Impact case study (REF3b)

Institution: Queen's University Belfast
Unit of Assessment: 2
Title of case study: The Global Monitoring of Cardiovascular Disease

1. Summary of the impact

Research in the MONICA project set the standards for national cardiovascular health surveys in Europe, by establishing quality assessment benchmarks for how cardiovascular health should be monitored in populations. These standards were subsequently adopted by the European Union, and by local health bodies, to improve their commissioning decisions. This research has had an important impact on public health monitoring, enabling robust epidemiological comparisons across countries and the sort of analysis that policy makers need to inform the balance between primary and secondary prevention for cardiovascular health.

2. Underpinning research

By the 1970s coronary heart disease (CHD) mortality had fallen in western countries, but there were divergent trends in eastern Europe. The correct policy response to these trends was uncertain because both the incidence of and mortality from CHD is affected by the nature of the presentation, the location of the event and the speed and rigour of the diagnosis and medical intervention. To understand which of these factors could explain international differences in coronary mortality, the World Health Organisation sponsored the MONICA Project (Multinational **MONI**toring of trends and determinants in **CA**rdiovascular disease). Queen's University investigators led by Evans (Professor of Epidemiology, QUB from 1988-2010) were the first to join MONICA. Evans attracted the initial grant from the MRC, recruited and trained the staff and was responsible for the project's overall conduct in Northern Ireland. He recruited Kee (Professor of Public Health Medicine) who worked with him from 1994 onwards.

MONICA was a global epidemiological study on a scale never before matched covering 38 populations, 21 countries in 4 continents over 23 years. Under Evans' leadership, the project was responsible for the detailed assessment of the quality of reporting of populations-at-risk, risk factor and case definitions, and survivorship, all of which were subsequently collated as manuals and e-publications on the MONICA website http://www.thl.fi/publications/monica/. This huge effort pre-dated the current capability of digital communications and electronic data-capture.

The number of people who die of a heart attack each year comprise those having a heart attack and who die immediately, and the "early" survivors who reach hospital but die soon afterwards (within 28 days). The case fatality rate is this number divided by the total number of heart attack patients per year i.e. the incidence of heart attack. The key insights that Evans and the MONICA team made[1,2] were that among countries experiencing a decline in mortality, changes in case fatality (the proportion who die within 28 days) contributed only about a third of the overall improvement and that a major factor was variation in the measurement of incidence. Variability in the suspicion, recognition, and confirmation of non-fatal versus fatal events can create error in the mortality rates if these are not defined accurately. International standards are needed for fair population comparisons and for comparisons of coronary care, so that spurious drivers of overall mortality can be distinguished from real ones. For example, in some low incidence countries where case fatality in women was high, the application of MONICA criteria suggested that non-fatal events in women were less consistently recognised. Less complete recording of non-fatal events artefactually inflates case fatality rates, making the latter a poor proxy for the quality of coronary care. Using consistent case definitions and a uniform measurement of acute coronary care allowed the first comparisons of the pathways of care and mortality in different counties that had differing models of acute out-of-hospital care[3].

In summary, MONICA resulted in 120 publications, many confirming that classic risk factors (such

as high blood pressure, cholesterol and smoking) only partly explained the trends in heart disease. Residual variance across counties was attributable to difficulties in measurement and analysis[4,5].

3. References to the research

Research outputs from MONICA (>120 papers) relied on contributions from many partners. Evans led MONICA's dissemination efforts as the publication coordinator from 1990 and was the overall Steering Committee Chairman from 1994-1999, it's most productive period.

1. **Evans A**, Dobson A, Ferrario M, Kuulasmaa K, Moltchanov V, Sans S, Tunstall-Pedoe H, Tuomilehto J, Wedel H, Yarnell J, for the WHO MONICA Project. The WHO MONICA Project: changes in coronary risk in the 1980s. *Proceedings of the XIth International Symposium on Atherosclerosis; 5-9 October 1997, Paris, France. Elsevier Science, Atherosclerosis XI, 1998; 49-55.* This output can be supplied on request. *In this early output, an aggregate "risk factor score" in the MONICA populations, showed a secular downward trend, predicting a subsequent downward trend in mortality, the latter borne out by later analyses.*

2. Tunstall-Pedoe H, Kuulasmaa K, Mähönen M, Tolonen H, Ruokokoski E, Amouyel P, for the **WHO MONICA** (monitoring trends and determinants in cardiovascular disease) Project. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA Project populations. *Lancet* 1999; 353:1547-57. Doi: 10.1016/S0140-6736(99)04021-0. This output can be supplied on request. *Analyses in this highly cited paper showed that the factors driving the incidence of new coronary events helped explain the trends in overall mortality better than those affecting survival from heart attack.*

3. Moore W, **Kee F**, **Evans** AE, McCrum-Gardner EE, Morrison C, Tunstall-Pedoe H. Pre-hospital coronary care and coronary fatality in the Belfast and Glasgow MONICA populations. *Int J Epidemiol* 2005; 34 (2): 422-30. Doi: 10.1093/ije/dyh377

Analyses in this paper capitalised on having access to a detailed "MONICA" dataset, including the place of occurrence of all heart attacks in Belfast and Glasgow and the timing and adequacy of resuscitation and coronary care provided, demonstrating that any differences in coronary mortality between the cities could not easily be attributed to the provision of a medically manned out-of-hospital ambulance service in Belfast.

4. Kuulasmaa K, Tunstall-Pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, **Evans A**, Ferrario M, Tuomilehto J, for the WHO MONICA Project. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *Lancet* 2000; 355:675-87. http://www.scopus.com/record/display.url?eid=2-s2.0-0034716468&origin=inward&txGid=AE4E357CE735F20F9C6A52A9C808D38B.Vdktg6RVtMfaQJ4pNTCQ%3a13. *This paper showed that changes in the classic risk factors across the 38 MONICA populations partly explained the variation in population trends in CHD. Residual variance was attributable to difficulties in measurement and analysis, including assumptions about the time lag for risk factor effects, and to factors that were not included, such as medical interventions. The results supported prevention policies based on the classic risk factors but suggested potential for prevention beyond these.*

5. **Evans A**, Tolonen H, Hense HW, Ferrario M, Sans S, Kuulasmaa K, for the WHO MONICA Project. Trends in coronary risk factors in the **WHO MONICA Project.** *Int J Epidemiol* 2001; 30 (Suppl 1):S35-S40. http://ije.oxfordjournals.org/content/30/suppl_1/S35.full.pdf. *This paper used repeated cross sectional surveys in the MONICA populations to analyse trends in classic risk factors and revealed worrying trends in smoking in women and obesity among men that had significant public health implications.*

Related grants:
- **EC QLG2-CT-2002-01254** (GENOMEUTWIN). *Studies of European volunteer twins to identify genes underlying common diseases, 2002-2006, **Alun Evans** - £338,798.*
- **EC FP6 LSHM-CT-2004-005268** EUROCLOT *Genetic regulation of the end-stage clotting process that leads to thrombotic stroke, 2005-2008, **Alun Evans** - £34,780.67.*
- **EU FP6 037593** CARDIOGENICS. *The Cardiogenics project,* 2006-2011, **Alun Evans** -

£3,140.90.
- **MRC** G0601463 ID NO 80983 BIOMARKER. *Serum biomarkers in the MORGAM Project,* 2007-2010, **Alun Evans** and **Frank Kee** - £507,840.
- **EU FP7 201413**. *European network of genetic and genomic epidemiology (ENGAGE),* 2008-2012, **Alun Evans** - £316,560.
- **EC FP7 HEALTH-F2-2011-278913**. *BiomarcaRE Biomarkers for cardiovascular risk assessment in Europe,* 2011-2015, **Frank Kee** - £44,728.

4. Details of the impact

The impact of the MONICA studies was in the 2008 production of a European Health Examination Survey Manual. Under Evans's leadership the MONICA Manual established the necessary quality assurance procedures and collated the information with which to judge the reliability and comparability of data on risk factors and outcomes of coronary heart disease. This enabled unbiased international comparisons, which allowed policymakers in many countries to make informed decisions about the balance between primary and secondary prevention strategies for cardiovascular disease.

Evans was a member of the MONICA Steering Committee from 1990 and was its Publication Coordinator from 1992. He subsequently assumed responsibility for the revision of the MONICA Survey Manual, re-designing several elements to remove ambiguities. In 1994 he became Chairman of the MONICA Steering Committee and he led the MONICA EU Biomed Concerted Action from 1996-1999, during which the success of the standardization process was thoroughly assessed and published in a series of reports[1]. As Chairman and with senior colleagues from other participating centres, he also set the direction for the subsequent MONICA research outputs.

The insights gained from the research led to the promotion of uniform methods for cardiovascular surveys (collated as manuals and e-publications on the MONICA website[1]) and their adoption by initially 38 population centres of coronary heart disease registration.
Based on the MONICA Manuals, the European Commission supported the development of **the European Health Examination Survey (EHES).** This standardized national health examination surveys in the European countries. The Feasibility of the European Health Examination Survey (FEHES) programme assessed the capacity to conduct uniform national health examination surveys in all EU countries. This feasibility project[2] (2006-2008) led directly to the EHES Pilot. The pilot in 12 countries between 2009 and 2012supported by the EU Joint Action programme set up the EHES Reference Centre (EU Service Contract) led directly to the production of a European Health Examination Survey Manual[2].

MONICA's survey manual and consistency of approach has also permitted policy makers to draw robust inferences about trends in CHD and the impacts of prevention and healthcare policies on them. For example, research based on MONICA survey data demonstrated that approximately 60% of the substantial CHD mortality decline in Northern Ireland between 1987 and 2007 was attributable to major cardiovascular risk factor changes and approximately 35% was attributable to treatments. These findings were launched by the Chief Medical Officer for Northern Ireland and the Minister for Employment and Learning in April 2012[3]. Similar conclusions have been replicated in many countries[4] and would not have been possible but for the adoption of MONICA's harmonised survey methods. Editorials in major journals have long testified to the need for data, such as are available in MONICA, for policy making[5,6].

Other direct beneficiaries of the research include commissioners of health services. A careful analysis of MONICA data from Belfast and Glasgow[7] showed little additional benefit in Belfast of having more expensive medically staffed coronary care ambulances. As a result, local commissioners moved away from supporting a medically manned mobile coronary care ambulance service and supported more paramedic-led coronary care models, appropriate to local geography and service needs.

The adoption of the MONICA survey methods also paved the way for a further important commissioning decision at EU level, namely to support the **MORGAM** programme[8], which has already successfully provided follow-up for cardiovascular disease of the cohorts defined by the MONICA risk factor surveys and other similar European population surveys. This has formed an important data harmonization infrastructure for the epidemiology, genetics and biomarkers of CHD in Europe which is now impacting on CHD service research and delivery in Europe.

The Deputy Head of Unit for Research and Innovation for Advanced Therapies and Systems Medicine at the EU stated that "under Professor Alun Evans's careful chairmanship and planning, the outputs from MONICA laid the foundation for many subsequent decisions that the EU took concerning our investment in the dissemination of uniform methods for population health surveys" and that he felt it "a privilege to see the legacy of MONICA mature in the genomic age."[9]

5. Sources to corroborate the impact:

Several editorials and commentaries in leading journals testified to the impact of the MONICA project including:

1. (http://www.ktl.fi/publications/monica/). *This source documents the MONICA quality assessment procedures themselves.*
2. (http://www.julkari.fi/bitstream/handle/10024/78265/2008b21.pdf?sequence=1). *This source shows how the CHD aspects of EHES have been informed by previous MONICA quality assessment procedures.*
3. (http://www.northernireland.gov.uk/index/media-centre/news-departments/news-del/news-del-march-archive-2011/news-del-030311-obesity-costing-economy.htm). *This source highlights the NI Minister of Health's role in helping launch the findings of a policy analysis which was conducted for Northern Ireland based on MONICA data,* available in: *Heart* 2013;99:1179-1184 Doi:10.1136/heartjnl-2013-303921
4. Capewell S et al. Cardiovascular risk factor rends and potential for reducing coronary heart disease mortality in the United States of America. *Bulletin of the World Health Organization* 2010; 88:120-130. Doi: 10.2471/BLT.08.057885. *This source is one of many, internationally, demonstrating how analysing MONICA data can inform policy on CHD prevention.*
5. Grover S. Role of WHO-MONICA Project in unravelling of the cardiovascular puzzle (Editorial) *Lancet 2*000; 355: 668-9. Doi: 10.1016/S0140-6736(00)00016-7. *This source testifies to the relevance of MONICA for prevention policy analysis.*
6. Alpert JS. Coronary heart disease: where have we been and where are we going? (Editorial) *Lancet* 1999; 353: 1540. Doi: 10.1016/S0140-6736(99)00154-3. *This source testifies to the relevance of MONICA for prevention policy analysis.*
7. Wayne R, Johnson A-M. Commentary: Modern day 'flying ambulances' for coronary care: a tale of two cities. *Int. J. Epidemiol.* (April 2005) 34(2): 431-432. Doi: 10.1093/ije/dyi018. *This editorial testifies to how use of carefully quality assured MONICA data informed the policy debate on models of out of hospital coronary care.*
8. Evans A, Salomaa V, Kulathinal S et al. MORGAM (an international pooling of cardiovascular cohorts. *Int. J. Epidemiol.* 2005 Feb; 34(1):21-7. Doi:10.1093/ije/dyh327. *This source demonstrates how MONICA gave birth to the MORGAM study.*
9. Key decision makers have offered personal written testimonies to the impact claimed including: The Deputy Head of Unit European Commission DG Research & Innovation, and The Medical Director Northern Ireland Ambulance Service Health and Social Care Trust.