PROPOSED RESEARCH PROJECT

a Title:
In-depth study of the cost-effectiveness of the Risk Assessment and Management Programme for Hypertension (RAMP-HT) for patients with uncontrolled hypertension in primary care in Hong Kong

b Introduction:
Hypertension (HT) is an important risk factor for stroke, coronary heart disease (CHD), heart failure and renal diseases\(^1\), and the leading risk factor of global disease burden\(^2\). A multitude of interventions have proven efficacy in lowering blood pressure and reducing long term HT complications, including pharmacologic treatment, DASH diet (Dietary Approaches to Stop Hypertension), exercise, weight reduction, smoking cessation, alcohol moderation and self-monitoring of blood pressure\(^1\) \(^3\) \(^4\). A few studies had examined the effects of coordinated multidisciplinary management programmes for HT patients to maximize the effectiveness of these interventions, but the long term benefit or cost-effectiveness of such programmes are uncertain\(^5\).

In Hong Kong, over 200,000 patients with HT are being managed in public primary care clinics (i.e. General Out-patient Clinics (GOPCs) and Family Medicine Clinics (FMC)) under the Hospital Authority (HA); but more than 45% HT patients have still not achieved target blood pressure control (HA Internal communication). In order to improve the quality of care for patients with uncontrolled HT at GOPCs, the evidence-based \(^1\) \(^4\) \(^6\), structured protocol-driven multidisciplinary Risk Assessment and Management Programme – Hypertension (RAMP-HT) was launched since October 2011 by the HA with the support from the Food and Health Bureau. Standardized cardiovascular risk factor assessment, hypertensive complication screening and assessment on patient adherence to treatment are carried out on enrolled patients (Appendix A). Patients are stratified into low,
medium or high risk groups according to the 10-year cardiovascular disease (CVD) risk calculated from their relevant risk factors by the Joint British Society 2005 Equation\textsuperscript{4}. A multidisciplinary team comprised of doctors, nurses, dieticians, physiotherapists and/or occupational therapists would then deliver individualized management targeted to the patient’s risk factors according to standardized risk-stratified guidelines (Appendix B).

In our evaluation of quality of care of RAMP-HT as part of the Extended Study on Evaluation of Quality of Care of Chronic Disease Management and Public-Private Partnership Programmes of the HA (HMRF Reference no: EPC_HKU-2), we have found that, among patients whose baseline blood pressure was not controlled (≥140/90mmHg), RAMP-HT patients had significantly greater reduction in mean systolic blood pressure (SBP), low-density lipoprotein cholesterol (LDL-C) and estimated 10-year CVD risk after 12 months than matched HT patients receiving usual care from GOPCs ($p<0.001$ for all parameters). In addition, a significantly greater proportion of patients in the RAMP-HT group achieved target blood pressure (i.e. SBP/DBP<140/90mmHg) after 12 months compared to usual care group; the Number Need to Treat (NNT) for achieving one more target blood pressure was 14. These preliminary findings on improvement in blood pressure and CVD risks are very encouraging, suggesting that RAMP-HT may be effective in preventing cardiovascular and renal complications in primary care HT patients.

c Aim, objectives and Hypotheses:

Aim and objectives:
The aim of this study is to evaluate the cost-effectiveness of the RAMP-HT of the HA in primary care patients with uncontrolled hypertension.

The objectives are to
1. Evaluate the long term (5-year) effectiveness of RAMP-HT compared to usual care in reducing cardiovascular complications, end-stage renal disease and all-cause mortalities in a cohort of primary care patients with uncontrolled hypertension at baseline
2. Estimate the direct medical cost of RAMP-HT and other health services
among primary care HT patients with or without complications

3. Evaluate the cost-effectiveness of RAMP-HT, compared to usual care, in gaining one Quality-Adjusted Life Year (QALY) in primary care patients with uncontrolled hypertension

Hypotheses:
1. RAMP-HT is more effective in reducing 5-year cardiovascular complications, end stage renal disease and all-cause mortality among primary care patients with uncontrolled hypertension compared to usual care
2. The direct medical cost of RAMP-HT patients, for the same disease complication status, is not higher than that of usual care except for the RAMP-HT cost
3. The direct medical cost of HT patients with one or more complications is higher than that of HT patients without any complication
4. RAMP-HT is cost-effective compared to usual care, i.e. the incremental cost-effectiveness ratio (ICER) per QALY gained is below the threshold value of 1 annual GDP (Gross Domestic Product) per capita of Hong Kong (HK$295,303, 2013\(^7\)), which is the benchmark recommended by the World Health Organization\(^8\)

**Plan of Investigation:**

(i) **Study design**
   A retrospective study on public primary care population-based matched cohorts of patients with uncontrolled hypertension in Hong Kong

(ii) **Subjects**
   All patients who have enrolled into the RAMP-HT between 1 Oct 2011 and 31 March 2012, fulfilled the following inclusion criteria and without any exclusion criterion will be included in the RAMP-HT cohort. The same number of matched patients receiving usual care in GOPCs who have never enrolled into RAMP-HT on or before 31 March 2017, fulfilled the following inclusion criteria and without any exclusion criterion will be randomly selected from the HA clinical management system (CMS) to form the usual
Inclusion criteria
1. Age ≥18 years old and <80 years old
2. Coded with ICPC-2 of K86 on or before baseline* (*date of RAMP-HT enrolment for RAMP-HT cohort, and 31 March 2012 for usual care cohort)
3. Had uncontrolled blood pressure (i.e. average Systolic Blood Pressure (SBP) ≥140mmHg OR Diastolic Blood Pressure (DBP) ≥90mmHg between 6 months before and 3 months after baseline*)

Exclusion criteria
1. Patients who had a diagnosis of any HT complications defined by relevant ICPC-2 and/or ICD-9-CM diagnosis codes (defined in the “Methods” section) on or before baseline*
2. Patients diagnosed to have Diabetes Mellitus (DM) on or before 31 March 2017, defined by ICPC-2 codes of T89 or T90
3. Patients exclusively managed by Specialist Out-Patient Clinic (SOPC) on or before baseline*

To reduce selection bias, the RAMP-HT and usual care subjects will be matched in baseline covariates using the propensity score matching method:

Baseline Covariates
The covariates are categorized into demographics, co-morbidities, clinical parameters and treatment modalities. Demographics include sex, age, smoking status and whether the patient is a recipient of Comprehensive Social Security Assistance (CSSA). Co-morbidities include history of chronic lung disease, cancer or psychological condition indicated by the presence of the relevant ICPC-2 or ICD-9-CM codes in the CMS. These factors reflect the patient's baseline health status. Clinical parameters data including blood pressure (systolic and diastolic), lipid profile (including triglyceride level) and
body mass index (BMI) and treatment modalities including hypertensive
drug(s) and lipid-lowering agent(s) used account for HT disease severity
and individual CVD risk.

**Propensity Score Matching**

Propensity score matching was first introduced in 1983\(^9\). The technique
summarises relevant baseline characteristics of each eligible HT patient into
a single-index variable (the propensity score); HT patients in usual care will
be matched to patients in the RAMP-HT group based on the value of the
propensity score\(^9-11\). The propensity score will be generated for each patient
by logistic regression, modelling the RAMP-HT as dependent variable and
baseline covariates of patients as independent variables. The propensity
score mapping will be performed by using the “psmatch2” command\(^12\) with
one-to-one matching without replacement and a callipers of 0.001 approach
in the STATA.

**Sample size calculation**

a. For the long-term effectiveness evaluation, the difference in 5-year
incidence of CVD between the RAMP-HT and usual care group is the
primary outcome. From the result of our RAMP-HT QOC study, the
observed 1-year incidence of CVD in the RAMP-HT and usual care
group was 1.33% and 1.76% respectively. A conservative estimate of
the 5-year incidence of CVD in RAMP-HT and usual care group would
be 7% and 8%, respectively. A minimum sample size of 7,116 subjects
from each group will be needed to detect a difference of 1% in incidence
rates of CVD between RAMP-HT and usual care group with 90% power
and at 5% level of significance\(^18\).

We have identified from the HA CMS data set of the RAMP-HT QOC
study 8,681 eligible RAMP-HT patients and 8,681 usual care patients
who fulfilled the inclusion criteria and without any exclusion criterion
matched by propensity score matching. These two matched cohorts will
be the subjects of this long-term effectiveness and cost-effectiveness
study. The flow chart of subject selection is attached in Appendix C.

b. For the costing analysis, 140 subjects from each of the RAMP-HT and usual care groups will be required to show that the direct medical costs of RAMP-HT patients (excluding RAMP cost) is not higher than that of usual care HT patients by independent one side t-test with 0.3 effect size and 80% power at 5% significance level.

307 RAMP-HT and 291 usual care patients had been recruited from May 2013 to March 2014 in GOPCs across Hong Kong for the longitudinal evaluation of patient reported outcomes (PRO) in the RAMP-HT QOC study. These patients will be follow-up from May 2015 to March 2016 as part of our RAMP-HT QOC study; telephone survey on private health service utilization will be conducted at the same time. Taking 25% attrition rate into account, 230 RAMP-HT and 218 usual care patients will complete the questionnaire. This sample will be adequate for the comparison of private medical cost between RAMP-HT and usual care group.

(iii) Outcome Measures

The primary outcomes of this study are:
1. The 5-year incidence of CVD among RAMP-HT and usual care HT patients
2. The direct medical costs of RAMP-HT and usual care HT patients with and without complications
3. The ICER of cost per QALY gained by RAMP-HT compared to usual care group

The secondary outcomes of this study are:
4. The 5-year incidence of end stage renal disease (ESRD) and all-cause mortality among RAMP-HT and usual care HT patients
5. The hazard ratio of CVD, ESRD and all-cause mortalities between
RAMP-HT and usual care group

6. The Number-Need-to-Treat (NNT) to reduce one CVD, ESRD and mortality in 5 years by RAMP-HT

(iv) Data Collection

HA CMS Data Extraction of Incidence of HT Complications and All-cause Mortality

Our RAMP-HT QOC study will have collected anonymous 3-year follow up HA CMS data of the cohorts available by November 2015. This study plans to extend the follow up period for an additional 2 years to measure the 5-year incidence of CVD, ESRD and mortality outcomes of these HT patient cohorts from 1 Oct 2011 to 31 March 2017. The data extraction will be carried out by the HA statistics team. Each patient in the cohorts (RAMP-HT and usual care groups) will be observed from baseline to the first occurrence of any of the outcome events until 31 March 2017, with CMS documented diagnoses defined by the relevant ICPC-2 and ICD-9-CM codes below:

1. Cardiovascular disease (CVD) is defined as the presence of any of coronary heart disease (CHD), heart failure or stroke. CHD includes all ischaemic heart disease, myocardial infarction (MI), coronary death or sudden death as indicated by the ICPC-2 K74 to K76 or ICD-9-CM 410.x, 411.x to 414.x, 798.x codes. Heart failure is defined as the ICPC-2 K77 or ICD-9-CM 428.x codes. Stroke (fatal and non-fatal stroke) is defined by the ICPC-2 K89 to K91 or ICD-9-CM 430.x to 438.x codes.

2. End Stage Renal Disease (ESRD) is defined by any of ICD-9-CM 250.3x, 585.x, 586.x, or an estimated Glomerular Filtration Rate (eGFR) <15mL/min/1.73m², according to the definition of the National Kidney Foundation13.

3. Mortality is defined by a documented death in the Hong Kong Death Registry.
The definitions of each HT complication are determined by the clinician co-investigators and endorsed by clinicians of the HA.

**Direct Medical Costing Studies**

The costing studies will be evaluated from the healthcare provider’s perspective.

*(i) In-depth costing of RAMP-HT*

The cost of RAMP-HT comprises of three components: (a) set-up costs; (b) ongoing intervention costs; and (c) central administrative costs. Set-up costs refer to one-off expenses incurred in the course of setting up the programme, which include costs related to staff training, additional equipment, information technology and infrastructure. Ongoing intervention costs refer to the recurrent costs for the programme operation and maintenance, which include costs of staff, printing and consumables in the clinics. The evaluation of the set-up costs will be primarily based on the data reported by the clusters, who are responsible for maintaining detailed inventory of supplies purchased and distributed to the clinics. Central administrative costs refer to recurrent costs incurred by the GOPCs for running RAMP-HT (i.e. project team cost in Head Office).

The set-up and intervention costs will be collected by two sets of questionnaires to be completed by RAMP-HT programme co-ordinators of the HA clusters and GOPCs that provide the RAMP-HT service (Appendix D); The central administration costs will be collected from the Finance Office in HA Head Office by a structured questionnaire. These questionnaires are adapted from the costing questionnaires that were used in our in-depth study on the cost-effectiveness analysis of RAMP-DM that had proven feasibility and validity (HHSRF # EPC_HKU-1A).

*(ii) Direct Medical Costs of HT patients*
The medical cost analysis will focus on the direct medical costs involved in the care of HT patients without or with specific HT complications (i.e. CHD, heart failure, stroke and ESRD) in both public and private healthcare sectors; indirect cost (e.g. opportunity cost) and non-medical costs (e.g. transportation cost, carer cost) will not be measured.

Public medical costs will be estimated from products of the unit costs (published in the HKSAR Government Gazette and Hospital Authority ordinance (Chapter 113) of charges for non-entitled persons) and the utilization rates of 1) dispensed drugs (note: self-financed drugs will be considered as private medical cost, see below), 2) laboratory tests and investigations, 3) healthcare services including general outpatient clinics (GOPC), specialist outpatient clinics (SOPC), allied health services (e.g. dietician, physiotherapist or occupational therapist), accident and emergency (A&E) department and 4) admissions to hospital in the 12 months before baseline and at 12, 24, 36, 48 and 60 months after study enrolment for each patient in the study cohorts. The data extraction will be carried out by the HA statistics team.

Private direct medical costs include the cost of all private Western doctor and Chinese medicine practitioner consultations, private hospitalisation and self-medications inclusive of self-financed medications prescribed by the HA. 598 HT patients (307 RAMP-HT patients and 291 usual care patients) who were recruited from HA GOPCs for the longitudinal evaluation of patient reported outcomes (PRO) in the evaluation of QOC RAMP-HT study from May 2013 to March 2014 will be invited to complete a “private medical cost of HT questionnaire” (Appendix E) by telephone. The questionnaire is adapted from the costing questionnaire that was used in our in-depth study on the cost-effectiveness analysis of RAMP-DM that had proven feasibility and validity (HHSRF # EPC_HKU-1A).

Health Preference of HT Patients
Health-related quality of life (HRQOL) measured by the SF-12v2 collected in our previous PRO surveys of the evaluation of QOC of RAMP-HT study from May 2013 to March 2014 will be converted to SF-6D health preference values by the HK algorithm\textsuperscript{14, 15} for HT patients with or without complications (CVD, end stage renal disease).

Our team has successful collaboration with the HA statistics Department to extract the relevant data as part of our evaluation of QOC and short-term effectiveness of RAMP-HT study (HHSRF commissioned project EPC\_HKU-2). The detailed data schema is attached in the Appendix F.

(v) Data processing and analysis

**Long Term Effectiveness of RAMP-HT**

Descriptive statistics will be performed on the clinical parameters (e.g. blood pressure (BP), lipid profile, BMI) and incidence of CHD, heart failure, stroke, ESRD, HT-related mortality and all-cause mortalities of the RAMP-HT and usual care cohorts. Differences in each outcome between groups will be tested using independent t-tests for continuous variables such as mean BP, or chi-square tests for categorical variables such as proportion of patients with BP control or CVD incidence. The number needed to treat to reduce one CVD, each specific HT complication and death by RAMP-HT will be calculated from the unadjusted 5-year rates between RAMP-HT and usual care HT cohorts.

Multivariable Cox proportional hazards regression will be performed to estimate the adjusted effect of RAMP-HT on the dependent variable of each first HT complication event, adjusting for all baseline covariates of patients. Cox model has been widely used to evaluate the effectiveness of primary care intervention in previous study.\textsuperscript{16} For each model, survival curves will be estimated by Kaplan-Meier method and the differences between RAMP-HT and usual care groups will be compared using the
log-rank test. The effectiveness of RAMP-HT will be measured by Hazard ratio with 95% confidence intervals in the regression models. Predictive accuracy of Cox models will be assessed and compared using Harrell’s discrimination C-index, ranging from zero to one. A value of 0.5 indicates no predictive discrimination, and values of 0 or 1.0 indicate perfect separation of patients\textsuperscript{17}. Goodness-of-fit for Cox regression model will be assessed using Akaike information criterion and Bayesian information criterion.

**Cost Analysis of RAMP-HT**

Descriptive statistics will be used to summarize the costs of RAMP-HT and annual direct medical costs for RAMP-HT and usual care patients at baseline and over each of 5 subsequent years, overall, and by the presence of complications. The cost of each healthcare service will be derived by multiplication of the unit cost from Gazette and Hospital Authority ordinance and the number of respective services used by the patients. To avoid double counting the cost of drugs and laboratory tests, the Government Gazette cost of each GOPC and SOPC attendance will be adjusted by a factor of 0.7 to include only the manpower cost\textsuperscript{18}. The total public medical costs will be calculated by summing up all costs of drugs, laboratory tests and each healthcare service utilisation. The private medical costs will be estimated by summarizing the self-reported costs of private consultations, self-medication and private hospitalisation. The average annual public and private direct medical costs per patient will be analysed by HT complication status (CHD, heart failure, stroke and ESRD), and by RAMP-HT and usual care HT groups. To determine whether the direct medical costs of the RAMP-HT cohort is higher than the usual care HT cohort, one sided independent t-test will be performed.

**Health Preference by HT Complication Status**

The SF-6D preference will be calculated by the HK population specific
algorithm\textsuperscript{15} by HT complication status. Independent t-test will be used to compare the SF-6D values of HT patients with each complication to those without any complication, and between RAMP-HT and usual care HT patients.

All above statistical analyses will be performed using STATA Version 13.0 (StataCorp LP. College Station, Texas, U.S.). All significance tests will be two-tailed and those with a p-value less than 0.05 will be considered statistically significant.

\textbf{Cost Effectiveness Analysis of RAMP-HT by Markov Modeling}

To evaluate the long term cost-effectiveness of RAMP-HT, a Markov model will be developed based on the natural history of a patient population, with similar distribution of age and gender as the RAMP-HT cohort, to simulate disease development over a lifetime. The structure of the model will be established as shown in Figure 1. At the end of each year, each HT subject may die, develop one HT complication or stay alive without complications. For subjects who develop complications, they may die immediately from the complication, die from other cause of death or stay alive in the complication health state.

The transition probabilities of developing complications and death from year to year will be estimated from the observed complication rates from the 5-year cohort study for RAMP-HT and usual care HT patients as described above. HT complication related mortality rates will be estimated by a review of published and unpublished local and overseas literature. Hong Kong standard life table\textsuperscript{19} will be used as a benchmark of survival presenting HT related mortality and mortality from other causes in Hong Kong local population among different demographic groups (e.g. age and sex). The cumulated life-years of the RAMP-HT and usual care cohorts will be calculated. The average cost and preference values for each HT disease state (with or without specific complication) obtained from the cost and
preference studies described above will be applied to the model to determine the cumulative quality adjusted life years (QALY) and lifetime costs for RAMP-HT and usual care cohorts.

The measure of cost-effectiveness of RAMP-HT will be the incremental cost-effectiveness ratio (ICER) in term of cost per QALY gained by RAMP-HT group compared to usual care. By comparing the between-group-differences in average lifetime costs (ΔC) and quality adjusted life years (QALYs) gained (ΔE), the ICER will be calculated by dividing the incremental cost (ΔC) by the incremental effectiveness (ΔE) in terms of QALYs gained by the RAMP-HT intervention compared to usual care. The ICER will be compared against the threshold value of 1 GDP (Gross Domestic Product) per capita of Hong Kong / QALY (HK$295,303, 20137) to determine lifetime cost effectiveness of RAMP-HT.

The Markov models will be analysed by the TreeAge Pro Suite (TreeAge Software, Inc, Williamstown, MA) which can run Markov models.

Data sources are summarized in the table below:

<table>
<thead>
<tr>
<th>Propose</th>
<th>Item/ unit</th>
<th>Data collection methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness</td>
<td>Incidence of CVD, ESRD and all-cause mortality</td>
<td>Anonymous 5-year dataset of diagnosis record (ICPC-2 and ICD-9-CM) to be extracted by HA statistics team from the HA CMS database#</td>
</tr>
</tbody>
</table>
| Direct Medical Costs | (i) Cost of RAMP-HT                        | (i) In-depth costing of RAMP-HT by  
- set-up and operation costs questionnaires to be completed by HA clusters, GOPCs  
- central administration cost questionnaire completed by |

# HA CMS database: Hong Kong Hospital Authority Clinical Management System database.
<table>
<thead>
<tr>
<th>Calculation of quality adjusted life years (QALY)</th>
<th>SF-6D Health preference values of HT patients without and with complications</th>
<th>SF-12v2 HRQOL data from 410 RAMP-HT and 388 usual care HT patients collected in our previous PRO surveys from May 2013 to March 2014 will be converted to SF-6D preference values.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort Life-time Mortality estimates</td>
<td>(i) HT related mortality (ii) Mortality from other causes</td>
<td>(i) Annual HT-related mortality rates will be estimated from the annual incidence of HT complications and published mortality rates of the respective complications. (ii) Hong Kong standard life table(^{19}) will be used as a</td>
</tr>
</tbody>
</table>

(ii) Public medical costs of RAMP-HT and usual care group; with complications and without complications

(iii) Private direct medical costs

Finance Office in HA Head Office

(ii) Public healthcare service cost will be estimated by the products of:

- Public healthcare service utilization rates will be extracted from the 5-year HA CMS dataset.
- Unit cost of each healthcare service published in the HKSAR Government Gazette

(iii) Private medical cost questionnaire administered by telephone survey on 230 RAMP-HT and 218 usual care HT subjects
The Markov modelling will run on the following assumptions:

1. Each HT patient will develop only one HT complication in his/her lifetime.
2. HT patients without complications will not die from HT related death, but may die from other cause of death.
3. HT patients with complications may die from either HT-related death or other cause of death.
4. RAMP-HT is effective in reducing HT complications for a period of 5 year; thus the transition probability adjustment of CVD/ESRD development (as determined by the annualized hazard ratio obtained from our long-term effectiveness analysis) will be applied to the model of the RAMP-HT cohort in the first five years. After 5 years, the RAMP-HT will have the same transition probabilities of developing HT complications as usual care HT cohort.
5. RAMP-HT is repeated every 12-24 months and the effectiveness of RAMP-HT will not decrease over time; thus the 5-year effect of RAMP-HT can be annualized. Adjustment will be made on the average duration of repeat RAMP-HT based on available empirical data in order to avoid over-estimation of the RAMP-HT cost.
6. The medical cost (public and private) of HT patients in usual care and RAMP-HT programme is the same for the same HT health status except for the additional RAMP-HT cost.
7. All costs and health preference will be discounted by an annual rate of 3.5% as recommended by the guidance of National Institute for Health and Clinical Excellence (National Institute for Clinical Excellence 2008).

<table>
<thead>
<tr>
<th>Timeline</th>
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<tr>
<td>Project timeline (0-24 month)</td>
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[Word Court: 3968 ]
<table>
<thead>
<tr>
<th>Time Frame</th>
<th>Activity</th>
<th>Tasks</th>
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<tbody>
<tr>
<td>April – July, 2016</td>
<td>Study planning</td>
<td>a) Recruitment, training of RA and literature review</td>
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<tr>
<td>(0-4 month)</td>
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<td>b) Data schema and operational definition confirmation with the HA</td>
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<td>Statistics Team</td>
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<tr>
<td></td>
<td></td>
<td>c) Costing data collection</td>
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<tr>
<td></td>
<td></td>
<td>questionnaires development and field testing</td>
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<td></td>
<td></td>
<td>d) Extraction of 3-year outcome and public medical cost data from HA</td>
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<td></td>
<td></td>
<td>CMS data for interim analysis</td>
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<tr>
<td>August – November, 2016</td>
<td>Cost Data Collection</td>
<td>a) Costing data collection</td>
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<tr>
<td>(4-8 month)</td>
<td></td>
<td>b) Feedback on results of cost of RAMP-HT to HA RAMP-HT programme</td>
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<tr>
<td></td>
<td></td>
<td>team to assure validity</td>
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<tr>
<td>December, 2016 –</td>
<td>Preliminary Model development based</td>
<td>a) Analysis of annual direct public and private medical costs of</td>
</tr>
<tr>
<td>March, 2017 (9-12</td>
<td>on 3-year data</td>
<td>RAMP-HT &amp; usual care subjects</td>
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<tr>
<td>month)</td>
<td></td>
<td>b) Preliminary analysis of ICER of RAMP-HT Vs. usual care</td>
</tr>
<tr>
<td>April – November, 2017</td>
<td>Final Data analysis</td>
<td>a) Extraction of 5-year outcome and public medical cost data from HA</td>
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<tr>
<td>(13-20 month)</td>
<td></td>
<td>CMS</td>
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<tr>
<td></td>
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<td>b) To evaluate the 5-year long-term effectiveness of RAMP-HT</td>
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<td></td>
<td></td>
<td>c) Final Markov model on cost-effectiveness of RAMP-HT based on 5-year</td>
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<tr>
<td></td>
<td></td>
<td>outcome and cost data.</td>
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<tr>
<td>December, 2017 –</td>
<td>Preparation of final report and</td>
<td>a) Two manuscripts for submission to peer-reviewed international</td>
</tr>
<tr>
<td>March, 2018 (21-24</td>
<td>manuscripts</td>
<td>journals</td>
</tr>
<tr>
<td>month)</td>
<td></td>
<td>b) Final report ready for submission</td>
</tr>
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</table>
f) Existing Facilities:
The Department of Family Medicine and Primary Care (FMPC) has more than 20 years of experience in health services research with a focus on quality of primary care and patient-reported outcomes. Our research team of clinical academic staff, postdoctoral fellows, statisticians and research assistants has a track record of close collaboration with the HA in the extraction and analysis of longitudinal data from the HA CMS in the past five years in the evaluation of QOC studies of various enhanced primary care programmes including the RAMP-HT, RAMP-DM and Patient Empowerment Programme (PEP) which involved over 400,000 patients and have published 10 papers from these studies.

Relevance of Past Studies Conducted
As explained above, we have already identified the required cohort of over 16,000 HT patients and will have collected their 3-year clinical data by 30 November 2015, which provides an opportunity for an extended 5-year study. Our research team in the Department of Family Medicine and Primary Care in collaboration with our School of Public Health and School of Nursing also has a track record of cost-effectiveness analysis studies including an on-going in-depth study of the cost-effectiveness of the RAMP-DM and PEP to be completed in 2016.

g) Justification of Requirements:
The funding request in this application is to cover the staff and other cost for the extended and additional data collection and data analysis from April, 2016 to March, 2018, which does not overlap with the previous evaluation of QOC of RAMP-HT from 2012 to 2016.

Proposed Budget (All costs are in HKD)

<table>
<thead>
<tr>
<th>Item</th>
<th>Description/Justification</th>
<th>Cost</th>
</tr>
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<tbody>
<tr>
<td>1. Staff related costs</td>
<td></td>
<td></td>
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<tr>
<td>1 Full time Senior</td>
<td>Senior Research Assistant with expertise in cost-effectiveness</td>
<td>$1,030,164</td>
</tr>
<tr>
<td>Research Assistant</td>
<td>analysis and biostatistics is needed to carry out the large</td>
<td></td>
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<tr>
<td></td>
<td>amount of complex data</td>
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<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 Full time Research Assistant for two years</td>
<td>analysis of longitudinal data and coordinate the whole project and liaise with the HA Statistics Department.</td>
<td>$795,360</td>
</tr>
<tr>
<td></td>
<td>Research Assistant is required to liaise with the HAHO, RAMP-HT cluster coordinators and RAMP-HT clinic in-charge, assist data cleaning and data analysis, literature review and preparation of manuscripts and reports.</td>
<td>$234,804</td>
</tr>
<tr>
<td>2. General Expenditure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Service charge by the HA</td>
<td>for CMS data extraction by the Statistics Department of the HA</td>
<td>$100,000</td>
</tr>
<tr>
<td>Computers and Statistical software</td>
<td>Two high speed &amp; memory computers for handling a large database and the licenses of TreeAge Pro Suite (TreeAge Software, Inc, Williamstown, MA) and STATA software (STATA Corp, College Station, Texas) are needed for the analysis of a large data set.</td>
<td>$34,300</td>
</tr>
<tr>
<td>Overseas conference</td>
<td>Conference attendance to disseminate results</td>
<td>$10,000</td>
</tr>
<tr>
<td>Publication fee</td>
<td></td>
<td>$10,000</td>
</tr>
<tr>
<td>Audit fee</td>
<td></td>
<td>$10,000</td>
</tr>
<tr>
<td>Printing and consumables</td>
<td></td>
<td>$5,500</td>
</tr>
<tr>
<td>Total:</td>
<td></td>
<td>$1,199,964</td>
</tr>
</tbody>
</table>
h Purpose and Potential:

This study addresses the HMRF thematic priority of enhanced primary care and multi-disciplinary treatment of the most common chronic disease. The results will provide empirical evidence on the long term effectiveness and cost effectiveness of the multidisciplinary RAMP-HT in improving health of patients with hypertension. This can inform policy on whether special intervention programmes such as the RAMP-HT should be implemented.

i) Key References:


12. Leuven E, Sianesi B. PSMATCH2: Stata module to perform full Mahalanobis and propensity score matching, common support graphing, and covariate imbalance testing. Statistical Software Components 2012.


**List of additional Materials**

I. Figure 1. The Structure of Markov Model

II. Table 1. Clinical and costs parameters inserted to Markov model

III. Appendix A Protocol for the RAMP-HT programme

IV. Appendix B Workflow of the RAMP-HT programme

V. Appendix C Flow Chart of the Process of Matching Subjects

VI. Appendix D Cost questionnaires (cluster and clinic)

VII. Appendix E Telephone Survey on the Cost of Private Medical Care
VIII. Appendix F Data schema for Cost-Effectiveness Analysis
Figure 1. The Structure of Markov Model

Table 1. Clinical and costs parameters inserted to Markov model

<table>
<thead>
<tr>
<th>Natural history of Hypertension</th>
<th>Transition probability from without complication to Coronary Heart Disease*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Transition probability from without complication to Stroke*</td>
</tr>
<tr>
<td></td>
<td>Transition probability from without complication to Heart Failure*</td>
</tr>
<tr>
<td></td>
<td>Transition probability from without complication to End Stage Renal Failure*</td>
</tr>
<tr>
<td></td>
<td>The rate of other death unrelated to Coronary Heart Disease, Stroke, Heart Failure or end stage renal disease</td>
</tr>
<tr>
<td></td>
<td>The rate of HT-related death from Coronary Heart Disease, Stroke, Heart Failure or end stage renal disease</td>
</tr>
<tr>
<td></td>
<td>Survival rate of Hong Kong population</td>
</tr>
</tbody>
</table>

*The hazard ratio obtained from the results of long-term effectiveness of RAMP-HT will be applied to adjust the transition probabilities of Coronary Heart Disease, Stroke, Heart Failure and end stage renal disease in the first 5-year after baseline

<table>
<thead>
<tr>
<th>Costs</th>
<th>Cost of RAMP-HT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Direct medical costs for each health status (i.e. Hypertension without complications, HT with Coronary Heart Disease, HT with Stroke, HT with Heart failure or HT with End Stage Renal Disease)</td>
</tr>
</tbody>
</table>

| Health utility | Health utility for each health status (i.e. Hypertension without complications, HT with Coronary Heart Disease, HT with Stroke, HT with Heart failure or HT with End Stage Renal Disease) |