HEALTH ECONOMICS
Health Econ. **24**(Suppl. 2): 164–177 (2015)
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/hec.3287

A WINDOW ON GEOGRAPHIC VARIATION IN HEALTH CARE: INSIGHTS FROM EUROHOPE

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ABSTRACT

The aim of EuroHOPE was to provide new evidence on the performance of healthcare systems, using a disease-based approach, linkable patient-level data and internationally standardized methods. This paper summarizes its main results. In the seven EuroHOPE countries, the Acute Myocardial Infarction (AMI), stroke and hip fracture patient populations were similar with regard to age, sex and comorbidity. However, non-negligible geographic variation in mortality and resource use was found to exist. Survival rates varied to similar extents between countries and regions for AMI, stroke, hip fracture and very low birth weight. Geographic variation in length of stay differed according to type of disease. Regression analyses showed that only a small part of geographic variation could be explained by demand and supply side factors. Furthermore, the impact of these factors varied between countries. The findings show that there is room for improvement in performance at all levels of analysis and call for more in-depth disease-based research. In using international patient-level data and a standardized methodology, the EuroHOPE approach provides a promising stepping-stone for future investigations in this field. Still, more detailed patient and provider information, including outside of hospital care, and better data sharing arrangements are needed to reach a more comprehensive understanding of geographic variations in health care. Copyright © 2015 John Wiley & Sons, Ltd.

Received 6 March 2014; Revised 8 October 2015; Accepted 8 October 2015

KEY WORDS: performance measurement; healthcare system; acute care practice; geographic variation; health outcomes

1. INTRODUCTION

Introduction of the principles of evidence-based medicine some decades ago has not (yet) resulted in uniform medical practice. In fact, there is ample evidence for substantial variation in health care along geographical lines and within the same region (Skinner, 2011; Newhouse *et al*., 2013; Corallo *et al*., 2014; McPherson *et al*., 2013). The quantity and quality of health care provided and the way health care is delivered differs, while the treatment patients presenting with similar signs and symptoms receive may depend on location or setting. The burning question is whether such differences in the practice of health care also lead to differences in health outcomes and in the efficiency of care in the respective populations.

The EuroHOPE project was conceived to study such geographic variation in healthcare practice and in outcomes of care. Five specific diseases (acute myocardial infarction (AMI), breast cancer, hip fracture, stroke and infants born with very low birth weight (VLBW) and/or very low gestational age (VLGA) (further referred to as VLBW/VLGA infants) were selected to serve as case studies and for which countrywide

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patient data were collected in the participating countries (Finland, Hungary, Italy,[1] the Netherlands, Norway, Scotland and Sweden) (Fattore *et al*., 2015; Hagen *et al*., 2015a, 2015b; Malmivaara *et al*., 2015; Medin *et al*., 2015; Numerato *et al*., 2015; Peltola *et al*., 2015; Smith *et al*., 2015). In addition, one study was carried out with the hospital as unit of analysis and including all diseases treated in the hospital (Kittelsen *et al*., 2015). For this analysis, hospital patient data from the Nordic countries only were used. An important aim of EuroHOPE, for which patient data from 2006 to 2008 were collected, was to develop an internationally standardized approach regarding data management, selection of study populations and data analysis (Häkkinen *et al*., 2013; Moger and Peltola, 2014). Using such methods, the further aim was to explore variations between countries, regions and providers and to study the reasons behind these differences. In EuroHOPE, regions were defined according to the geographical organization of health care in a country or the OECD NUTS-3 definition in countries without regional healthcare authorities.[2]

The objective of this paper is to provide an overview of geographic variations in medical practice and outcomes as observed in the EuroHOPE studies. More specifically, the aim is to summarize the main results of the project, concentrating on (1) the methodologies developed; (2) the extent to which geographic variation was present; (3) the causes of variation that were identified; and (4) unmeasured explanatory factors.

The structure of the paper is as follows. In Section 2, a brief review of the literature on the existence and causes of healthcare variation is presented, as well as a description of what the EuroHOPE project aimed to contribute to this field of study. In Section 3, we discuss two methodological issues the EuroHOPE project elaborated upon, namely risk adjustment and costing methodology (Moger and Peltola, 2014; Smith *et al*., 2015; Iversen *et al*., 2015). Section 4 brings together the main insights from the disease-specific studies on geographic variation, aiming to formulate overall results and implications of the project. The main conclusions are presented in Section 5.

2. LITERATURE ON GEOGRAPHIC VARIATION IN HEALTH CARE

In theory, how healthcare systems 'perform' in terms of the use of procedures, resources and health is affected by demand and supply (Cutler *et al*., 2013; Skinner, 2011). Factors on the demand side include household income or patients' preferences. Factors on the supply side include prices, supplier inducement and physician beliefs, for example. As far as such explanatory factors are grouped geographically, such as medical doctors with similar training and beliefs practicing in the same geographic area, they may cause regional variation in medical practice, healthcare use and health outcomes.

Studies at the *country level* have clearly demonstrated the association between national income and aggregate health spending or population health (Getzen, 2006; OECD, 2013a; Joumard *et al*., 2010). The role of other demand factors, such as population ageing, appears to be smaller and often insignificant at the country level (Getzen, 2006; Hitiris and Posnett, 1992). Institutional characteristics of health systems have been studied as well, demonstrating that the financing system (showing higher spending in social health insurance systems, for example) or the reimbursement system (showing higher utilization in fee-for-service systems, for example) may affect healthcare use and cost, although the impact on health outcomes is unclear (Gerdtham *et al*., 1992; Asiskovitch, 2010; Wagstaff, 2009; Moreno-Serra and Wagstaff, 2010; Street *et al*., 2011; Wubulihasimu *et al*., 2015). Recently, OECD researchers did not find any indication that (grouped) institutional characteristics of health systems affect health outcomes and health system efficiency (Joumard *et al*., 2010).

[1]It should be mentioned that the Italian data were not nationally representative and covered relatively wealthy Italian regions.

[2]The number of regions and their size varied between the five cases. The regions were bigger for VLBW and VLGA infants (e.g. university hospital regions in Finland and Sweden) compared with the analysis of other conditions (e.g. hospital districts in Finland and counties in Sweden). In addition, in the regional analysis of stroke and hip fracture, regions with less than 100 patients were excluded. In Kittelsen *et al.* (2015), hospitals were the spatial units of analysis.

DOI: 10.1002/hec

Other researchers have focused on *regional variations within a single country*. Studies from the USA (Medicare) and Europe showed that a substantial part of regional variation in health spending is related to differences in demography and health status in particular (Zuckerman *et al*., 2010; Newhouse *et al*., 2013; Gopffarth *et al*., 2015; Reich *et al*., 2012; Skinner, 2011). Dissimilar impacts of institutional and supply factors have been reported across studies and countries. For example, in the USA, Medicare spending was found to vary between regions largely because of differences in post-acute care, while in the private insurance market variation in spending was explained by prices mostly (Newhouse and Garber, 2013). In Germany, the impact of price differences on regional variations was limited (Gopffarth *et al*., 2015). Disparity in quality of care may explain regional differences in spending as well. In Canada, higher spending regions had lower mortality rates, after controlling for demand characteristics such as socio-economic and lifestyle factors (Cremieux *et al*., 1999). In contrast, a recent Institute of Medicine study reported the absence of a relationship between measured quality of care and spending (Newhouse *et al*., 2013). Fisher *et al.* showed that after controlling for various patients' (demand) characteristics, mortality was not lower in higher-spending regions in the USA, while functional status or satisfaction with care were not better (Fisher *et al*., 2003a, 2003b). The authors interpreted this as providing evidence for the existence of variation in efficiency of healthcare delivery between US regions.

A few international comparisons of healthcare practice have been conducted at the *disease level* (McClellan and Kessler, 2002; OECD, 2003; Bech *et al*., 2009). The OECD studied costs and outcomes of care across countries for ischaemic heart disease, stroke and breast cancer to conclude that social health insurance systems tend to provide high-level technology with more access to modern technologies (OECD, 2003). Public-integrated systems seemed to exert a strong level of control over costs, while also limiting the use of certain technologies, particularly for the very old patients. The literature provides more evidence from disease-specific studies focusing on regional variations *within* countries, for example regarding cardiovascular care and the use of beta-blockers (Wennberg and Birkmeyer, 1999), tonsillectomy rates (Suleman *et al*., 2010) or asthma hospitalization rates (Lougheed *et al*., 2006). An important source of variation at the disease level is the status of the evidence for efficacy and effectiveness of treatments. In certain disease groups, treatment standards have created converging patterns of utilization, such as in the prescription of beta-blockers for cardiovascular disease. Before reaching this point, however, different dynamics of the adoption process may create regional variation in medical practice and utilization in the short run (Bradley *et al*., 2005). In other disease groups, variation was observed to be rather persistent, and it appeared difficult to empirically distinguish the contribution of different explanatory factors. In these areas, evidence may simply be insufficient to be able to capture what constitutes optimal care in clear-cut guidelines, and greater regional variation is to be expected (Skinner, 2011). Moreover, the impact of institutional or supply factors is expected to be greater where decisive evidence is lacking and/or benefit is dubious.

Illustrative is the case of cardiovascular disease and in particular AMI. This is one of the fields of medicine for which international consensus formation and defining of standards of care is highly advanced, based on large international clinical trials (Steg *et al*., 2012; Hamm *et al*., 2011). Nonetheless, still many questions remain, and new ones continue to emerge, as to what the most effective treatments are. In the case of AMI, there is now strong evidence that percutaneous coronary intervention (PCI) for ST elevation myocardial infarction results in better outcomes than medical treatment when performed within 2 hours after presentation. This implies that the infrastructure is highly relevant: the regional spread of specialized centres being equipped to perform PCI, and transportation to the hospital. Thus, even though consensus exists on an important aspect of treatment, this does not apply to treatment as a whole and in all contexts. In the literature, variation in coronary angiography and PCI rates between countries was found indeed (Widimsky *et al*., 2010; Laut *et al*., 2013; Ko *et al*., 2010; Matlock *et al*., 2013; Chung *et al*., 2014). These variations appear to be associated with healthcare supply (physicians, nurses and beds) (Laut *et al*., 2013) but not with reimbursement type (Medicare Advantage versus Medicare Fee-for-Service) (Matlock *et al*., 2013).

One of the main limitations of the analyses reported in the literature is that previous studies often used a particular perspective, such as focusing on a single country or on a single disease or treatment group. Furthermore, most international studies concentrated on outcomes at the macro-level. The EuroHOPE study aimed to add

DOI: 10.1002/hec

evidence to the literature using more comprehensive data, combining the international and the regional perspective, and including nationwide patient-level data for multiple patient groups and countries. Furthermore, internationally standardized data management and statistical analysis was conducted (Häkkinen *et al*., 2013).

3. RISK ADJUSTMENT AND COSTING METHODOLOGY IN EUROHOPE

3.1. Risk adjustment

In comparing outcomes and resource use, it is crucial to adjust for geographic variation in population characteristics (e.g. demographics or disease severity) that affect demand for health care and the potential for health improvement. The possibilities for risk adjustment in EuroHOPE were limited by data-sharing restrictions in some of the participating countries. In order to partially circumvent these limitations, several statistical approaches were taken: (1) The coefficients of pooled-data risk adjustment models (including those countries that could share data) were used to calculate expected outcomes at the patient level and risk-adjusted outcomes (using the observed/expected approach) at the regional level, (2) Pooled-data models were estimated (excluding countries with non-transferable data), including risk adjusters as covariates and random effects to estimate the performance of countries, regions or hospitals, (3) Outcomes and risk adjustment variables were aggregated at the regional level and included in regional-level regression analysis, (4) Meta-analytic techniques were used to combine the results of country-specific models. It was shown that the choice of reference data had little impact on outcomes (Moger and Peltola, 2014). In studies reported in two papers, the regional-level analysis was supplemented with analyses using the pooled patient-level data from five countries (Hagen *et al*., 2015b; Peltola *et al*., 2015), whereas in the studies reported in two other papers, solely pooled patient-level data were used (Häkkinen *et al*., 2015; Kittelsen *et al*., 2015).

3.2. Costing

In general, comparing treatment cost across countries is associated with some challenges: accounting systems that differ between countries, differences between patient populations (risk adjustment is required) and a lack of cost figures at the individual patient level. In the disease-specific EuroHOPE analyses, three approaches were followed to deal with these issues (Iversen *et al*., 2015).[3] In addition, and in contrast to most previous studies, special attention was given to defining treatment episodes in a comparable manner and including treatment information beyond the first hospital stay (to account for hospital transfers). In the first approach, the relative costs of the different components of resource use (procedures and hospital length of stay (LOS)) were approximated on the basis of patient cost data from Sweden and converted to euros by means of a purchasing power parity index for hospital services. In this manner, only variation in the use of procedures and in LOS could affect treatment cost. In the second approach, the between-country variation in the cost of 'production' of a hospital service is accounted for by using cost estimates of the local diagnosis related group (DRG) systems. In the third approach, the Nordic DRG grouper was used to compare treatment costs between Nordic countries. Following that, risk-adjusted cost functions were estimated, employing three alternative estimation methods, by means of data for AMI patients. Using data from breast cancer patients, cost functions were estimated using ordinary least squares regression and quantile regression to test for parameter heterogeneity (Smith *et al*., 2015).

These analyses provided several conclusions with important relevance for health policy. First, risk adjusters explained only a small proportion of the variation in calculated costs across patients. Second, the ranking of countries depended on the cost indicator used and on the length of the observation period. Third, the ranking of countries depended neither on the risk adjusters included nor on the specification of the cost function. This

[3]In Kittelsen *et al.* (2015), costs were collected at the hospital level only. The DRG-based approach to costing individual patients could not be used because the Nordic DRG grouper was instead used to aggregated outputs.

DOI: 10.1002/hec

means that ranking of countries according to crude costs gave the same result as ranking of countries according to the estimated expected costs adjusted for variation in disease severity. Finally, the breast cancer regression models showed that costs may need to be considered beyond an average point estimation.

4. SUMMARY AND IMPLICATIONS ACROSS DISEASE-SPECIFIC STUDIES IN EUROHOPE

EuroHOPE provides new evidence on geographic variation in health care using international patient-level data for multiple patient groups. The case studies covered a few of the most highly prevalent conditions (stroke, AMI and hip fracture). In addition, a relatively rare condition was selected with a major health burden and requiring intensive treatment that has hardly been studied from a comparative health economic perspective (VLBW). The level of evidence regarding treatment effectiveness varies for these cases. For AMI and stroke, international guidelines exist and evidence indicates that certain treatments are more effective than others. The evidence is weaker regarding treatment of hip fracture and in particular VLBW and VLGA infants. Still, regional variations may be expected for AMI and stroke as guidelines change on a regular basis and many countries have issued national guidelines (in particular for stroke). Moreover, reaching the standards of care recommended in these guidelines requires a particular organization of care and availability of services, which may not be present in all countries and regions. Geographic variation in the organization and availability of care may therefore cause variation in healthcare use and in health outcomes. The main results of these four disease-specific studies and the Nordic hospital-level study are summarized in Table I.

4.1. Summary of results across diseases

In general, the AMI, stroke and hip fracture patient populations were similar with regard to age, sex and comorbidity across the EuroHOPE countries. Differences were somewhat larger for VLBW and VLGA infants in particular for specific variables. For example, the percentage of multiple births was rather low in the Dutch VLBW and VLGA dataset (mainly due to data limitations), and the percentage of first deliveries was relatively high in the Swedish data.

In terms of health outcomes, the results showed that 30-day mortality rates for AMI, stroke, hip fracture and VLBW/VLGA infants varied to similar extents, that is, with a 10% to 15% point difference between the best-performing and worst-performing country. In the Nordic hospital-level study, differences were smaller, with a case mix-adjusted mortality ranging from 0.32% to 0.45% of the much larger sample of patients including all disease groups. Hungary and Scotland showed relatively high mortality rates, with Hungary having the highest age-sex adjusted 30-day mortality for AMI, stroke and hip fracture. Scotland showed the second highest 30-day mortality for stroke and AMI. Italy fared better, having the lowest mortality rates, except for AMI (where mortality was lowest in Norway). VLBW/VLGA infants showed a different pattern with high mortality in Hungary, followed by the Netherlands, Italy and Finland, and low mortality in Scotland and Sweden. In all cases, regional differences within countries were substantial, but estimates from region-by-region comparisons often showed overlapping confidence intervals. Remarkable was that some countries showed high within-country variation for one disease but low within-country variation for other diseases. Demand-side and supply-side variables explained regional variation in mortality only to a limited extent (limited explanatory power). Moreover, the impact of various patient and region characteristics varied between countries and diseases, except for age and comorbidity. Most often, significant effects were found for some countries only.

Variation in the use of procedures was analysed for AMI, where PCI use was relatively high in Sweden, the Netherlands and Hungary (the country with the highest mortality). In comparison with what was found for mortality rates, the degree of variation between regions was much larger (10% to 60% in each country) for PCI use. PCI rates for AMI patients were associated at the regional level with population size and the number of catheterization labs.

Length of stay was low in Hungary for both hip fracture and stroke patients. However, for AMI and VLBW/VLGA infants, opposite results were found, with LOS being highest in Hungary. For AMI, LOS was low in

DOI: 10.1002/hec

Table I. Main EuroHOPE results by case study, by type of measure (mortality, LOS/costs, procedures) and by type of result ((1) degree of variation[a] and (2) explanatory factors significantly ($p < 0.05$) associated with the outcome))

	Mortality	LOS/costs	Procedures
AMI	1. Degree of variation	1. Degree of variation	1. Degree of variation
	Country level - Age-sex adjusted 30-day mortality (%): 5.5 (NOR)–18.2 (HUN) - Age-sex adjusted 30-day mortality (CV): 11.4 (NETH)–23.3 (SCO) - Age-sex adjusted 1-year mortality (%): 12.0 (NOR)–28.2 (HUN) - Age-sex adjusted 1-year mortality (CV): 11.1 (NETH)–14.1 (FIN)	*Country level* - Age-sex adjusted LOS first episode days: 7.4 (SCO)–10.6 (ITA) - Age-sex adjusted LOS first episode (CV): 6.9 (NETH)–11.7 (NOR) - Age-sex adjusted LOS 1 year (days): 8.1 (SCO)–17.3 (HUN) - Age-sex adjusted LOS 1 year (CV): 7.6 (HUN)–11.1 (NOR)	*Country level* - Age-sex adjusted PCI within 2 days (%): 17.9 (SCO)–43.4 (NETH) - Age-sex adjusted PCI within 2 days (CV): 17.7 (NETH)–37.8 (SCO)
	2. Explanatory variables	2. Explanatory variables	2. Explanatory variables
	(a) Individual-level 30-day mortality (age, sex and comorbidity adjusted) Country indicators (FIN (+) HUN (+), ITA (−), NOR (−) SWE (−)), PCI rate (pooled data and all countries (−)), population size ((pooled data, NOR, SWE) (+)), regional unemployment (pooled and SWE) (+), regional share 70+ (NOR) (−), regional GDP (NOR) (−)	*(a) Individual level* Not reported	*(a) Individual-level 2-day PCI rate (age, sex and comorbidity adjusted)* Country indicators (ITA (−), SWE (+)), regional number of catheterization labs ((pooled data, HUN, NOR, SWE) (+), ITA (−)), regional GDP (ITA (+), NOR (−)), regional population size ((pooled data, NOR, SWE) (+), ITA (−)), regional unemployment (NOR) (−), regional share 70+ (NOR) (−)
	(b) Regional-level 30-day risk-adjusted mortality (pooled data models) Country dummies (HUN (+), ITA (−), SCO (+), SWE (−)), population size (+), unemployment rate (+)	*(b) Regional level* Not studied	*(b) Regional-level 2-day PCI rate (pooled data models)* Country dummies (FIN (−), NETH (+), NOR (+), SCO (−), SWE (+)), regional catheterization labs (+), population size (+), global budget (−)
	c) Hospital-level 30-day survival Country dummies (FIN (−), HUN (−), ITA (−), NOR (+), reference SWE), university/teaching status (FIN) (+), existence of catheterization lab (pooled data, FIN, HUN, NOR and SWE (+)), HHI ((HUN and NOR) (−)), regional GDP (FIN, HUN, ITA (+)), population density (HUN, ITA (+))	*c) Hospital level* Country dummies (FIN (−), ITA (+), NOR (+), reference SWE), university/teaching status (pooled data, FIN SWE) (+)), existence of catheterization lab (all models (+)), HHI (pooled data HUN, NOR, SWE) (−)), regional GDP (pooled data FIN, SWE (−)), regional population density (pooled data (+))	*c) Hospital level* Not studied
Hip fracture	1. Degree of variation *Country level* - Age-sex adjusted 30-day mortality (%): 4.0 (ITA)–13.7 (HUN) - Age-sex adjusted 30-day mortality (CV): 11.9 (NETH)–25.8 (FIN) - Age-sex adjusted 1-year mortality (%): 19.1 (ITA)–39.7 (HUN) - Age-sex adjusted 1-year mortality (CV): 5.4 (NETH)–13.1 (NOR)	1. Degree of variation *Country level* - Age-sex adjusted LOS first episode (days): 9.6 (NOR)–18.7 (ITA) - Age-sex adjusted LOS first episode (CV): 7.3 (NETH)–27.5 (FIN) - Age-sex adjusted LOS 1 year (days): 12.7 (HUN)–23.3 (ITA) - Age-sex adjusted LOS 1 year (CV): 7.8 (NETH)–23.0 (HUN)	Not studied
	2. Explanatory variables *(a) Individual level* Not reported *(b) Regional-level risk-adjusted 30-day mortality (pooled data model)* Country dummies (SWE (−), HUN (+), ITA (−), reference FIN), regional share of men in one model (+), clinical guidelines (−)	2. Explanatory variables *(a) Individual level* Not reported *(b) Regional-level risk-adjusted LOS first episode (pooled data model)* Country dummies (SWE (+), ITA (+), NETH (+), SCO (+), reference FIN), regional share of men in one model (−)	

(*Continues*)

DOI: 10.1002/hec

Table I. (Continued)

	Mortality	LOS/costs	Procedures
	(c) Regional-level risk-adjusted 1-year mortality (pooled data models) Country dummies (HUN (+), ITA (−), SCO (+), reference FIN), clinical guidelines (−)	*(c) Regional-level risk-adjusted LOS 1 year (pooled data model)* Country dummies (SWE (+), HUN (−), ITA (+), reference FIN), regional share of men in one model (−), clinical guidelines (+)	
	(d) Hospital level (30-day survival) Country dummies (HUN (−), ITA (+), NOR (+), reference SWE), regional GDP (pooled data (+))	*(d) Hospital level* Country dummies (FIN (−), HUN (−), ITA (+), NOR (−), reference SWE), university/teaching status (pooled data, SWE) (+)), HHI (FIN) (−), regional GDP (pooled data (−)) NOR (+)	
Stroke, cerebral infarction	1. Degree of variation *Country level* - Age-sex adjusted 30-day mortality (%): 7.5 (ITA)–16.3 (HUN) - Age-sex adjusted 30-day mortality (CV): 14.3 (NETH)–17.3 (FIN) - Age-sex adjusted 1-year mortality (%): 15.7 (ITA)–31.1 (HUN) - Age-sex adjusted 1-year mortality (CV): 6.1 (NETH)–13.3 (FIN)	1. Degree of variation *Country level* - Age-sex adjusted LOS first episode (days): 9.8 (ITA)–17.3 (SCO) - Age-sex adjusted LOS first episode (CV): 4.4 (NET)–23.8 (SCO) - Age-sex adjusted LOS 1 year (days): 11.6 (ITA)–30.3 (SCO) - Age-sex adjusted LOS 1 year (CV): 4.9 (NETH)–17.8 (SCO)	Not studied
	2. Explanatory variables *(a) Individual-level 1-year mortality (pooled data models, including four countries)* Regional GDP (−), regional population density (+), effort (−)	2. Explanatory variables *(a) Individual-level LOS (country-specific models)* Age (HUN, NETH, SCO, SWE) (+), age 85+ (FIN) (−), male (ITA, NETH, SWE) (−), LOS of previous year (FIN, HUN, NETH, SWE) (+), some comorbidities (varying) (±), some weekdays (varying) (±)	
	(b) Regional-level risk-adjusted 1-year mortality (pooled data) Regional GDP (−), regional population density (+)	*(b) Regional-level risk-adjusted LOS* None	
	(c) Hospital level (30-day survival) Country dummies (HUN (−), ITA (+), reference SWE), university/teaching status (pooled data, HUN(+)), regional GDP (pooled data, FIN (+)), regional population density (pooled ITA (−))	*(c) Hospital level* Country dummies (FIN (−), HUN (−), reference SWE), university/teaching status (SWE), HHI (pooled data, FIN and HUN) (−)),regional GDP (pooled data (−), ITA SWE (+)), regional population density (SWE (−))	
VLBW/ VLGA infants	1. Degree of variation *Country level* - Unadjusted 30-day mortality (%): 8.0 (SWE)–15.7 (HUN) - Unadjusted 1-year mortality (%): 9.4 (SWE)–18.1 (HUN)	1. Degree of variation *Country level* - Unadjusted LOS first year (days): 36.5 (SWE)–69.9 (FIN)	Not studied
	2. Explanatory variables *(a) Individual-level 30-day mortality (country-specific models)* Low gestational age (+), Apgar score at 5 min (−), small at gestational age (FIN, HUN, ITA, NETH, SCO, SWE) (+), presence of malformations (FIN) (+), presence of malformations (NOR)	2. Explanatory variables *(a) Individual-level LOS 1-year (country-specific models)* Gestational age >23 weeks and <31 weeks (+), Apgar score at minutes (±), low weight at gestational age (NETH, NOR, SCO, SWE) (+), presences of malformations (ITA,	

(*Continues*)

DOI: 10.1002/hec

Table I. (Continued)

	Mortality	LOS/costs	Procedures
	(−), multiple births (FIN, HUN, NETH, SCO) (+), male (HUN), regional GDP (FIN, HUN) (+), regional HHI (FIN) (−), birth in level III hospitals (FIN, HUN) (−), hospital transfer (FIN, HUN) (−), regional unemployment (FIN, HUN) (+)	NOR, SCO) (+),presences of malformations (FIN) (−), multiple births (except NOR) (−), hospital transfer (FIN, ITA, HUN, SWE) (+), unemployment (HUN) (−), unemployment (NETH) (+), regional GDP (HUN) (+), regional population density (HUN) (+), birth in level III hospitals (HUN, ITA) (+)	
	(b) Individual-level 1-year mortality (country-specific models) Low gestational age (+), Apgar score at 5 min (−), small at gestational age (HUN, ITA, NETH, SWE) (+), presence of malformations (NOR) (−), presence of malformations (HUN, SWE) (+), multiple births (FIN, HUN, NETH, SCO, SWE) (+), male (HUN, NOR), regional GDP (FIN, HUN) (+), regional HHI (FIN) (−), birth in level III hospitals (FIN, HUN) (−), hospital transfer (FIN, HUN) (−), regional unemployment (HUN) (+)		
	(c) Regional level Not studied	*(c) Regional level* Not studied	
	(d) Hospital level Not studied	*(d) Hospital level* Not studied	
Nordic hospital-level study	1. Degree of variation	1. Degree of variation	Not studied
	Country level −30-day mortality (%): 0.32 (NOR)–0.45 (FIN). Between-hospital variation from 0.29% to 0.66%.	*Country level* - LOS: 1.46 (FIN)–1.68 (NOR/SWE)	
	- 365-day mortality 0.64%–0.83%. Lowest in Finland/Norway, highest in Sweden	- Higher costs per DRG point in Sweden, lowest in Finland	
	- Highest readmission rates in Norway (12%), lowest in Denmark (6%)	- Large within-country variation	
	- Patient safety indices show little significant differences between countries but are likely to be insufficiently coded		
	2. Explanatory variables:	2. Explanatory variables	
	Individual level Age, gender, transfers, LOS, comorbidity. These have great impact	Costs *Hospital level* Size in patients, case-mix index, university or capital city hospital. Only case-mix index has significant impact on costs	
	Regional level Population, unemployment, social assistance, single families, percent foreign-born, travel time to hospital. The municipal variables have generally little impact	*Regional level* Population, Unemployment, Social assistance, Single families, Percent foreign-born, Travel time to hospital. These have generally little impact, except travel time in Norway	

CV, coefficient of variation (excluding Italy); LOS, length of stay; GDP, gross domestic product; HHI, Herfindahl–Hirschman Index; VLBW, very low birth weight; VLGA, very low gestational age; FIN, Finland; HUN, Hungary; ITA, Italy; NOR, Norway; NETH, Netherlands; SCO, Scotland; SWE, Sweden.

[a]Based on regional data used in articles of this supplement. The indicators are available in the Atlas Map Report (http://www.eurohope.info/).

DOI: 10.1002/hec

Scotland, where, however, LOS was high for stroke and VLBW and VLGA infants. For both stroke and hip fracture, regional variation in LOS could not be explained by any of the demand-side or supply-side variables (not studied for AMI).

Summarizing, the results of the regression analyses showed that various demand-side and supply-side variables did not explain regional and hospital variation in terms of mortality, LOS or utilization of procedures. The variables considered that proved to be statistically non-significant in most cases were the following: population density (except for mortality after stroke), population size (except for PCI use and mortality in AMI patients), HHI,[4] disease incidence, availability of primary or comprehensive stroke centres (analysed for stroke care only), education level (analysed for AMI only) and elderly as share of the total population (analysed for AMI only). The macroeconomic indicator gross domestic product (GDP) showed a significant association only with mortality after stroke and AMI (in Norway). When studied on a per-country basis, the regional characteristics (e.g. HHI) showed significant associations for some countries. In many cases, the HHI variable was negative, meaning that higher degrees of concentration of regional care of the condition were associated with lesser use of resources. Regarding the hospital or regional-level variables in the Nordic hospital-level study, only average travelling time had a significant effect on costs.

4.2. Interpretations

The results confirm that health outcomes (30-day and 1-year mortality) and LOS may vary as much for hip fracture and VLBW/VLGA infants as for stroke and AMI (both within and between countries). Particular patterns were found. Hungary systematically showed the highest mortality rates, while those in Italy were amongst the lowest in all cases, except for VLBW/VLGA infants. These variations may reflect differences between the countries in health status of the general population. Furthermore, in the case of Hungary, these outcomes may be associated with socio-economic conditions, as indicated by its relatively low GDP and high Gini coefficient. In fact, previous studies have reported a relationship between these two measures and health outcomes. Also, Scotland has a relatively high Gini coefficient, which may explain the high mortality for AMI and stroke there. In the regression models, we found an association between GDP and mortality at the regional level for stroke. As a result, it may be questioned whether these outcomes reflect variation in healthcare performance per se or are rather related to general socio-economic conditions.

Results further demonstrate that some explanatory variables may be more important or relevant in one country than in another. For example, university hospitals in Sweden generally had high cost/LOS compared with other Swedish hospitals, whereas this was not the case in other countries. Besides these more or less consistent findings, various results did not seem to fit into a pattern. For example, mortality rates for Finnish AMI patients were rather high, whereas in contrast, survival of Finnish patients was much better for stroke and hip fracture. In these two latter cases, hip fracture and stroke, results indicated an inverse relationship between LOS and mortality at the country level. At the same time, hospital-level analysis showed no indication that a cost–quality trade-off existed for the two conditions. A weak trade-off between readmissions and costs was found in the Nordic hospital-level study including all diseases, but here again, there was an inverse relationship for mortality, where high quality was significantly associated with low costs.

Noteworthy are the large variations between and within countries that we found for AMI, in our analysis of regional variation in treatment choices, in terms of PCI use. As was expected, these variations were clearly associated with the supply of cardiac services in the region. The further association between PCI use and mortality rates indicated that this may translate into variation in health outcomes as well. Interestingly, country-level results here do not mirror findings at the regional level and that of the individual. At the patient level, higher PCI use was associated with lower mortality. However, a lower effect of PCI on mortality was found in a country with the lowest mortality, while Hungary showed the highest mortality in combination with high PCI use.

[4]Herfindahl–Hirschman Index for the concentration of service utilization.

DOI: 10.1002/hec

This could indicate that the role of explanatory variables also differs across aggregation levels of analysis. The results of more detailed analyses in Finland and Norway suggested that the effect of socio-economic factors on mortality *through* the use of PCI was small (Hagen *et al*., 2015b). In Hungary and Finland, there seemed to be a trade-off between survival and use of resources at the hospital level, indicating that better quality may require more resources in these countries.

The differences in health outcomes and use of resources (LOS) after case-mix adjustment, in combination with a lack of significance of several explanatory variables, indicate that there is room for improvement in healthcare performance. Alternatively, health production possibilities may differ between regions having different health production functions. This could be the result of variation in the adoption of effective technologies, in the quality of doctors and other healthcare providers, or in physician beliefs about treatment effectiveness. Regarding this latter point, a recent study from the USA indicated that physician beliefs may be an important explanatory factor for regional variation in health spending (Cutler *et al*., 2013). Although we could hardly statistically test the impact of institutional factors in this study, another explanation is that differences in institutional factors do not determine performance as much as theory suggest, in accordance with the results of the OECD study (Joumard *et al*., 2010).

4.3. Limitations

The reliance on registries that are used for administrative purposes—the only feasible way to achieve nationwide coverage—also has its drawbacks. Probably, the most important limitation is the lack of detail on clinical variables that give insight into disease severity. This applies especially to AMI and stroke, where information on baseline severity was not available. Thus, although sophisticated risk adjustment was performed, these important prognostic variables could not be taken into account. Furthermore, this type of source provides insufficient information to be able to evaluate the appropriateness of treatment. Detailed insight into the timing of procedures (relevant for AMI, stroke and hip fracture) would assist in better understanding the true degree of variation in performance.

As far as hospital infrastructure is concerned, differences between countries were encountered in the categorization of hospitals and services that are given in hospitals. The most important differences in this respect concerned the status of rehabilitation, in some countries forming part of hospital care, in others offered outside the hospital setting. Nevertheless, we were able to separate out rehabilitation from our LOS and cost analysis, in order to guarantee better comparability. This confirms the need for patient-level information across different types of care and different functions.

Furthermore, information on pre-hospital and post-hospital care could further enrich our understanding of regional variations. In some regions, more AMI or stroke patients may die before/without reaching the hospital. As a result, hospital patient populations may differ (even though we found rather similar patient populations across countries by the available characteristics). This confirms the importance of adding information on disease severity. Also, the availability and quality of follow-up care may affect the outcomes of treatment and LOS. In case these variables vary along geographical lines, they affect regional variations in outcomes.

4.4. The way forward

Previous studies comparing regions or countries in the fields of medicine covered by EuroHOPE often were restricted to selected hospitals or diseases, or to ‘metadata’, or to only one of the aspects of outcomes or healthcare pathways. A noteworthy exception is the recent study by Chung *et al*. (2014) on AMI that used nationwide registries with detailed patient-level information on all hospital admissions. Unfortunately, such registries currently exist only in the UK and Sweden and only for AMI. In addition, linkage with other registers, such as those on medication use and preferably costs, is needed to comprehensively assess the cost-effectiveness of healthcare systems.

The EuroHOPE case studies are unique in having collected nationwide data at the level of the patient in multiple countries, for several diagnoses, and with well-defined criteria for selecting patients at first hospital

DOI: 10.1002/hec

admission and following them up until 1 year after the index admission. Linkage of records made it possible to clearly delineate episodes of care, follow patients over time and assess vital status. This creates comprehensive information on geographic variations in healthcare performance across levels (country, region, hospital). Future studies that build upon this approach may focus on acquiring additional information that was lacking in the current study. In particular, disease-specific patient characteristics and quality-of-care indicators would prove beneficial for better insight into the causes of regional variation and into the performance of regions. Additionally, it seems important to improve the registration of diagnostic procedures and treatment procedures that determine treatment outcome and cost. Furthermore, it would be useful to have better understanding of differences in coding practices across countries.

It seems that outcomes and relationships between outcomes and explanatory factors may vary across levels of analysis (national, region, hospital, individual). For a better understanding of regional variations, it is worthwhile to analyse such 'inconsistencies' across levels in more detail. Also, research could be extended to other diseases or regions to validate the findings. The differences in geographic variation between disease groups that were found to exist call for more use of disease-based approaches in future healthcare performance research. In which countries results of hospital treatment were best, clearly depended on the type of disease. At the same time, consistent differences in outcomes across diseases, providers and countries also point to the existence of systematic performance effects (Häkkinen *et al*., 2015; Kittelsen *et al*., 2015). Explanations for such across-the-board variation are to be sought in ownership structures, financial incentives and health sector practices that differ between countries and regions in ways that may influence overall performance. In other words, both disease-specific studies and studies including a broad range of diseases are needed to provide a comprehensive picture.

Finally, although administrative data may provide a 'big data' and possibly relatively cheap information source, substantial effort was required in the EuroHOPE project to create comparable datasets that cover the healthcare pathway of individual patients as well as health outcomes. Moreover, privacy issues prevented the sharing and pooling of national datasets into a single EuroHOPE database, limiting the possibilities for risk adjustment or multilevel modelling. In addition, the performance at hospital level could not be studied in all countries because it was not allowed in all countries to share outcomes at the hospital level. Such experiences should be taken into account in future studies, in particular because the possibilities for linking and sharing data appear to vary widely between countries (OECD, 2013b). Therefore, as this type of research may provide the necessary step forward in the monitoring and evaluation of healthcare systems and policies, these data infrastructure issues require close attention.

5. CONCLUSION

A major aim of the EuroHOPE project was to develop a methodology for standardizing administrative patient data in several countries in a manner that makes them suitable for comparative purposes. In principle, this would enable regular population-based monitoring as an ongoing international comparison, without the need for costly survey research, centre enrolment or manual consultation of hospital records. It may be concluded that EuroHOPE has shown that such an enterprise is feasible. The methodological framework developed provides a solid starting point for further elaborating an international performance assessment toolkit. Given the differences in geographic variation between disease groups found, more future studies are recommended to apply disease-based approaches to healthcare performance research. Still, more detailed patient and provider information, including outside of hospital care, and better data sharing arrangements are needed to reach a comprehensive understanding of variations in medical practice and health outcomes across countries and regions.

CONFLICT OF INTEREST

The authors have no conflict of interest.

DOI: 10.1002/hec

ACKNOWLEDGEMENT

This project was undertaken within the European Union 7th Framework Programme 'European Health Care Outcomes, Performance and Efficiency' (EuroHOPE), contract no 241721.

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