COHORT PROFILE

Cohort Profile: The electricity generating authority of Thailand study

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Accepted 18 October 2010

How did the study come about?

During the past 30–40 years, there has been a tremendous increase in the prevalence of cardiovascular disease (CVD), especially in developing countries. The change from an agricultural to an industrial society, and the introduction of new technology, make people less likely to engage in physical activity and more likely to adopt a sedentary lifestyle. Modern medicine has markedly reduced the mortality from infectious disease and has improved human longevity, consequently leading to more deaths from chronic diseases, particularly cancer and CVD. Thailand, a medium-sized middle-income country, is one of those nations that is encountering this epidemiological transition and is anticipated to experience much greater increases in CVD compared with Western countries over the next 20 years.1,2

Observational studies in Western populations suggest that the well-established risk factors for CVD (obesity, diabetes mellitus, elevated blood pressure, dyslipidemia and cigarette smoking) account for most of the attributable risk for CVD. But the manifestations of CVD and prevalence of its risk factors are often different among Western and Asian populations. For instance, stroke is much more common among many Asian populations compared with the USA or European Union. Most CVD events are potentially preventable through modification of risk factors. To prioritize the preventive measures for maximum benefit, and influence change, a clear understanding of the attribution of risk factors in the local environment is needed. Consequently, following the model of the Framingham study, the first cohort study of chronic disease in Thailand was set up by a group of cardiologists at Ramathibodi Hospital, Bangkok, in 1985. Their basic aim was to examine the effects of cardiovascular risk factors, as identified by Framingham and other studies, on health in the Thai population, specifically to see if the same risk factors worked in the same way as elsewhere. Due to issues with contacting participants in a general population setting within Thailand, it was decided to site this study within an occupational workforce. Initial funding was provided by Mahidol University, the Thai Heart Association and the Electricity Generating Authority of Thailand (EGAT) corporation. Later, the National Research Council, Thailand Research Fund and Praman Chansue Foundation became major funders.

What does it cover?

The EGAT study began in Bangkok in 1985. The initial survey for first cohort (Figure 1) mainly covered details of established CVD risk factors in other settings, nutrition and toxicology. Blood samples were stored for future use, e.g. in genetic and biomarker studies. This cohort is now called EGAT 1.

The second cohort, EGAT 2, started in 1998 and covered risk factors for a wider range of diseases, including liver diseases, neurological problems, kidney diseases and malignancies. This cohort was designed to be a parallel study to EGAT 1, in which the majority comes from rural areas of Thailand. Together with the first cohort, this cohort will explore the differences between cardiovascular risk factors and mortality patterns among urban and rural populations. In the second survey of EGAT 2, in 2003, a team of dentists joined the programme and added detailed questions on periodontal disease.
The third cohort, EGAT 3, was started in 2009. The baseline survey expanded the range of questions further by exploring psycho-social conditions with the addition of three multi-purpose health surveys that measure psychological distress, overall health status, functional status and health-related quality of life. These are the Kessler psychological distress scale (K-10), Short-Form 36 Health Survey Version 2.0 (SF-36) and EuroQoL 5-Dimensions (EQ-5D) questionnaires, respectively. This cohort also had additional questionnaires on obstructive sleep apnoea, allergies and gynaecological problems. This cohort was also designed to look at cardiovascular risks pre- and post the epidemiological transition in Thailand by comparison with the EGAT 1 and 2 cohorts. The majority of the study population came from the urban middle class, similar to EGAT 1.

The primary outcomes for all EGAT cohorts are as follows:

- stroke (fatal and non-fatal, ischaemic and haemorrhagic);
- CHD (fatal and non-fatal); and
- total CVD.

Secondary outcomes are as follows:

- all-cause mortality; and
- other major causes of death.

The primary analytical method is to use Cox proportional hazard regression models, adjusted for age, sex and potential confounders to calculate hazard ratios and their confidence intervals.

Who is in the sample?

EGAT was established on May 1, 1969 by the promulgation of the EGAT Act B.E. 2511, which merged assets and operations of the three previous state enterprises. Presently, it is a state enterprise under the Ministry of Energy. EGAT cohorts are located at the headquarters of EGAT in the Bangkok metropolitan area and at three different sites in Western and Northern Thailand (Figure 1), where hydro-electric dams are located. In 1985, 3499 workers of EGAT in Bangkok and the surrounding area (half of the total employees) were randomly enrolled. The age range was selected as 35–54 years old, to maximize the probability of CVD events, given that the retirement age in EGAT in 1985 was 55 years. Since EGAT was one of the largest enterprises in Thailand at that time, participants came from a wide range of socio-demographic backgrounds and EGAT 1 had representatives from more than 30 different occupations. EGAT 2 randomly enrolled 2999 employees who worked at hydro-electric plants in remote areas. Although half of them were brought up in Bangkok, these people spend most of their life in the communities that have been provided by EGAT, surrounding the dams. There are schools, primary health-care units, open markets, police stations and temples in every community. If workers have a medical emergency, they can go to a public community hospital outside the complex, or go to a provincial hospital, as would the non-EGAT population in that area. The age and sex of this population were frequency matched with the EGAT 1 population. Any employee
who had already been sampled in EGAT 1 was excluded.

Similar to EGAT 1, the EGAT 3 cohort was sited at the headquarters of EGAT in Bangkok, but the age range was expanded to 25–54 years old. There were 2584 participants, age/sex matched to EGAT 1, randomly recruited in 2009. Again, participants in earlier waves of EGAT were excluded.

The response rates in the first and second cohorts was >95%, but in EGAT 3 it dropped to 76% in the 35–54 year age group and 71% in 25–34 year age group, which were independently sampled. The major reasons for this reduced response rate are thought to be that some selected participants were due to leave for periodic work in the sites outside Bangkok, and the fear of contracting swine flu in examination centres in 2009. The mean ages were not different between responders and non-responders (each was 41 years; \( P = 0.78 \)), but responders were less likely to be male (74 vs 78%; \( P = 0.004 \)).

These numbers, taken together, resulted in the total number of 9082 participants in the EGAT study.

How often have they been followed up?

The EGAT 1 cohort was resurveyed in 1997, 2002 and 2007 (Figure 2). Each time, the same individuals were contacted by telephone and invitation letter, or else information about the cause of death was sought for those known to have died during the interim. The EGAT 2 cohort was resurveyed in 2003 and 2008. According to the plan, the next surveys for EGAT 1, 2 and 3 will be held in 2012, 2013 and 2014, respectively.

What has been measured?

Baseline

In EGAT 1 and 2, among the items recorded at the baseline assessment were age, sex, educational level, occupation, tobacco smoking, alcohol drinking, family history of cancer or CVD, and whether the participant had ever been diagnosed as having CHD, stroke, diabetes, hypertension, dyslipidemia, tuberculosis, allergy, autoimmune diseases, osteoarthritis, recent fracture or Parkinson’s disease. EGAT 3 contained additional questionnaires on physical activity, socio-demographic, K-10, SF-36 v2 and EQ 5D (Table 1).

Physical examinations were performed by clinicians in each survey. These included measuring blood pressure, heart rate, weight, height and waist and hip circumference. Thorough history taking and examination by a cardiologist, neurologist and gastroenterologist were available when an end-point disease was suspected. Dental examinations were included from the 2003 survey onward in all three waves.

Blood was collected in a fasting state at all eight survey visits to date. Laboratory tests subsequently carried out every time included glucose, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides, creatinine, total protein, albumin, total bilirubin, direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGT) and a full blood count. Some special blood tests were added in certain surveys; for example, cystatin-C, high sensitivity C-reactive protein, HbA1C and an oral glucose tolerant test. DNA was also extracted for future genetic studies from 1997 onwards.

Electrocardiograms and chest X-rays were routinely recorded in every survey.

Figure 2 Overview of EGAT cohorts. Each box represents a survey of an EGAT cohort between 1985 and 2009, plus the current projections. Deaths are up to the last resurvey for EGAT 1 and EGAT 2. \( n \) is the number of people who were surveyed at each time.
Outcomes

Mortality

Information on causes of death among the participants in EGAT 1 and EGAT 2 have, to date, been obtained up to the end of 2007 and 2008, respectively. To do so, details of study members who did not participate in resurveys were cross-checked against databases maintained by the National Health Security Office (who hold hospital discharge records) and the Department of Provincial Administration of the Ministry of the Interior (who compile death certificates) to ascertain vital status. For those death records from which cause could not be determined, we utilized a range of other sources for information on the last 48 h of life: hospital records, an interview with the primary physician, relatives, colleagues and neighbours. Cause of death was verified by an independent adjudication committee comprising two cardiologists, one neurologist, one gastroenterologist and one internist, and classified as being due to one of the

Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Cohort</th>
<th>EGAT 1 n = 3499</th>
<th></th>
<th>EGAT 2 n = 2999</th>
<th></th>
<th>EGAT 3 n = 2584</th>
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<td>Demographics</td>
<td></td>
<td>Men</td>
<td>Women</td>
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<td>Women</td>
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<td>Age (years)</td>
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<td>Range</td>
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<td>35–54</td>
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<td>25–54</td>
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<td>43 (5.2)</td>
<td>42 (4.5)</td>
<td>43 (5.0)</td>
<td>43 (5.1)</td>
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<td>Sex (%)</td>
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<td>27</td>
<td>26</td>
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<td>Alcohol (%)</td>
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<td>37</td>
<td>35</td>
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<td>Exercise (%)</td>
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<td>Prevalence of disease (%)</td>
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<tr>
<td>Hypercholesterolaemia</td>
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<td>48</td>
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<td>Hypertension</td>
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<td>27</td>
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<td>Diabetes</td>
<td>7.5</td>
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<td>7.7</td>
<td>7.7</td>
<td>5.3</td>
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<td>Physical examination (mean, SD)</td>
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<td>Height (cm)</td>
<td>166 (5.7)</td>
<td>155 (4.8)</td>
<td>164 (7.8)</td>
<td>164 (7.4)</td>
<td>169 (6.8)</td>
<td>158 (7.1)</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>23 (3.1)</td>
<td>23 (3.1)</td>
<td>24 (3.6)</td>
<td>24 (3.5)</td>
<td>25 (3.5)</td>
<td>22 (3.8)</td>
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<td>Waist/hip ratio</td>
<td>0.96 (0.06)</td>
<td>0.96 (0.05)</td>
<td>0.88 (0.07)</td>
<td>0.88 (0.06)</td>
<td>0.90 (0.05)</td>
<td>0.82 (0.06)</td>
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<td>Systolic blood pressure (mmHg)</td>
<td>122 (16.1)</td>
<td>116 (16.0)</td>
<td>125 (19.4)</td>
<td>124 (18.1)</td>
<td>123 (13.9)</td>
<td>113 (14.4)</td>
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<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>77 (11.0)</td>
<td>71 (10.3)</td>
<td>78 (12.7)</td>
<td>77 (11.7)</td>
<td>82 (10.2)</td>
<td>76 (10.4)</td>
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<td>General chemistry (mean, SD)</td>
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<td></td>
<td></td>
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<tr>
<td>Fasting plasma glucose (mmol/l)</td>
<td>5.0 (1.05)</td>
<td>4.7 (0.88)</td>
<td>5.1 (1.31)</td>
<td>5.2 (1.62)</td>
<td>5.3 (1.47)</td>
<td>4.9 (1.13)</td>
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<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.8 (1.12)</td>
<td>5.7 (1.10)</td>
<td>6.1 (1.23)</td>
<td>6.2 (1.32)</td>
<td>5.6 (1.05)</td>
<td>5.5 (0.92)</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/l)</td>
<td>1.2 (0.29)</td>
<td>1.4 (0.30)</td>
<td>1.5 (0.39)</td>
<td>1.5 (0.38)</td>
<td>1.3 (0.28)</td>
<td>1.5 (0.33)</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/l)</td>
<td>3.8 (1.07)</td>
<td>3.8 (1.04)</td>
<td>3.9 (1.12)</td>
<td>3.9 (1.18)</td>
<td>3.9 (0.97)</td>
<td>3.6 (0.88)</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.9 (1.41)</td>
<td>1.2 (0.64)</td>
<td>1.9 (1.77)</td>
<td>1.8 (1.61)</td>
<td>1.6 (1.09)</td>
<td>1.0 (0.61)</td>
</tr>
</tbody>
</table>

aPrimary, secondary and tertiary education in EGAT 1 means 0–6, 7–12 and >12 years of education, respectively. In EGAT 2 and 3, it means 0–9, 10–12 and >12 years of education. Original work. SD = standard deviation.
following eight broad causes: coronary heart disease (fatal myocardial infarction or sudden unexplained death), stroke (including subarachnoid haemorrhage within 30 days after the event), other vascular death (e.g. heart failure, valvular heart disease or peripheral arterial disease), respiratory disease (excluding malignancy), gastrointestinal or hepato-biliary disease (excluding malignancy), malignancy (of any kind), injuries (including suicide) or other. In 2007, there were 172 subjects (4.9% of the EGAT 1 population) for whom we could not retrieve their vital status.

Morbidity
The individual national identification numbers of EGAT cohort participants were sent to the national health reimbursement database system. This returns the ICD code associated with any treatment in either in-patient or out-patient units in Thailand. Participants whose names were not returned, but who did not show up on the resurveys were treated as potential additional cases or deaths. They were then investigated using telephone calls or home visits. The search team asked for documentation from hospitals if there was any discrepancy in medical history or ambiguous ICD codes (e.g. unknown or unspecified heart disease).

What has been found? Key findings and publications
At the time of writing, 13 papers have been published, or are about to be published. A further three papers are in progress. The results from EGAT 1 were published in 2003, and reported the worsening of levels of most vascular risk factors over the 12-year period between 1985 and 1997. The associations between baseline risk factor levels and vascular mortality were consistent with those observed in other populations. After age adjustment to the world population, it was shown that the annual cardiovascular mortality rate in EGAT 1 over the first 12 years was relatively low, similar to rates in France or Spain. The rate was about one-third to one-half of that in the USA and UK. Comparing baseline data from each cohort, the mean systolic and diastolic blood pressure, body mass index (BMI) and fasting plasma glucose are on the rise. However, when comparing baseline data from EGAT 3 with the National Survey for England in 2008, the prevalence of obesity in the EGAT 3 study population is far lower than in England in both sexes, as is the prevalence of overweight in women (Figure 3). Despite the relatively advantaged status of EGAT workers, we have still seen a significant health inequality by level of education, income or occupation.

The EGAT heart score and EGAT diabetic score have been created to be used as simple tools for predicting future CV events and diabetes. The EGAT heart score was found to have greater sensitivity and specificity than the Framingham study CVD score in predicting CV events in this population (Figure 4).

Expanding the utilization of the EGAT data, the EGAT study has been involved in two international collaborations. The EGAT 1 cohort was chosen as the Thai representative in the Asia Pacific Cohort Study Collaboration (APCSC). Similarly, EGAT 3 is included in a multi-ethnic cohort study to identify biological, lifestyle and psychological factors associated with individual trajectories of cardiovascular risk factors in south-east Asia (the LIFECARE study). This collaboration study started in 2008 and includes four south-east Asian countries; Thailand, Malaysia, Indonesia and the Philippines. Unlike APCSC, individual studies in LIFECARE share a common protocol and it was this that
prompted the expanded age range and coverage of the questionnaire in EGAT 3.

What are the main strengths and weaknesses?

The major strength of EGAT is the detailed mortality ascertainment, which is likely to be unique in such a geographical population. Other advantages are that the EGAT enterprise itself is large enough to employ a large variety of people, from illiterates working as cleaners to truck drivers, security guards, office clerks, administrators, architects, engineers, field explorers, lecturers, lawyers, health-care practitioners and those on executive boards. Due to the wealthy profile of this enterprise, good working conditions, leisure facility and the excellent health-care scheme that is always available to employees, immigration is kept to a very low rate. The repeat surveys are also a great strength for investigating longitudinal changes in risk factors and subsequent disease incidence. The long time span and continued funding to enable future resurveys are also important for obtaining robust results. Finally, the breadth of risk factor ascertainment and the foresight in banking bloods add great value to the project. Few, if any, such comprehensive studies are available from this part of the world.

One drawback is that the workers in EGAT cannot be said to be representative of Thailand as a whole. The socio-economic status of EGAT employees is not comparable with the many economically disadvantaged Thais and the ‘healthy worker effect’ (severely ill and disabled are ordinarily excluded from employment) will come into play. Thus, baseline CVD risk factor profiles from the EGAT study may not align with those in the entire country, whereas death rates are likely to be lower than those in the general population. However, we would expect the relative risks, which are the primary outputs from our analysis, to be robust estimates of the general situation in Thailand. The EGAT 1 and 3 cohorts represent the working Thai urban middle classes in the mid-1980s and at the current time, respectively. EGAT 2 represents working Thais in rural areas in the late 1990s. The EGAT 3 cohort will provide a clear picture of the health transition in the Thai urban middle class, when compared with the EGAT 1 cohort.

Other weaknesses are the withholding of the EGAT 1 study in 1990 because of the tragic loss of the first project leader. This left a gap of 12 years between the first and second surveys in EGAT 1. Since then, regular 5-yearly resurveys have been conducted. Lastly, the adoption of newly developed questionnaires in EGAT 3, both to introduce new variables and to revise previous questions, such as those on socio-demographics and physical activity, makes for issues of comparability between cohorts. Such issues are inevitable as the study has evolved and received attention from new researchers.

Can I get hold of the data? Where can I find out more?

The data are held by the data manager and are not available for use by outsiders. Individuals who wish to work on the data have to obtain prior approval from the Executive Committee. Initial enquiries should be made to the principal investigator (Professor Piyamitr Sritara) in Thailand. Further details on the EGAT study, and an English language version of the questionnaire, are available on request from the corresponding author.

Funding

Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok; the National Research Council; the Thailand Research Fund; the Thai Heart Association; the Thai Health Foundation; the Electricity Generating Authority of Thailand and the Praman Chansue Foundation.

Acknowledgements

We thank the EGAT and their people for their help in establishing the study. We, in memorandum, wish to express our greatest respect to Professor Somchart Lochaya and Professor Vichai Tanphaichitr, the founders and the first and second principal investigators of this study. The Executive Committee: T. Yipintsoi, R. Rajatanavin, B. Sathapatayavongs, P. Tatsanavivat

Conflict of interest: None declared.

References