PRODEMOS

Work package 6

Health economic analysis plan

Final

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1.BACKGROUND

PRODEMOS aims at making an evidence-based dementia prevention strategy using mobile Health accessible to those at increased risk of dementia who are usually not reached by preventive medicine. From a global perspective, PRODEMOS will target socio-economically deprived populations in the UK and a population at risk of dementia in China. The final aim is to implement this flexible fully adaptable mHealth platform in a culturally appropriate form in a range of health care settings across the globe.

Description of work

Health economic assessment in high income countries targeting populations with low socio-economic status and in the population in middle-income country China

This task will focus on the health economic properties of the mHealth platform versus standard care in populations with low SES in a high-income setting (UK) and in the population of China. Because prevention of dementia and costs of living with dementia have a long time horizon (decades), a three step analytic framework will be conducted (for details, see further text below):

1.Cost consequence analysis: Within trial analysis

2.Cost effectiveness of the intervention: the incremental costs per epidemiological outcomes

3.Cost utility analysis of the intervention: the incremental costs per gained quality-adjusted life year (QALY)

2.EPIDEMIOLOGICAL AND HEALTH ECONOMIC CONSIDERATIONS OF PRODEMOS

The basic intervention approach in PRODEMOS has strong similarities to prevention projects.

Roughly there are two types of interventions that can be considered:

1) “Low risk”): Large community populations are the target for the interventions where the individual risk for a particular condition/disease is rather low. Such projects usually demand large sample sizes and long follow-up periods. The content of the intervention is to a great extent focussed on life-style changes and/or on well known risk factors. These interventions can most often be described as primary prevention.

2) ”High risk”: ”Small populations” (clinical), where people with a higher risk are identified and given a more targeted intervention, based on individual risk profiles. These interventions can most often be described as tertiary prevention. Secondary prevention programs where there is an established disease/condition and the aim is to prevent new episodes can, depending on the shape of the disorders, have characteristics of both low and high risk programs.

In the field of dementia research, primary prevention can be seen as preventing a shift from “normal” cognitive function to mild cognitive impairment, while secondary prevention aims to prevent a shift from mild cognitive impairment to dementia. Since underlying neuropathology, for instance Alzheimer’ Disease (AD)-pathology, may occur also in individuals with normal cognitive function the approach presented above may be questioned as the AD pathology may already have initiated the brain damaging process.

Based on the considerations above PRODEMOS, can be mainly be regarded as a primary prevention project. Some other projects within the same research group focus on groups identified as “at risk” of developing dementia (FINGER, MAPT, HATICE), whereas others focused on the general population (preDIVA). The target population in PRODEMOS is at increased risk based on the presence of risk factors, but no cognitive impairment, and as such can be considered as primary prevention.

Health economic analyses of prevention programs in the field of dementia are complicated for several reasons.
The great challenge is the time aspect. If the aim is to focus on long-term cost-effectiveness, the time period may need to be as long as 15-20 years from early symptoms to death and even longer if the focus is on persons with neuropathological changes but no cognitive impairment. The program costs may be high in the beginning whilst benefits may occur many years later. Since, for practical reasons, it is hardly possible to follow study populations for such long periods, alternative analytical approaches need to be considered. Furthermore, the effects on resource use and costs during the trial period will probably be very low and thus “within-trial cost-effectiveness analysis” with various approaches will probably be of limited value. The major cost drivers in dementia care are the costs of long-term care and informal (unpaid family) care. Long-term care will probably be very rare or none during the intervention period, at least for reasons linked to dementia. Informal care in terms of support in instrumental activities of daily living may occur but is unlikely to be at a magnitude that may be of use for an analysis of differences between the trial arms in PRODEMOS.

We have developed a dementia prevention model (Zhang, 2011), based on conversion to dementia. This work is based on progression/conversion from the EURODEM and CAIDE project (Kivipelto, 2006), which started at a rather young age and we did not have data for risk equations for older people.
However, due to the sample size and length of the intervention in PRODEMOS, the number of persons developing dementia will be too few to base the health economic evaluation on within trial results.

Based on these considerations we propose a dementia conversion model, which is based on a risk prediction model that functions as the link between trial outcomes and long-term dementia conversion. In PRODEMOS, the CAIDE score will be used for this purpose.

3.EVALUATIONS

3.1. Cost-consequence analysis of the within trial results

The resource use and costs linked to the intervention will be assessed as well as the effects of the intervention on dementia risk score. This analysis will have a cost consequence analysis approach (Mauskopf, 1998), where costs and consequences over the follow-up period of the trial are listed in a tabular format, making it possible for readers to get a comprehensive view of the intervention.
The costs of the intervention include not only the costs for the technical equipment and software (for example the application), but also the costs of the infrastructure to implement the intervention (staff etc). These resources will be quantified as far as possible and multiplied by unit costs. For quantifying the costs of implementation, we will use estimations of the time spent on coaching, such as hours per week. The numbers of messages will also be registered. Experiences from the HATICE project indicated that the coaching time on average was 9 hours over 18 months. Project driven costs (such as for assessors) will not be included. Due to the cognitive status of the study populations, it is not realistic to expect any significant resource use in terms of hospitalizations, production losses, long term care or informal care and thus such assessments will not be assessed or only in an aggregated form.
However, as mentioned above, it is unlikely that the within trial analysis will show any significant results, but of main interest is to look at the intervention cost.

3.2. Cost-effectiveness

For prevention, the “traditional” health economic outcomes need to be completed by more epidemiological related outcomes, which in PRODEMOS will be:

The number of dementia cases avoided, the number needed to treat (NNT) to avoid one case of dementia and dementia free survival. Since the content of PRODEMOS most likely also will influence cardiovascular morbidity, the survival period, the number of avoided deaths and the NNT to avoid one case of death can be analysed. All these outcomes can be related to the cost to avoid one case of dementia, the cost to avoid one case of death, the cost for one dementia free year.

3.3. Cost-utility analysis

In a cost utility analysis, the outcome is expressed in terms of a utility score, most often as QALYs (quality adjusted life years). This approach is frequently used (particularly in pharmaco-economics and for drug reimbursement decisions) since it gives opportunities for comparisons between different diagnostic entities. In PRODEMOS, a simulation model, starting in asymptomatic people will be applied, including risk of conversion to dementia, disease progression and survival, with associated and state dependent (and age dependent if available) costs and QALYs.

Based on the estimated reduction in dementia incidence, the long-term effects on the societal costs of dementia in UK and China will be calculated. Besides the inputs from the intervention in PRODEMOS, inputs regarding the care system in UK and China (such as patterns of resources for home care, institutional care, day care, informal care) as well as data on resource use and costs of dementia will be used to get stage related costs of dementia, as much as available from the literature. Non-available inputs will be estimated by expert opinion.

The year of cost is 2020. All costs and effects will be discounted according to UK guidelines for health-economic analysis.

A lifetime horizon was operationalized by running the simulation up to the age of 100.

3.4 Modelling

Modelling techniques as Markov model will be used for steps 2 and 3. We have developed a modelling framework where the effects on costs of different sectors of the care system can be analysed.

A situation in which the target population was exposed to the PRODEMOS intervention (i.e. intervention) will be compared to a situation in which the target population was not exposed to the PRODEMOS intervention (i.e. control). The control situation intends to reflect usual care.

The results will in its first phase be applied on the countries in the project, UK and China. However, after some adaptions (mainly due to care system differences, but, if possible, also to other dementia risk patterns), global consequence can also be highlighted.

The model choice was based on several considerations. A non-systematic review described three models for the evaluation of primary prevention interventions for dementia (Handels, 2017). They discussed the limited ability of the models to reflect possible cardiovascular effects. This would argue for a general health model (e.g. PACSim (Kingston, 2018a; Kingston, 2018b), Future Elderly Model (Goldman, 2005), Dynamic Aging Process (Lin, 2014)). However, insufficient resources were available to generate the required input estimates on all included risk factors and diseases specific for the UK and specific for China. Therefore, we non-systematically reviewed models for the evaluation of a lifestyle intervention on cardiovascular diseases. We identified the model described by Campbell et al. (2015), which estimated the incidence of coronary heart disease (CHD), stroke and type 2 diabetes (T2D). We intend to reverse engineer this model and add the component of dementia to it and make additional adaptations where considered relevant. We will use 2 model structures in our analysis. The first model structure was similar to two models from the review (Zhang, 2011; Baal, 2016) and a subsequently developed model specifically for the evaluation of the FINGER primary dementia prevention program. The second model structure was based on a combination of the model by Campbell et al. (2015) and the first model.

3.5 Sensitivity analysis

Since the long-term effects of PRODEMOS, a set of one-way comprehensive sensitivity analyses is needed.

1.The key element in PRODEMOS is its impact on dementia risk. Any method we use for this risk estimate, we need to vary this.
2.Another issue is whether or not the intervention should be repeated regularly over a specific time interval (completely or partly) to 'boost' the effects. Various scenarios of how the intervention will take place is needed to test, as well as the costs for the intervention.
3.The age in PRODEMOS is 55 and older (55+). A later start will have a population of greater risk and an earlier start a lower risk for dementia. Different ages of the study population will be tested in the modelling (such as 45+ and 65+).

4.The management of the Hawthorne effect is a great challenge in any intervention study. Although PRODEMOS has taken several steps to compensate for the Hawthorne effect, one option with no Hawthorne effect (assuming no positive effects at all in the control group) will be tested.
5. The base discount rate will be varied.
6. The model length in the base option is chosen to fit the assumption that more than 95% of the persons in the model have died. It may be of interest to see if different model lengths results in different patterns of cost effectiveness (due to survival effects etc). Thus, shorter model lengths will be tested.

In a one-way sensitivity analysis, one uncertain parameter at a time is analysed (and perhaps two or three parameters in two and three way sensitivity analysis, but such analyses are difficult to overview). If possible, in a probabilistic sensitivity analysis (PSA) a set of uncertain parameters with a distribution are analysed in the same model, if to a sufficient extend empirically based distributions of all relevant parameters are available.

4. DELIVERABLES

All analytic approaches will be delivered at month 60, given the assumption that inputs from the intervention has been delivered.

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