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Title: Contemporary roles of registries in clinical cardiology: insights from the Western and Eastern European countries

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Commentary

Despite substantial advances in the management of cardiovascular disease, it remains a major cause of morbidity and mortality worldwide [1]. Globally, cardiovascular disease is expected to account for over 23 million deaths by the year 2030, mostly attributable to an increasing incidence in low and middle income countries [2]. Within the World Health Organisation European Region, cardiovascular disease accounts for over 4 million deaths per year. However, this rate varies considerably between European countries with evidence from observational databases to suggest that mortality rates from cardiovascular disease are higher in countries of Central and Eastern Europe, Central Asia, Finland and Malta.

Clinical registries are observational databases which focus on a clinical condition, treatment or population [3]. Data are collected systematically with broad inclusion and limited exclusion criteria. The role of clinical registries is to capture generalisable and representative information to, therefore, provide insights into patient characteristics, patterns of care and outcomes for `real world' populations and clinical settings. While randomised control trials (RCTs) are the gold standard for determining treatment efficacy, that is, in a controlled clinical environment, clinical registries play an important role in contributing to the evidence representing care and outcomes in the environments in which healthcare is practiced. Both type of studies are complementary for the assessment of the safety of interventions or medical therapies. Clinical registries, in particular, are powerful resources for studying long term outcomes and temporal trends, identifying novel associations and monitoring inequalities in care and outcomes which cannot always be achieved in a

randomized controlled trial setting due to ethical constraints as well as their cost. Cardiovascular registries are increasingly used for comparative effectiveness research, a priority area for the Institute of Medicine [4]. Through collecting and reporting real world data, clinical registries have a central role in cardiovascular quality improvement as well as research.

To date, clinical registries of cardiovascular disease have been predominantly founded in high income and Western countries. The Myocardial Ischaemia National Audit Project (MINAP) is a clinical registry of acute coronary syndrome hospitalisations in England and Wales [5]. It was started in 2000 and has information pertaining to over 1.2 million events (Figure 1). Participation in the registry is near-universal and, in recent years, has been mandated by the Department of Health. The clinical registry collects information that characterises the pre-hospital and hospital course of patients experiencing an acute coronary syndrome, with the number of data fields expanding steadily since inception. Data are self-reported by hospital-based clinicians or clerks into standardised electronic forms, and uploaded to central servers. The MINAP data application has error-checking routines, including range and consistency checks. An annual data validation exercise requires participating hospitals to re-enter 20 data items from the medical records of 20 randomly selected patients. Other countries with cardiovascular registries include Sweden (Register of Information and Knowledge about Swedish Heart Intensive care Admissions, SWEDEHEART/RIKSHIA) [6], France (French Registry on Acute ST-elevation and non ST-elevation Myocardial Infarction, FAST-MI) [7] and the United States (Acute Coronary Treatment and Intervention Outcomes Network Registry —

Get With The Guidelines, ACTION Registry-GWTG)/National Cardiovascular Data Registry, NCDR) [8].

However, only a minority of countries have clinical registries of cardiovascular disease, and not all are mandatory which can lead to potential participation bias. A recent review of the literature suggested that most central and eastern European countries did not have published acute coronary syndrome care and outcomes data [9]. Of those that did, there was evidence for wide variation in emergency strategies for the reperfusion of ST-segment elevation myocardial infarction (STEMI) [10]. Moreover, a significant East-West gap across European countries was evident in recent comparative studies of aggregate national and regional registry survey data despite recent improvements in the quality of care and increased rates of reperfusion strategies for STEMI [11, 12]. Explanations for geographical variations in emergency strategies and mortality rates are not always clear. Many studies have focused on differences in social, economic, cultural and clinical risk factors. Indeed in the MONICA study improvements in mortality rates during a 10-year period showed a greater relationship with a decline in pre-hospital mortality rates [13]. Beyond the quality of care provided in hospitals, differences in pre-hospital logistics, management and time delays strongly influence patients' outcome. This is particularly true for the Central and Eastern European countries [12, 14, 15]. Differences in social and economic factors play a crucial role in risk profile, acute coronary care and secondary prevention and need to be considered when comparing East-West patient populations. In 2010, the International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-TC; ClinicalTrials.gov: NCT01218776) was launched, aiming to collect real world registry data concerning the quality of care and clinical outcomes of patients hospitalised across 11 Central and Eastern European countries with acute coronary syndrome [16]. The ISACS-TC is both a

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retrospective (over a one year period) and prospective registry. Currently there are 29 tertiary healthcare services providing advanced medical investigation and treatment including percutaneous coronary intervention (PCI) and/or cardiac surgery, and 28 secondary healthcare services providing intensive coronary care. Participating hospitals are instructed to record data from consecutive hospital admissions and to register these data into standardised electronic charts on an internet-based database system before being uploaded to the data bank of the international coordinating centre [16].

To date this international clinical registry has revealed substantial opportunities for healthcare improvement among patients with acute STEMI (as reflected in long times to reperfusion and high 30 day mortality rates), and reported the efficiency of early β blockade following acute coronary syndrome (associated with improved left ventricular systolic function and higher in-hospital survival rates)[14, 17]. A recent study from the ISACS-TC registry reviewed current practice in antithrombotic therapy and reported that STEMI patients who fail to receive any reperfusion therapy benefit in terms of survival from unfractioned heparin - clopidogrel combination therapy without significant increases in risk of bleeding as compared to combined enoxaparin and clopidogrel therapy [18]. These findings are of note if we consider that non-reperfused STEMI patients are a major concern despite advances in emergency management. Moreover, recommendations in current guidelines for non-reperfused STEMI patients are based mostly on expert opinions rather than on evidence from clinical trials or clinical registries.

Whilst there are several reports of between country comparisons of acute myocardial infarction care and outcomes, typically these have either compared high performing

countries with each other,[19-21] eastern countries with each other,[14, 16] or used aggregated data[11, 22, 23] to compare many countries. There are limited contemporary comparisons of care for acute myocardial infarction between eastern and western European countries which have used patient-level data derived from a range of clinical registries [10]. International comparisons contextualise the quality of care provided in different countries and highlight opportunities for improvement. Moreover, variation between hospitals in quality of care and clinical outcomes provides useful insight into the performance of national health systems. For example, comparative research has shown that specific aspects of cardiovascular care are better and vary less between hospitals in Sweden than in the United Kingdom and that this is associated with many potentially avoidable deaths in the United Kingdom [19, 20].

As such we are left with a gap in the knowledge base about how eastern European countries directly compare with Western countries in their management of acute myocardial infarction. A concerted effort is needed to establish an international research consortium that will enable harmonised cardiovascular data collection and standardised reporting across Eastern and Western European countries. Such a research 'arc' would enable targeted quality improvement to reduce unwarranted variation in mortality across Europe. The implementation of international quality indicators for the evaluation and comparison of achievement of standards of acute cardiovascular care is a critical role that clinical registries will soon need to adopt. In addition, there is huge scope for novel research – using individual patient data meta-analyses to study rare cardiovascular events, repurposing clinical data for the design of multinational studies and the conduct of efficient registry-based randomised controlled trials [24].

It is clear that a new approach to the international study of cardiovascular care is justified. Clinical registries are not only important to assess the effectiveness and safety of health interventions but are critical for the assessment of the quality of healthcare systems and more so, for quality improvement. For this reason, promotion of comparable national clinical registries, mandatory rather than volunteer, using similar definitions for diseases, interventions and outcomes should be fostered across Europe [25]. This is an urgent need for Eastern European countries, where there may be a greater need of cyclical clinical evaluation for research and particularly for identification of targets for quality improvement initiatives.

FIGURE LEGEND

Figure 1: Random sample of acute coronary syndrome events in England and Wales from the Myocardial Ischaemic National Audit Project clinical registry, 2003-2013
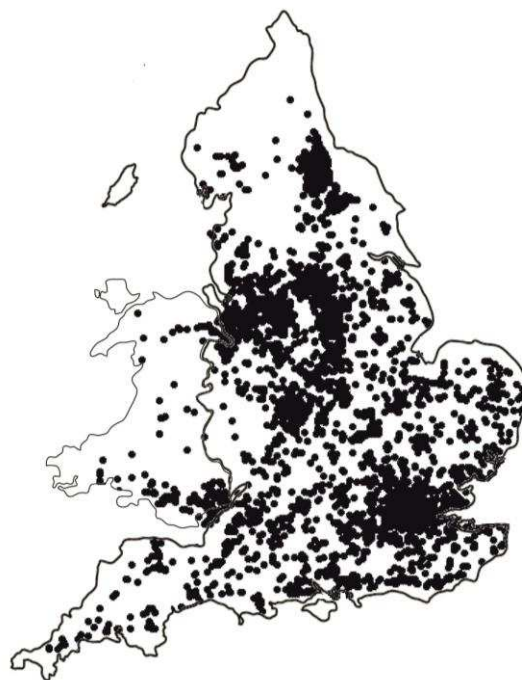
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