive treatment, (ii) how to use the excel risk estimation tool, (iii) correctly filling the information sheet (see a sample in the attachment) and expressing the individualized information in an identical way as in the information sheet. They have to pass an exam of practice which includes all the aforementioned contents after the training. During the study, the intervention process and effects will be monitored in patients of the intervention group.

*** Blinding:**

(i) Patients will be blind to the hypothesis of the study, but not to their grouping status. In the informed section, they are only going to be told about the purpose of the study, but the expected direction of behavior changes will be held from the patients.

(ii) Doctors will be blind to patients' grouping status.

(iii) Health educators, interviewers and researchers in charge of data analyses will be aware about patients' grouping status.

*** Follow-up:**

Interviewers will be in charge of patients' follow-up. Telephone interview will be conducted at two weeks, three months, and six months after the intervention. Patients in the control group will receive the individualized antihypertensive information in the last time follow-up. Contents of the survey include:

(1) Medication use of antihypertensive treatments;

(2) Life style changes;

(3) Knowledge and attitudes to antihypertensive treatments;

(4) Any possible contamination during the study, doctors' attitudes and the effects on patients decisions or behaviors.

6. Statistical analyses:

*** Sample size calculation:**

$$n = \frac{2\left(u_\alpha + u_\beta\right)^2 \bar{P}(1-\bar{P})}{(P_1 - P_2)^2}$$

Inequality test for two proportions is applied in the calculation.

Sample sizes in two groups are assumed to be equal.

$\alpha = 0.05$ (For preplanned subgroup analysis: on/ not on antihypertensive drug therapy);

Power: $1 - \beta = 0.80$

Rate difference between groups: $\Delta P = 0.20$

Pharmacological treatment rate in control: $P_1 = 0.75$

$n_1 = n_2 = 90$

A total of 100 patients are going to be recruited in each group, when the rate of loss to follow up is assumed to be 10%.

This predefined sample size in each group is able to detect the difference of 0.20 in rate of good adherence between groups, with the significant level of 0.05, power of 0.80 and the baseline rate of 0.40.

*** Outcomes analyses:**

The two groups will be compared at baseline on demographic features, life style characteristics, knowledge and attitudes to antihypertensive drug therapy, as well as medical use, by *t*-test for continuous variables and chi-square test for binary variables. Regression model for longitudinal data will be applied to examine the effects of intervention on the changes of primary and secondary variables from baseline during follow-up. The software of SPSS 16.0 (SPSS, Inc., Chicago, IL) will be used for baseline comparisons and mixed effects linear model, and Stata 10 for mixed effects logistic model.

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Appendix: Information for intervention

(Baseline CVD risk is assumed to be 20% in this example.)

得了高血压，要不要吃药？应该考虑这几个方面：不吃药的后果，吃药的好处、坏处和花费，家里的经济条件，以及治疗是否必要和划算。

我先跟您聊聊不吃药会有什么后果。不吃药，血压一直比较高，病人得中风、冠心病、心力衰竭、肾功能衰竭等的可能性会增加。

您以前有没有听说过中风或者冠心病？有没有见过这样的病人？如果见过，他们都是什么样的？（**如果不清楚，需解释：**得了中风，病人可能会出现瘫痪--胳膊和/或腿不能活动、不能讲话或讲话口齿不清、看不见东西、嘴歪、眼斜等表现。得了冠心病，病人的心脏功能可能会明显下降，连爬一层楼、走几十米，甚至起床、穿衣、上厕所都会觉得费力。）

除了残疾、生活不能自理外，更严重的，病人可能死亡。另外，得了病以后，无论是治疗，还是请人照顾病人，都要花掉很多钱，病人和家人的生活质量也都会明显下降。

不吃降压药，万一得了中风或者冠心病，后果是不是很严重的？（**如果觉得不严重，需解释：**您可以想想其他疾病，比如说普通的感冒，就算不去管它，一到两周也就好了；再比如脚气，不治肯定不会死人。跟这些病比起来，得了中风或者冠心病是不是很可怕的？）

也不是说后果很严重就一定要采取行动去预防，还要考虑可能性的大小。就像出门有被车撞的可能，坐飞机有遇到飞机失事的可能，但是似乎很少有人因此就不出门、不坐飞机了。因为出门被车撞，坐飞机出事儿的可能性都很小很小，就因为这个不出门、不坐飞机，完全没有必要。

所以除了要知道不吃药的后果，还要知道可能性的大小。我们利用我国最可靠的方法，对您得病的可能性进行了估算。跟您情况类似的 100 名患者中，大概有 A. 20 人在以后 10 年中会得中风或冠心病，其余的 B. 80 人不会得中风及冠心病。

得病可能性的大小是相对的，同样一个 A. 20 %的可能性，有的人会觉得很高，有的人会觉得还可以接受。您可以结合得中风或冠心病的后果想一想，您觉得您在以后的 10 年中，得病的可能性是高还是低。

如果吃了降压药，得病的可能性可以降低到多少呢？我们利用国际上的专家他们的研究结果，给您计算了一下。跟您情况类似的这 100 名患者如果都吃药，原本会得中风或冠心病的那 A. 20 个人中，约有 C. 5 个人就不得病了， D. 15 人还是会得病；其余的 B. 80 个人，不管吃不吃药，都不会得病。也就是说，有 C. 5 个人因为治疗而避免了中风或冠心病的发生，其余的 E. 95 个人，得不得病，跟吃不吃药，没什么关系，就是说，吃了药，本来要得病的人还是会得病，本来不得病的人也还是不得病。

吃药好处的大小也是相对的，把得病的可能性从 A. 20 %降低到 D. 15 %，有些人会觉得收益非常大，有些人却觉得好处一般般，这是没有绝对的错对之分的。您可以想一想，对您来说，吃药的好处大不大？是不是把您得病的可能性降低到了您可以接受的范围？

（对于基线风险和吃药的好处，如果患者难以理解，可尝试用后面的图进行解释。）

需要提醒您注意，目前我们只能知道您在以后 10 年中得中风或冠心病的可能性的大小，但是没有人能绝对准确地知道您在未来一定得或不得这些疾病，也就是说，您可能是那 B. 80 个人中的一个，也可能是 A. 20 个人中的一个。也没法知道您是否一定会因为吃药就不得这些病了，也就是说，您可能是那 C. 5 个人中的一个，也可能不是。

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说完吃药的好处，再跟您说说吃药的坏处。降压药物长期吃，一部分病人会出现不良反应，但一般来说都不会很严重。较为常见的有疲劳、入睡困难、头痛、下肢浮肿、咳嗽、心功能抑制、低血压、阳痿等。在 100 个服药者中，大约有 15 人会出现这些副作用。副作用出现后，停药或者换其他降压药物，副作用就会消失。所以对于副作用，大可不必太过担心。

费用方面，您有没有算过，您每年吃降压药要花多少钱？（**如患者目前没有在吃药：**我国高血压患者每年降压药物的花费大约在 2000 元左右。）您可以想一想，这样的花费，大概会占到您家庭收入的百分之多少，会不会和家里其他的重要支出有冲突。再跟吃药带来的好处比一比，想一想钱花得值不值得。当然对于这个问题，也是不同人会有不同的看法。

除了吃药，健康的生活习惯，也可以帮助降低您在以后得中风和冠心病的可能性。

1) 饮食方面：多吃蔬菜和水果，少吃油腻，不要吃得太咸。
2) 经常锻炼身体，尽量保证每周运动 3-5 次，每次持续 20-60 分钟。
3) 不抽烟、少喝酒：不提倡喝酒，如喝酒，男性每天喝葡萄酒不超过一杯（150ml），或啤酒不超过一听半（500ml），或白酒不超过 1 两。女性减半。不喝高度烈性酒。
4) 适当减肥：体质指数控制在 20-24，体质指数=体重(公斤)/身高(米)^2。

可以说，心血管病基本上都是由吃得不健康、运动太少、抽烟、喝太多酒、肥胖等引起的，不管您最终是不是打算吃药，我们都希望您能按照上面的建议改变您的生活方式。

目前您的大致情况就是这样。对于您的这种情况，不同的人可能会做出不同决定，因为 A. 20 %得病的可能性，在有人看来很高，但也有人觉得还可以接受；10 年花两三万块钱，把中风或冠心病的可能性降低 C. 5 %，有人会很愿意，但有人会觉得很不值；也可能有人虽然想吃药，但是因为考虑到家里目前有比这个更紧迫的事情要用钱，暂时还是先不吃药。

病人的情况、想法千差万别，这就好比做衣服，不同的顾客有不同的身材、尺寸。裁缝当然是要给顾客量体裁衣，吃药的问题上也是一样，要根据病人的具体情况，具体分析，再做吃不吃药的决定。

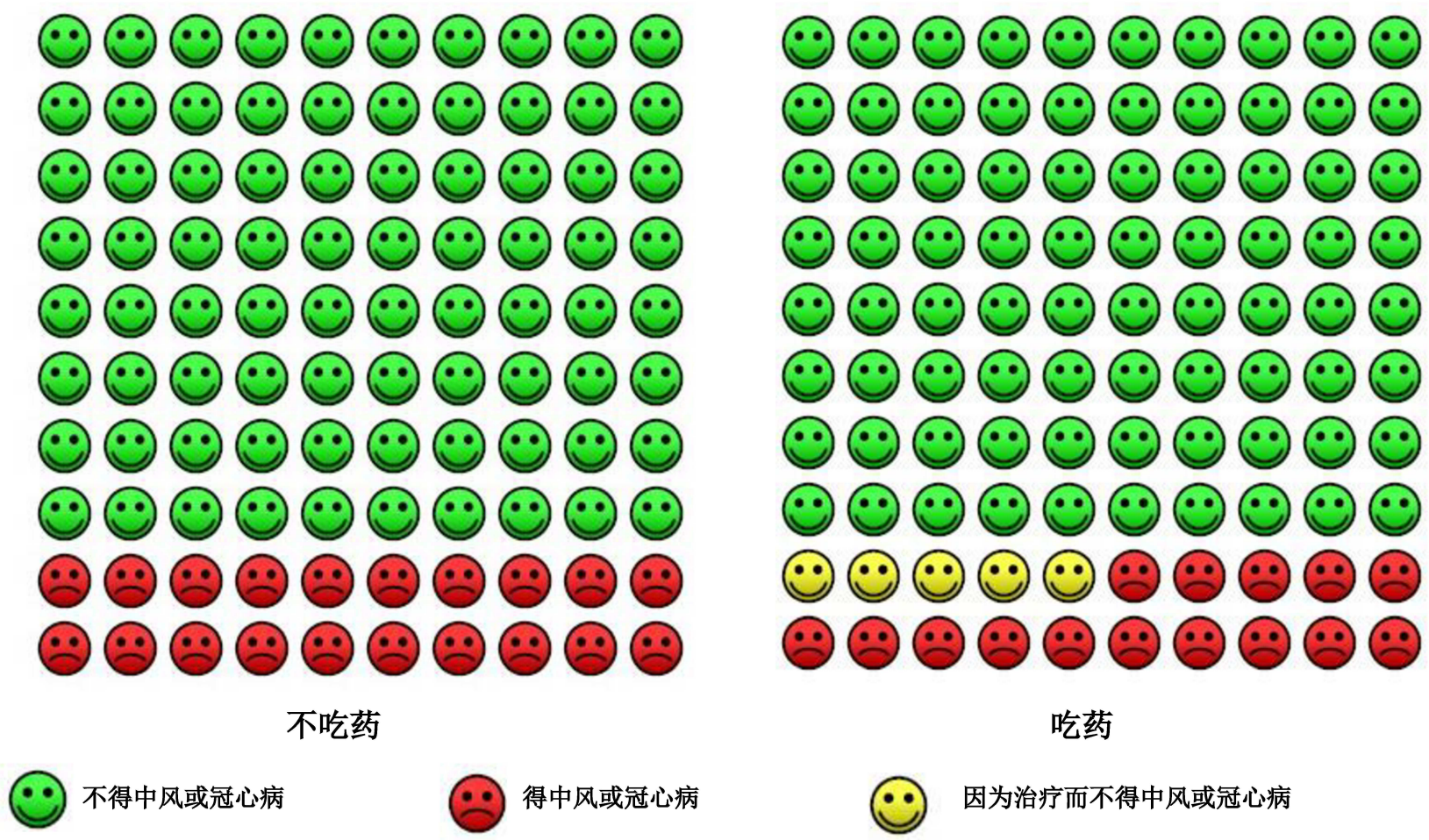
要在吃不吃降压药的问题上“量体裁衣”，需要病人来做决定,或者至少是病人参与到做决定的过程中，因为只有病人自己才最了解自己的情况和需要。就像买房、买车，卖房、卖车的人只是为顾客提供足够的信息，是不是要买、买哪一个，最终还是要由顾客权衡之后来做决定。

目前我们已经跟您讲了，您在以后 10 年中得这些病的可能性是 A. 20 %，不吃药得了中风或冠心病后果您也觉得很严重，吃药能把 A. 20 %的可能性降低到 D. 15 %，降压药长期吃，会有一些比较轻的副作用。吃降压药大概就是这样的情况，需要您一年大概出 2000 元，您可以根据自己家里的经济情况，权衡一下吃药是否必要和划算，看一看是不是要吃药。

需要提醒您注意，您在未来发生高血压相关疾病的风险可能会发生变化，一般会随年龄增加而增加。如果您现在不接受降压治疗，建议您监测血压，并每隔 3-5 年到医院进行一次全面的检查和评估。另外，在监测血压的过程中，如果您的血压一直都比较高，或者波动比较大，建议您要去找医生看一下。

Di M, *et al. BMJ EBM* 2019; 0:1–7. doi: 10.1136/bmjebm-2019-111197

Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang



Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

CURRICULUM VITAE OF ALL INVESTIGATORS.

Title: Prof.	Surname: TANG	Forename(s): Jin-Ling

Education/Training:

- PhD in Epidemiology, University of London, UK, 1991
- MSc in Epidemiology, London School of Hygiene and Tropical Medicine, UK, 1988
- MB in Public Health, Peking University Medical School, Beijing, China, 1983

Position and Honours

- Acting Director (External Affairs and Collaboration), School of Public Health and Primary Care, the Chinese University of Hong Kong, Hong Kong
- Head, Division of Epidemiology, School of Public Health and Primary Care, the Chinese University of Hong Kong, Hong Kong
- Director, Hong Kong Cochrane Branch, the Chinese University of Hong Kong, Hong Kong
- Convenor, Asia Pacific Evidence-Based Medicine Network

Recent Relevant Publications:

1. **Tang JL**, Hu YH. Drugs for preventing cardiovascular disease in China. [Editorial] [BMJ 2005; 330(7492): 610-1.
2. **Tang JL**, Wang WZ, An JG, et al. How willing are the public to pay for anti-hypertensive drugs for primary prevention of cardiovascular disease: a survey in a Chinese city. Int J Epidemiol 2010; 39 (1): 244-54
3. Wang WZ, **Tang JL**, Hu YH, et al. Gap between evidence and physicians'knowledge and practice regarding hypertension and its drug treatment: a survey in a Chinese city. Chin Med J (Engl) 2011; 124(8): 1235-41.
4. **Tang JL**, Dickinson JA, Liu JL. Coronary risk assessment methods and cholesterol lowering. Lancet 1999; 353: 1095-96.
5. Wu HM, **Tang JL**, Lin XP, Lau J, Leung PC, Woo J, Li YP. Acupuncture for Stroke Rehabilitation. The Cochrane Library, 2007.
6. **Tang JL**, Wang S. Defining and providing essential evidence for practice. Clinical Evidence Nov. 17, 2008.
7. Di MY, **Tang JL**. Adaption and application of the four phase trials to traditional Chinese medicines. Evid Based Complement Alternat Med. 2013; 2013: 128030.
8. **Tang JL**, Morris JK, Wald NJ, et al. Mortality in relation to tar yield of cigarettes: a prospective study of four cohorts. BMJ 1995;3 11(7019): 530-3.
9. Law M, **Tang JL**. An analysis of the effectiveness of interventions intended to help people stop smoking. Arch Intern Med 1995; 155(18): 1933-41. 25.
10. **Tang JL**, Law M, Wald NJ. How effective is nicotine replacement therapy in helping people to stop smoking. BMJ 1994;308(6920): 21-6.
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15. **Tang JL**. Data analysis and interpretation in clinical epidemiological studies. In: Li Li-Ming: Clinical Epidemiology. Beijing: People's Medial Press, 2011.
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Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

Title: Dr.	Surname: DI	Forename(s): Mengyang

Education/Training:

- PhD candidate in Epidemiology, The Chinese University of Hong Kong, Hong Kong SAR, China, expected in 2015
- MD, Peking Union Medical College, Beijing, China, 2012
- MBBS, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, 2009

Recent Relevant Publications:

1. **Di MY**, Tang JL. Adaption and application of the four phase trials to traditional Chinese medicines. Evid Based Complement Alternat Med. 2013; 2013: 128030.
2. Yang ZY, Wu XY, Huang YF, **Di MY**, Zheng DY, Chen JZ, Ding H, Mao C, Tang JL. Promising biomarkers for predicting the outcomes of patients with KRAS wild-type metastatic colorectal cancer treated with anti-epidermal growth factor receptor monoclonal antibodies: a systematic review with meta-analysis. Int J Cancer. 2013; 133(8):1914-25.
3. Yang ZY, Yuan JQ, **Di MY**, Zheng DY, Chen JZ, Ding H, Wu XY, Huang YF, Mao C, Tang JL. Gemcitabine plus erlotinib for advanced pancreatic cancer: a systematic review with meta-analysis. PLoS One. 2013;8(3):e57528.
4. Wang J, Xie XM, Wang X, Tang J, Pan QQ, Zhang YF, **Di MY**. Locoregional and distant recurrences after breast conserving therapy in patients with triple-negative breast cancer: A meta-analysis. Surg Oncol. 2013.
5. **Di MY**, Bai R. Drug-induced Brugada ECG/syndrome. Adv Cardiovasc Dis. 2010, 31(4): 501-4.

Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

Title: Prof.	Surname: MAO	Forename(s): Chen

Education/Training:

- Doctor degree of Epidemiology, Southern Medical University, Guangzhou, Guangdong, China, 2011
- Master degree of Epidemiology and Biostatistics, Anhui Medical University, Hefei, Anhui, China, 2008
- Bachelor degree of Preventive medicine, Anhui Medical University, Hefei, Anhui, China, 2005

Position and Honours (in reverse chronological order with dates):

- 2011.08-Present, Instructor, Division of Epidemiology, School of Public Health and primary care, Chinese University of Hong Kong, Hong Kong
- 2010.08-2011.08, Research Assistant, Division of Epidemiology, School of Public Health and primary care, the Chinese University of Hong Kong, Hong Kong

Recent Relevant Publications:

1. **Mao C**, Yang ZY, Hu XF, Chen Q, Tang JL. PIK3CA exon 20 mutations as a potential biomarker for resistance to anti-EGFR monoclonal antibodies in KRAS wild-type metastatic colorectal cancer: A systematic review and meta-analysis. Annals of Oncology.2011. Doi:10.1093/annonc/mdr464.
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3. **Mao C**, Liao RY, Qiu LX, Wang XW, Ding H, Chen Q. BRAF V600E mutation and resistance to anti-EGFR monoclonal antibodies in patients with metastatic colorectal cancer: a meta-analysis. Mol Biol Rep 2011; 38(4):2219-2223.
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7. **Mao C**, Qiu LX, Liao RY, Du FB, Ding H, Yang WC, Li J, Chen Q.KRAS mutations and resistance to EGFR-TKIs treatment in patients with non-small cell lung cancer: a meta-analysis of 22 studies. Lung Cancer 2010; 69(3):272-8.
8. **Mao C**, Yang ZY，He BF, Liu S, Zhou JH, Qiu LX, Luo RC, Chen Q, Tang JL. Toremifene versus tamoxifen for advanced breast cancer. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD008926. DOI: 10.1002/14651858.CD008926.
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Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

Title: Dr.	Surname: GUO	Forename(s): Hongbo

Education/Training:

- MBBS, Xiangnan College, Chenzhou, Hunan Province, 1981.

Position and Honours (in reverse chronological order with dates):

- Director and attending physician in Zhongxincheng primary care center, the People's hospital in Longgang, Shenzhen, Guangdong Province.

Recent Relevant Publications:

1. **Guo HB**, Sun YQ, Li YS, Luo DA, Ma HR, Luo YM. A survey on mental health in hypertensive patients in the primary care centers in Shenzhen. Chinese Journal of Misdiagnostics. 2010.
2. Li QF, **Guo HB**, Kang SY, Jiang KH. Survey and analyses on medical service seeking of immigrant workers in primary care centers in Shenzhen. Journal of Community Medicine. 2009.
3. Luo YM, Wan XH, Jiang DL, Wen D, Chu LX, **Guo HB**. Effect of simvastatin upon serum levels of interleukin-6 and high-sensitivity C-reactive protein in patients with acute coronary syndrome. China Journal of Modern Medicine. 2005, 15(15): 2245-9.

Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

Title: Dr.	Surname: JIANG	Forename(s): Kunhua

Education/Training:

- MBBS, Luzhou Medical College, Luzhou, Sichuan province, China, 1993

Position and Honours (in reverse chronological order with dates):

- Director and attending physician of Ziwei primary care center, the People's hospital in Longgang, Shenzhen.

Recent Relevant Publications:

1. Li QF, Guo HB, Kang SY, **Jiang KH**. Survey and analyses on medical service seeking of immigrant workers in primary care centers in Shenzhen. Journal of Community Medicine. 2009.

Title of project: Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.
Principle investigator: Jin-Ling Tang

Title: Dr.	Surname: YANG	Forename(s): Zuyao

Education/Training:

- PhD in Epidemiology, The Chinese University of Hong Kong, Hong Kong SAR, China, 2013
- MSc in Epidemiology and Biostatistics, Peking University Health Science Center, Beijing, China, 2010
- MB in Public Health, Peking University Health Science Center, Beijing, China, 2008

Recent Relevant Publications:

1. **Yang ZY**, Mao C, Tang JL. Bevacizumab and cancer treatment-related mortality. JAMA 2011; 305: 2291-2.
2. **Yang ZY**, Zhang Y, Wu SS, et al. The values of different study designs on the levels of evidence: a descriptive analysis of the researches published in four general medical journals in 2009. Chinese Journal of Internal Medicine 2010; 49: 1006-9.
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4. **Yang ZY**, Zhan SY, Wang B, et al. Fatality and secular trend of bloodstream infections during hospitalization in China: a systematic review and meta-analysis. Journal of Peking University (Health Sciences) 2010; 42: 304-7.
5. **Yang ZY**, Zhan SY. Chapter 24: New progress of randomized controlled trials. In: Zhan SY, ed. Progress in Epidemiology (volume 12). People's Medical Publishing House, Beijing, 2010.
6. **Yang ZY**, Zhan SY. Application of 'stepped-wedge design' methodology in randomized controlled trials. Chinese Journal of Epidemiology 2010; 31: 92-5.
7. Liu J, Shang PH, **Yang ZY**, et al. Analysis on concept of drug safety according to the result of systematic review. Chinese Journal of Pharmacovigilance 2009; 6: 257-60.

香港中文大學醫學院
Faculty Of Medicine
The Chinese University Of Hong Kong

醫院管理局
新界東醫院聯網
Hospital Authority
New Territories East Cluster

Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee
香港中文大學-新界東醫院聯網 臨床研究倫理 聯席委員會

Flat 3C, Block B, Staff Quarters, Prince of Wales Hospital, Shatin, HK
Tel : (852) 2632 3935 / 2144 5926 Fax : (852) 2646 6653 Website : http://www.crec.cuhk.edu.hk

To: Prof. Jin Ling TANG (Principal Investigator)
The Jockey Club School of Public Health and Primary Care
Prince of Wales Hospital

15 JAN '14

Ethics Approval of Research Protocol

CREC Ref. No.:	**CRE-2013.633**
Date of Approval:	**03 January 2014***
Study Title:	**Effects of individualized antihypertensive information on the medication use in hypertensive patients: An exploratory randomized controlled trial.**
Investigator(s):	**Jin Ling TANG, Mengyang DI, Chen MAO, Hongbo GUO, Kunhua JIANG and Zuyao YANG**

I write to inform you that ethics approval has been given for you to conduct the captioned study in accordance with the following document(s) submitted:

- Research Protocol, Version 1, dated 01 December 2013
- Subject Information Sheet and Informed Consent Form, Chinese Version 1, dated 01 December 2013
- Questionnaire (for baseline survey of intervention group), Chinese Version 1, dated 01 December 2013
- Questionnaire (for baseline survey of control group), Chinese Version 1, dated 01 December 2013
- Questionnaire (for follow-up survey of intervention group), Chinese Version 1, dated 01 December 2013
- Questionnaire (for follow-up survey of control group), Chinese Version 1, dated 01 December 2013

This ethics approval* will be valid for 12 months. Application for further renewal can be made by the submission of the Ethics Renewal and Research Progress Report Form to the CREC (Download the electronic form template from the http://www.crec.cuhk.edu.hk or http://ntec.home/Research%20Ethics/main.asp). You are kindly requested to report to the Committee upon completion of the study.

The Joint CUHK-NTEC Clinical Research Ethics Committee is organized and operated according to ICH-GCP and the applicable laws and regulations.

Phoebe Chan
CREC Officer
Joint CUHK-NTEC
Clinical Research Ethics Committee

Encl.
PC/ci

S3 Table. Sensitivity analyses: effects of individualized, evidence-based counseling on use of antihypertensive drugs when different cutoff values (days) were employed to define the outcome

Outcome variable	Control, n (%)	Intervention, n (%)	OR (95% CI)	*P* value
Cutoff value=1				
Baseline	78 (72.9)	75 (72.8)	1.00 (0.54, 1.83)	.989
Third follow-up	78 (72.9)	74 (71.8)	0.95 (0.52, 1.74)	.865
Cutoff value=2				
Baseline	75 (70.1)	74 (71.8)	1.09 (0.60, 1.98)	.780
Third follow-up	78 (72.9)	72 (69.9)	0.86 (0.47, 1.57)	.631
Cutoff value=3				
Baseline	73 (68.2)	73 (70.9)	1.13 (0.63, 2.04)	.677
Third follow-up	76 (71.0)	71 (68.9)	0.91 (0.50, 1.63)	.741
Cutoff value=4				
Baseline	71 (66.4)	72 (69.9)	1.22 (0.68, 2.18)	.512
Third follow-up	76 (71.0)	71 (68.9)	0.91 (0.50, 1.63)	.740
Cutoff value=5				
Baseline	71 (66.4)	72 (69.9)	1.18 (0.66, 2.11)	.581
Third follow-up	75 (70.1)	70 (68.0)	0.91 (0.50, 1.63)	.739
Cutoff value=6				
Baseline	71 (66.4)	71 (68.9)	1.13 (0.63, 2.01)	.691
Third follow-up	74 (69.2)	70 (68.0)	0.95 (0.53, 1.69)	.852
Cutoff value=7				
Baseline	69 (64.5)	71 (68.9)	1.22 (0.69, 2.17)	.496
Third follow-up	73 (68.2)	69 (67.0)	0.95 (0.53, 1.69)	.849
Cutoff value=8				
Baseline	65 (60.7)	70 (68.0)	1.37 (0.78, 2.42)	.277
Third follow-up	63 (58.9)	67 (65.0)	1.30 (0.74, 2.27)	.357
Cutoff value=9				
Baseline	65 (60.7)	68 (66.0)	1.26 (0.72, 2.20)	.429
Third follow-up	63 (58.9)	67 (65.0)	1.30 (0.74, 2.27)	.357
Cutoff value=11				
Baseline	61 (57.0)	64 (62.1)	1.30 (0.75, 2.28)	.349
Third follow-up	61 (57.0)	67 (65.0)	1.40 (0.80, 2.45)	.233
Cutoff value=12				
Baseline	59 (55.1)	63 (61.2)	1.28 (0.74, 2.22)	.420
Third follow-up	59 (55.1)	67 (65.0)	1.51 (0.87, 2.64)	.143
Cutoff value=13				
Baseline	57 (53.3)	60 (58.3)	1.20 (0.69, 2.07)	.514

Third follow-up	58 (54.2)	61 (59.2)	1.23 (0.71, 2.12)	.463
Cutoff value=14				
Baseline	55 (51.4)	55 (53.4)	1.08 (0.63, 1.86)	.827
Third follow-up	57 (53.3)	57 (55.3)	1.09 (0.63, 1.87)	.764

Abbreviations: OR, odds ratio; CI, confidence interval.

S4 Table. Sensitivity analyses: effects of individualized, evidence-based counseling on good adherence to treatment when different cutoff values were employed to define the outcome

Outcome variable	Control	Intervention	OR (95% CI)	*P* value
Cutoff value=10%				
Baseline	75 (70.1)	74 (71.8)	1.09 (0.60, 1.98)	.780
Third follow-up	78 (72.9)	72 (69.9)	0.86 (0.47, 1.57)	.631
Cutoff value=20%				
Baseline	73 (68.2)	73 (70.9)	1.13 (0.63, 2.04)	.677
Third follow-up	76 (71.0)	71 (68.9)	0.91 (0.50, 1.63)	.741
Cutoff value=30%				
Baseline	71 (66.4)	72 (69.9)	1.18 (0.66, 2.11)	.581
Third follow-up	75 (70.1)	70 (68.0)	0.91 (0.50, 1.63)	.739
Cutoff value=40%				
Baseline	71 (66.4)	71 (68.9)	1.13 (0.63, 2.01)	.691
Third follow-up	74 (69.2)	70 (68.0)	0.95 (0.53, 1.69)	.852
Cutoff value=50%				
Baseline	69 (64.5)	71 (68.9)	1.22 (0.69, 2.17)	.496
Third follow-up	73 (68.2)	69 (67.0)	0.95 (0.53, 1.69)	.849
Cutoff value=60%				
Baseline	65 (60.7)	68 (66.0)	1.26 (0.72, 2.20)	.429
Third follow-up	63 (58.9)	67 (65.0)	1.30 (0.74, 2.27)	.357
Cutoff value=70%				
Baseline	61 (57.0)	64 (63.4)	1.30 (0.75, 2.28)	.351
Third follow-up	61 (57.0)	67 (65.0)	1.40 (0.80, 2.45)	.234
Cutoff value=80%				
Baseline	59 (55.1)	63 (61.2)	1.28 (0.74, 2.22)	.420
Third follow-up	59 (55.1)	67 (65.0)	1.51 (0.87, 2.64)	.143
Cutoff value=90%				
Baseline	57 (53.3)	60 (58.3)	1.20 (0.69, 2.07)	.514
Third follow-up	58 (54.2)	61 (59.2)	1.23 (0.71, 2.12)	.463
Cutoff value=100%				
Baseline	55 (51.4)	55 (53.4)	1.08 (0.63, 1.86)	.827
Third follow-up	57 (53.3)	57 (55.3)	1.09 (0.63, 1.87)	.764

Abbreviations: OR, odds ratio; CI, confidence interval.