Board for Academic Medicine

Medical Schools Council

Health of Scotland

The international impact of Scottish medical schools

Introduction

Scotland has a proud heritage in medical research and our medical schools are at the forefront of internationally competitive research impacting on our patients and improving the health and wealth of the country. The recently completed census of research performance and quality, the Research Excellence Framework 2014 (REF2014), for the first time elicited documented examples of the impact that the research of medical schools is having in Scotland, the UK and worldwide. In *Health of Scotland: The international impact of Scottish medical schools* we have selected a series of 17 of the Scottish medical schools' most impressive impact case studies from a total of 90 submitted to REF2014. They exemplify the extraordinary breadth and depth of impact that results from work undertaken by Scottish medical schools.

The areas in which the research has had an effect on society are broad and wide ranging, but include: improving clinical practice, boosting the economy, delivering benefits to society which include public understanding of health issues and of science, and making improvements to health care internationally.

As you read this document, remember that these 17 examples are only a fraction of the 90 submitted by the Scottish medical schools and published on the REF website (www.ref.ac.uk). Taking a broad view, the impact of research in our Scottish medical schools has been profound. For example, work undertaken in Glasgow has contributed significantly to the reduction in morbidity and mortality associated with cancer, chronic inflammatory and cardiovascular diseases, including a reduction in mortality rates of 25% through pioneering lipid-lowering therapy and the mortality from heart failure by 24% due to the use of a specific class of drugs, the mineralocorticoid receptor antagonists. In terms of benefits to our economy and the NHS, for the case studies submitted to REF from the University of Edinburgh with a measurable health economic impact, researchers estimate the underpinning grant funding has generated annual cost savings for the NHS in the UK of £294 million, representing an annual return on public funding of a minimum of £147 for every £1 of grant income awarded. Research based in the University of Dundee Medical School has influenced major charities and shaped research priorities for Cancer Research UK; the Breast Cancer Campaign; the Wellcome Trust; the British Heart Foundation; Diabetes UK and the Juvenile Diabetes Research Foundation. Research undertaken at the University of Aberdeen Medical School has profoundly influenced UK policy in relationship to a range of health issues relating to food, including regulations and regulatory standards for specific pathogens in foodstuffs and the impact of allergen exposure during pregnancy to childhood allergy. Novel drug and diagnostic developments for infectious diseases of international importance, particularly for the developing world, featured in the impacts from St Andrews and Dundee universities.

The impact generated by our Scottish university medical schools has been demonstrated to reach in excess of 100 countries worldwide in all continents and to affect the lives of millions of individuals. The examples contained in this document cannot be comprehensive but demonstrate how researchers in our universities have influenced and defined practice for healthcare delivery organisations including, of course, the National Health Service, and national governments and global bodies including the World Health Organization.

It is important to recognise that this excellent, collaborative research is facilitated by significant investment and benefits from the strong UK-wide funding streams and infrastructure. The most recent figure from the Medical Research Council demonstrates that 11.5% of its UK funding comes to Scotland. In 2009–2010 medical research in Scotland received £65.98 million from the Medical Research Council; £45.84 million from the Wellcome Trust; and £28.05 million from Cancer Research UK, in addition to the £17.6 million of support from the Chief Scientist Office Scotland and £7.32 million from the Department of Health England. In summary, Scotland's community of medical researchers wins more research funding than would be expected on a simple share of population; winning 13.1% of UK research funding with a population of 8.4% of the UK total.

Scotland's medical schools also support vibrant training pathways for the next generation of clinical academics, equipping young researchers to address the challenges facing society, healthcare nationally and internationally, and the NHS in future years.

Professor John Iredale

Regius Professor of Medical Science & Vice Principal Health Services,
University of Edinburgh
for the Board for Academic Medicine and the Medical Schools Council

Fuller Longer: helping to develop a new health food range for Marks & Spencer

University of Aberdeen

Obesity and associated conditions are a major health concern. Helping people to make healthier choices is a priority for governments, health services, researchers and industry.

Research findings at Aberdeen have underpinned the development of the Fuller Longer range of products which are intended to support weight loss or weight maintenance diets. Aberdeen based studies conducted from 2008 onwards demonstrated that high protein and moderate carbohydrates sustain appetite control and weight loss. To come to their conclusions, the Aberdeen team conducted numerous studies with obese human volunteers which included psychological and physiological monitoring in and out of the laboratory. Researchers also used Positron Emission Tomography to understand how high protein moderate carbohydrate weight loss diets affect the brain. The findings showed that high protein moderate carbohydrate diets are as effective as diets that are high in protein, but low in carbohydrates. This means the valuable intake of fruit, vegetables and fibre can be maintained, unlike in other diets.

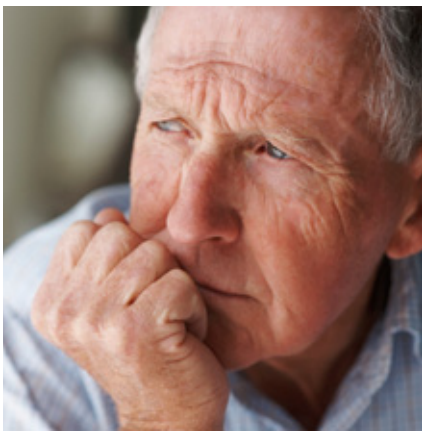
An interaction with Marks and Spencer (M&S) took the research findings through to the marketplace. Researchers worked closely with senior management and others within M&S to create an effective range of products. The Fuller Longer product range has represented a huge commercial success for the industry partner and is an established brand for the company's 20 million customers. Figures for sales in January 2012 indicate 1.5 million meals being sold in a week. This industry-academia partnership was a first for M&S, and has led to one of the UK's most popular retail healthy-eating food ranges.

As of 2015 the Fuller Longer range is rebranded to 'Balanced for You'.

Researchers: **Johnstone and team**

Discovery and commercialisation of an entirely new drug for the treatment of Alzheimer's disease

University of Aberdeen



The World Health Organization estimates that, over the next twenty years, the number of people with Alzheimer's disease will double to 65.7 million. Major new research undertaken at the University of Aberdeen forms the basis for an entirely new therapeutic approach to treating Alzheimer's – one that could effectively prevent disease progression. Work has concentrated on understanding the mechanism of action through which tau pathology, a characteristic hallmark of Alzheimer's disease, can be inhibited by compounds. This approach was a marked departure from the previous focus that has dominated Alzheimer's research and drug development, which had targeted amyloid with generally disappointing clinical results.

During a double-blind Phase 2 clinical trial which targeted tau of 321 people with mild Alzheimer's, it was found that taking methylthioninium chloride three times a day over a period of 50 weeks was successful in slowing down the development of Alzheimer's by about 81%.

Researchers then worked to improve subject-tolerability of the drug and, in 2007, developed the synthesis of the first ever stable, pharmaceutically acceptable version of the compound. In July 2008, Researchers presented their Phase 2 trial findings to seismic effect at the International Conference on Alzheimer's Disease in Chicago. Aberdeen's research had provided the first clinical evidence demonstrating that a treatment based on tau aggregation pathology may delay the progression of cognitive decline in both mild and moderate Alzheimer's.

Among the benefits described by both patients using the drug and their families are an improvement in levels of concentration and greater alertness, leading to recovered confidence and an ability to cope.

Although not yet commercially available, this drug has already benefited more than 100 patients and their families. A new spin-out company founded to develop the drug has created new jobs and attracted more than US$250 million in investment since 2008. Extensive media coverage of the research has generated increased public awareness of the disease and Aberdeen's cutting-edge research and ability to raise investment.

Researchers: **Wischik and Harrington**

National screening programme for diabetic retinopathy

University of Aberdeen

Diabetic retinopathy – a serious complication of diabetes – is a leading cause of blindness in people of working age and can progress to an advanced stage without any noticeable symptoms. Screening programmes for its early detection are crucial. Since 1996 the number of people with diabetes in the UK has increased from 1.4 million to 2.9 million and is predicted to rise to 5 million by 2025. Approximately 20% of people diagnosed with type 2 diabetes have early signs of retinopathy, but with early diagnosis and treatment, blindness will be prevented in 90% of those cases.

Aberdeen researchers developed software to detect those features common to the early onset of diabetic retinopathy: microaneurysms, haemorrhages and exudates. They evaluated the clinical benefit of the software and concluded there was a strong case both for commercialising the software itself and for introducing it into screening programmes for diabetic retinopathy.

The programme started at a time when retinal imaging technology was analogue and the early work on microaneurysm imaging involved the time-consuming and invasive technique of injecting dye prior to imaging (fluorescein angiography). As digital fundus cameras came on the market, the researchers showed that digital imaging was an effective method for detecting potentially sight threatening retinopathy, with technical failure rates lower than those of conventional photography. With this technology, dilation of the pupils was not normally required, reducing patient discomfort, and a single image of each eye (rather than the usual two) was sufficient. In addition, automated grading could improve efficiency by correctly identifying just under half the population as having no retinopathy.

A multidisciplinary team evaluated the efficacy and cost-effectiveness of the automated grading system using 14,406 images from 6,722 consecutive patients attending a screening programme. The software performed disease/no disease decision-making based on detection of microaneurysms and dot haemorrhages. They then recruited over 25,000 patients with a view to monitoring the performance of a new algorithm that incorporated macular exudate and blot haemorrhage detection, both signs that may require referral to an ophthalmology clinic. This demonstrated conclusively that the detection of observable/referable retinopathy was improved.

A licence agreement was negotiated with Medalytix which developed a commercial version of the software known as iGrading. A condition of the licensing was that the products should be made available to the Scottish screening service free of charge. Thus not only has industry benefited, but NHS Scotland has had free use of the software. The workload of screeners has been reduced by nearly 40%, and the estimated annual cost saving for NHS Scotland is around £200,000 per year. Since 2008, interest in using the software has also been shown by centres in other parts of the UK, Europe, South America, Africa and Australia.

Researchers: **Olson, Sharp and Forrester**

Provexis: A nutrition and health spinout company marketing a food ingredient for vascular health

University of Aberdeen

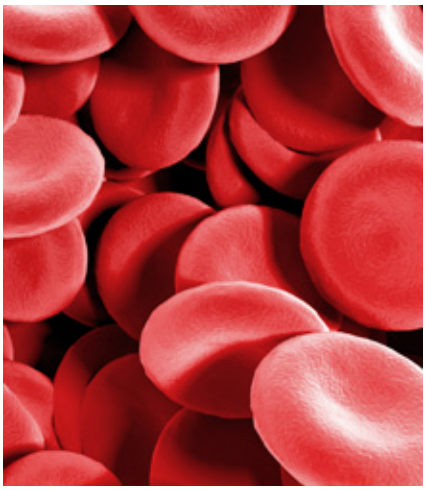
The World Health Organization estimates that annually worldwide more than 15 million people suffer a stroke and that total mortalities from all cardiovascular disorders exceed 17 million (the Atlas of Heart Disease and Stroke). Diet and lifestyle linked conditions such as stroke and coronary heart disease account for 5.5 million and 7.2 million deaths, respectively. Recent data has indicated that other conditions such as deep venous thrombosis affect approximately eight in 10,000 in the world population.

Researchers at the Rowett Institute of Nutrition and Health, now part of the University of Aberdeen, found that biologically active constituents in tomatoes inhibit blood platelet aggregation: a known cause of heart attack, stroke and venous thrombosis.

Research began in 1998 with a screening programme examining the effects of a range of fruit and vegetables on the function of platelets, an overabundance of which can cause cardiovascular disorder. This work expanded to include aqueous extracts of herbs and botanicals which revealed that aqueous tomato has far higher anti-platelet activity than other extracts. Further work identified the compounds with anti-platelet activity. The chemical properties of the active compounds indicated their potential suitability as therapeutic agents or as functional food ingredients.

By 2001, the body of evidence amassed was sufficient to secure funding for commercialisation. Provexis Ltd was formed and a work programme commenced focusing initially on characterisation of the concentrated tomato extract, followed by development of a prototype industrial extract. This was followed from 2003 by extensive human trials to demonstrate the efficacy of the extract.

The health claim around this product was deemed sufficiently detailed and evidenced to result in the landmark judgement from the European Food Safety Agency in 2009 that it would be the first product-specific health claim to be approved by the agency. The award set a benchmark for other companies to follow and demonstrated that the science-led approach adopted by the small company could compete successfully with the intellectual inputs



of major global players. This remains a definitive standard for the industry. Since then very few other companies have successfully gained similar approval.

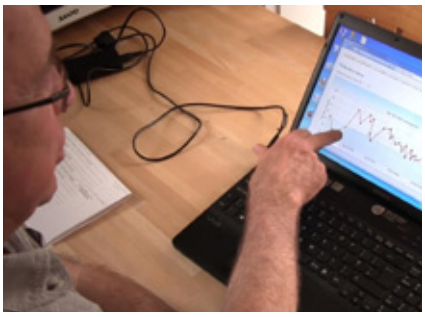
An alliance agreement was announced with DSM Nutritional Products in June 2010 to commercialise what was named 'Fruitflow' heart-health technology. The alliance partners have now worked to develop a powder concentrate of the Fruitflow technology which is being readied for tablet and capsule use. DSM is responsible for manufacturing, marketing, and selling via its global sales force while Provexis remains responsible for contributing the scientific expertise necessary for successful commercialisation.

In 2010 it was given awards for the 'Most Innovative Health Ingredient' and 'Best Innovation in the Heart Health' category at the Health Ingredients European Conference in Madrid. In 2011 it was awarded the Nutraward for 'Best New Ingredient' at the USA trade launch at the Nutracon conference in California.

Researchers: **Dutta-Roy and team**

Biomedical informatics transforming the care of people with diabetes, and with chronic diseases internationally

University of Dundee



Diabetes is a global health problem which poses severe risks for the world. The number of people living with diabetes is estimated to be 500 million by 2030. In response to this, researchers at Dundee developed a health informatics platform supporting chronic disease management nationally and internationally, along with a new record linkage tool for drug safety.

Initially, the Diabetes Audit and Research in Tayside, Scotland (DARTS) study tested the hypothesis that record linkage of routinely collected NHS data sources was an efficient and accurate methodology to create a regional diabetes register. The study linked information from the community health index (health identity number), hospital clinics, pharmacies, laboratories, and the retinal screening service. The Government commissioned further informatics research at the University of Dundee to develop DARTS into a national technology product, the Scottish Care Information-Diabetes Collaboration (SCI-DC). Its roll out to the whole of Scotland has allowed the study of the epidemiology, pharmacovigilance and outcomes research on a national basis. Since 2004 SCI-DC has been implemented in all 14 Scottish Health Boards, and since 2008 it has been used in 1,038 general practices and 38 hospitals, monitoring the care of over 271,000 people with diabetes. It represents the most comprehensive clinical information system for the care of people with diabetes internationally.

SCI-DC has supported the evaluation of improved regional and national health outcomes, such as a 40% reduction in amputation rates and a 40% reduction in sight-threatening retinopathy from 2003–2009. The associated recruitment of individuals to large genomic studies (over 40,000 subjects), and the linkage of phenotype to genotype, has been of great importance. This linkage between research, informatics and healthcare led Sir Mark Walport, then Director of the Wellcome Trust to write (The Times, 30th May, 2011) 'If you live in Dundee and suffer from diabetes, you have recently been taking part in a medical revolution'.

Researchers: Morris, Leese and McDonald

A new diagnostic and risk stratifying test in cardiology

University of Dundee

Around 900,000 people in the UK have heart failure, accounting for 1 million inpatient bed days per year and 5% of all emergency medical admissions to hospital. Financially, this adds up to some 2% of total healthcare costs. The diagnosis of heart failure is difficult because its symptoms are non-specific and the physical signs are often not obvious.

The research at Dundee on brain/B-type naturietic peptide (BNP) has helped to diagnose both types of heart failure (systolic and diastolic heart failure) and to identify high-risk aortic stenosis patients for surgery. The researchers were the first to show that plasma levels of BNP could be used in clinical practice to detect left ventricular systolic dysfunction (a left-sided heart failure). Aortic stenosis is the most common valvular disease in Western countries but identification of subgroups of symptomatic patients who may benefit from early surgery is a clinical challenge. The work demonstrated elevated plasma BNP in significant aortic stenosis.

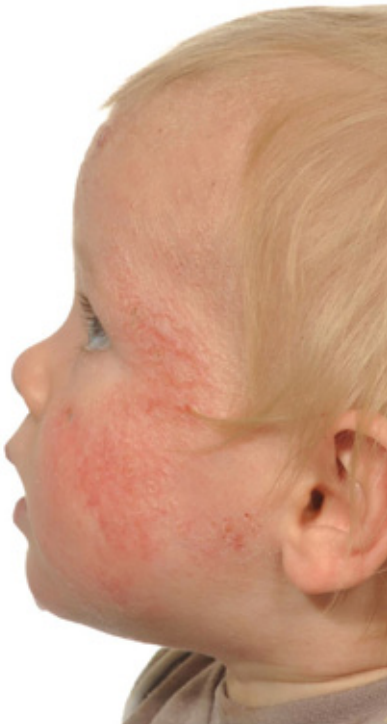
The availability of BNP as a diagnostic test has important implications. Firstly, when applied early in the diagnostic process in patients with suspected cardiac failure, a negative BNP test can help rule out congestive heart failure and thus avoid unnecessary tests and referral to clinics. Secondly, BNP assessment can hasten the correct diagnosis of heart failure allowing prompt delivery of evidence-based treatment. The inclusion of BNP testing in the recent 2010 NICE Guidelines will have a major clinical impact. BNP testing is cost-effective and measuring BNP is the single most useful test to add to the diagnostic process in primary care.

A costing report for implementing the 2010 NICE guidance on BNP testing to rule out heart failure estimated that there will be a £3.8 million net saving and a 23% reduced risk per patient of being admitted to hospital within the first six months of the implementation of BNP testing. In addition to establishing a clear role for BNP testing to diagnose heart failure and identifying at risk patients with aortic stenosis, the Dundee BNP research has prompted the development of commercial assays for BNP.

Researchers: **Struthers, Lang, Kennedy**

Filaggrin: The major predisposing gene for atopic disease and a target for stratified therapeutic intervention

University of Dundee



Atopic eczema is a complex trait in which multiple genetic risk factors interact with environmental factors in disease pathogenesis. Associated conditions – asthma, food allergy and hay fever – affect around 40% of the population in developed nations. They cause significant morbidity and create a multibillion-pound global healthcare burden. The common single gene skin disease, ichthyosis vulgaris (characterised by dry, scaly skin), is caused by loss-of-function mutations in the gene which encodes filaggrin. The gene product of filaggrin (FLG) is cleaved to produce monomeric filaggrin, which plays a role in keratin filament aggregation, skin barrier formation and cutaneous hydration in normal skin.

The Dundee group made a seminal discovery: they demonstrated that up to 50% of severe childhood eczema cases carry a loss-of-function mutation in the filaggrin gene (FLG). This creates a paradigm shift in the eczema/allergy field by showing that one of the primary driving forces underlying common atopic (allergic) disorders is impaired skin barrier function, which allows entry of allergens and irritants normally hidden from the immune system by an effective skin barrier, resulting in skin and systemic inflammation.

Longitudinal population-based genetic studies have confirmed that FLG is a major genetic factor in eczema, asthma and allergic rhinitis, and that FLG haploinsufficiency (in effect a filaggrin defect) is particularly associated with severe, early onset and persistent disease.

This paradigm shift in understanding eczema has changed the focus of clinical care to epidermal (skin) barrier function and this has informed the development of therapeutic guidelines. The increased public understanding of atopic eczema disease has improved compliance with emollient therapy. Clinical trials of barrier enhancement interventions are underway. The Barrier Enhancement for Eczema Prevention study (2010–2011) demonstrated a 50% reduction in eczema incidence in babies receiving daily emollients.

Researchers: McLean and Brown

The Global Registry of Acute Coronary Events (GRACE) risk score for the management of acute coronary syndrome

University of Edinburgh

The GRACE registry, for the first time demonstrated that lower-risk rather than higher-risk patients with acute coronary syndromes (ACS) received more intensive medical and interventional treatment. To optimise the targeting of treatment for ACS and using data from the registry, the GRACE risk score provides clinicians with a powerful yet user-friendly means of identifying higher-risk patients at the time of their first presentation.

The independent predictors of outcome in 21,688 patients presenting with ACS were derived and the predictions validated prospectively in a further 22,122 patients, with the aim of predicting both in-hospital and six-month risk of death, and death or myocardial infarction. Nine factors independently predicted both death and the combination of death or myocardial infarction and conveyed more than 90% of the risk.

The GRACE programme identified that survivors of non-ST elevation ACS (previously perceived as minor or threatened heart attacks) had higher long-term risks of death and recurrent myocardial infarction and ST-elevation myocardial infarction (ST elevation refers to a finding on an electrocardiogram, wherein the trace in the ST segment is abnormally high above the isoelectric line). By identifying these patients, appropriate interventional strategies could be put in place and lives saved.

The GRACE risk score was made freely available to download to a mobile device. The app provides a user-friendly interface of the variables that convey 90% of the risk. Clinicians use this information alongside their own clinical evaluation to guide management of the patient. By facilitating appropriate treatment the GRACE risk score has contributed to a change in practice and improved outcomes saving 30 – 80 lives for every 10,000 patients presenting with non-ST elevation ACS.

Researchers: Fox and Gore

Dolly the sheep – the first cloned mammal

University of Edinburgh

This scientific breakthrough in regenerative medicine is widely recognised as the key stepping stone between earlier amphibian-based work and the reprogramming of adult human somatic cells to a stem cell state.

Researchers, led by Ian Wilmut (Inaugural Director of the Centre for Regenerative Medicine), with colleagues from the Roslin Institute (now University of Edinburgh), focused their scientific efforts on the manipulation of eggs (female reproductive cells), oocytes (egg precursor cells) and stem cells (cells that can divide and self-renew, but also differentiate into diverse specialised cell types). They were particularly interested in utilising somatic-cell nuclear transfer to produce viable embryos. This technique involves transfer of the nucleus from a somatic cell (any cell that is not a reproductive or stem cell) into an oocyte or egg deprived of its own nucleus (cytoplast). Eventually this enabled the successful cloning of sheep from cultured cells derived from sheep embryos. Dolly – the first cloned adult mammal – was born on July 5, 1996, providing the first evidence that adult specialised cells are capable of driving the development of a complete and fertile animal.

Dolly has become a scientific icon, entering the public and educational lexicons in addition to scientific ones, stimulating rolling religious, ethical, cultural, political and scientific debates, and triggering public engagement with bioscience. For example, cloning principles are now part of high school education, including the International Baccalaureate, which is implemented in over 3,600 schools on five continents.

Dolly played a major role in clarifying the value of stem cell and regenerative medicine research to Government, contributing to the establishment of several high-profile initiatives, including the UK Stem Cell Initiative. In autumn 2012, the Chancellor of the Exchequer identified Eight Great Technologies of strategic importance to the UK and announced an additional funding of £600 million to help support their development. Regenerative medicine is placed among these great technologies.

Researchers: **Wilmut and team**

Reducing the global burden of stroke by using aspirin and avoiding heparin use in the treatment of acute stroke

University of Edinburgh

Each year, worldwide, about 15 million people suffer a stroke, of whom one third will die, and one third will survive in a disabled state.

The International Stroke Trial led by Edinburgh researchers was a randomised controlled trial in patients with acute ischaemic stroke within 48 hours of stroke onset, evaluating the safety and efficacy of aspirin, heparin, both or neither. The study recruited 19,453 patients and showed that for every 1,000 patients treated immediately with aspirin, 10 patients avoid early recurrent stroke or death, and at six months after stroke onset, 13 more were alive and independent.

The trial showed that patients allocated to heparin had a lower risk of early recurrent ischaemic stroke and pulmonary embolism, but a higher risk of intracranial and extracranial haemorrhage (bleeding), so overall heparin had no effect on the likelihood of death or of being alive and independent, and so should be considered ineffective.

To date, aspirin remains the agent of choice in ischaemic stroke and there is no evidence to support the routine use of any form of anticoagulation therapy. The effect of giving early aspirin to the 85% of the patients whose stroke is ischaemic and who have no contraindication to or intolerance of aspirin would be to reduce stroke deaths at three months by 15 out of 520, or 3%, and the number of patients who are either dead or dependent by 29, or 2%. This means that 1,800 people in the UK now avoid death or disability and are treated with a highly cost-effective drug.

The use of aspirin has been introduced into stroke treatment guidelines worldwide, reaching up to 50 million patients annually. In the UK, the administration of aspirin within 24 hours is a quality standard against which services are judged nationwide. In the UK, the estimated cost to health and social services of a dependent stroke survivor is £11,292, and the annual cost of an independent survivor £876. The avoidance of post-stroke dependency therefore can save the UK healthcare system substantial amounts.

Researchers: **Sandercock, Dennis, Wardlaw, Warlow**

Preventing deaths from pesticide self-poisoning in rural Asia

University of Edinburgh

Suicide accounts for over half of the 1.6 million violent deaths that occur every year worldwide. About 63% of global suicides occur in the Asia Pacific region. Most of these deaths occur in rural areas, where easy access to highly toxic pesticides turns many impulsive acts of self-poisoning into suicide. The World Health Organization's World Report on Violence and Health has recommended that suicide prevention be a priority issue.

In the early 1990s, Sri Lanka had one of the world's highest suicide rates, at around 52 per 100,000 per year (the UK suicide rate at this time was seven to eight per 100,000). Since then a collaboration of Sri Lankan and international researchers, led by a researcher at the University of Edinburgh, has searched for ways to prevent deaths from self-poisoning, through clinical and public health interventions.

They produced the first description of the clinical presentation and outcome of poisoning with many pesticides, showing very different clinical syndromes and lethality, despite the pesticides having the same World Health Organization toxicity classification. A series of studies dissected the roles of specific organophosphates, their hydrocarbon solvents, and treatments in deaths following self-poisoning. During this time, the first prospective cohort of patients with acute self-poisoning in the developing world was set up. The cohort continues today and now contains information on over 35,000 patients.

This work has profoundly impacted on clinical practice. It demonstrated that activated charcoal used to bind ingested poison was safe and reduced the need for hazardous gastric lavage (stomach washout), an intervention hitherto believed to be beneficial but which was associated with increased mortality. Crucially, the researchers found that pralidoxime, used with atropine to treat poisoning caused by specific pesticides, is hazardous for patients. As a result the guidance concerning treatment of organophosphate-poisoned patients has now changed across Asia. The 2010 Indian national guidelines demonstrate by citing the importance of this work, and a follow-up trial in Bangladesh to define the value of the group's recommendations on the use atropine showed a 60% reduction in deaths.

The work has led directly to national bans in Sri Lanka of the pesticides fenthion, dimethoate and paraquat, and influenced WHO policies regarding the prevention and treatment of pesticide poisoning leading, for example, to the withdrawal of pralidoxime from the World Health Organization's essential drug list. Based on 350,000 deaths from pesticide self-poisoning across Asia every year, the findings on the use of the antidotes atropine, pralidoxime and activated charcoal, and the bans of three toxic pesticides in Sri Lanka, are estimated to be saving around 10,000 lives per year in Asia.

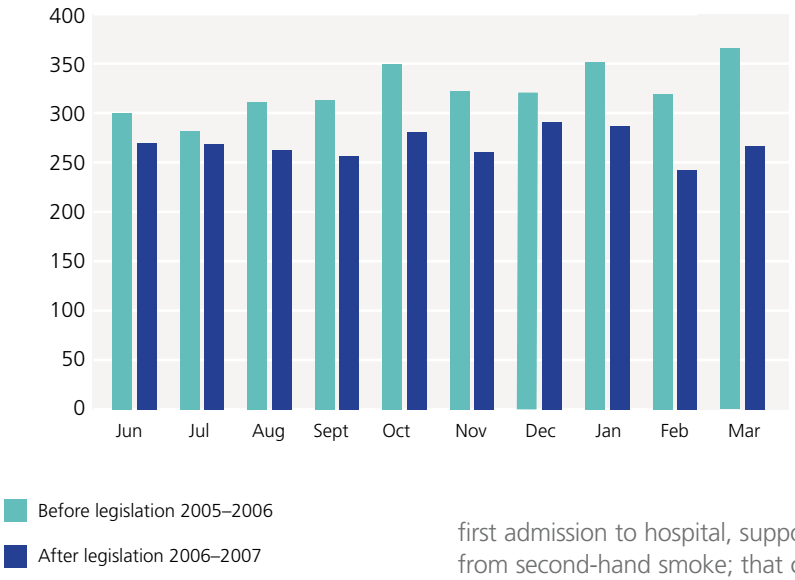
Researcher: Eddleston

The benefits of smoke-free policy in Scotland and worldwide

University of Glasgow

Since the end of March 2006, smoking has been prohibited by law in all enclosed public spaces throughout Scotland, with the specific aim of protecting non-smokers from the effects of second-hand smoke. Studies led by the University of Glasgow have provided the most robust available evidence that smoke-free laws have a significant impact on rates of heart disease, childhood asthma, complications in pregnancy, and stroke.

Admissions for acute coronary syndrome according to month before and after smoke-free legislation



From New England Journal of Medicine, Pell JP, Haw S, Cobbe S, Newby DE, Pell ACH, Fischbacher C, McConnachie A, Pringle S, Murdoch D, Dunn F, Oldroyd K, MacIntyre P, O'Rourke B, Borland W, *Smoke-free legislation and hospitalizations for acute coronary syndrome*, Volume 359, Pages 482–91.

The Glasgow team was the first to perform a prospective study that linked reductions in admission rates to smoke-free legislation. For ten months before the enactment of the smoking legislation in Scotland on the 26 March 2006, and the same ten months in the year following legislation, patients admitted with acute coronary syndrome (ACS) to nine Scottish hospitals were recruited to the study. Over the period studied, the number of hospital admissions for ACS in Scotland decreased by 17%. By comparison, a 4% reduction was reported during the same period in England, where no such legislation had been introduced.

Further studies found that 'never smokers' who were exposed to second-hand smoke had a higher risk of adverse events (such as death or rehospitalisation) within 30 days of first admission to hospital, supporting the argument for protecting non-smokers from second-hand smoke; that childhood asthma admissions had been increasing by about 5% each year prior to the introduction of the smoke-free law, but were reduced by 18% per year following introduction of the legislation; that, for women who conceived between 1995 and 2009, there was a drop of more than 10% in the overall number of preterm deliveries, and significant drops of 5% and 8% in the number of infants born either small or very small, respectively, for their gestational age; that the incidence of cerebral infarction, which accounts for 50% of all strokes, was increasing at around 1% per year but, following introduction of the smoke-free law, reduced by around 9%.

This evidence has been used to support policy debate and decision-making in Scotland, the rest of the UK, and around the world. It has also provided a focal point for an extended and high profile global public debate over smoking legislation, and underpins health advice and campaigns published by the World Health Organisation, World Heart Federation and other international bodies.

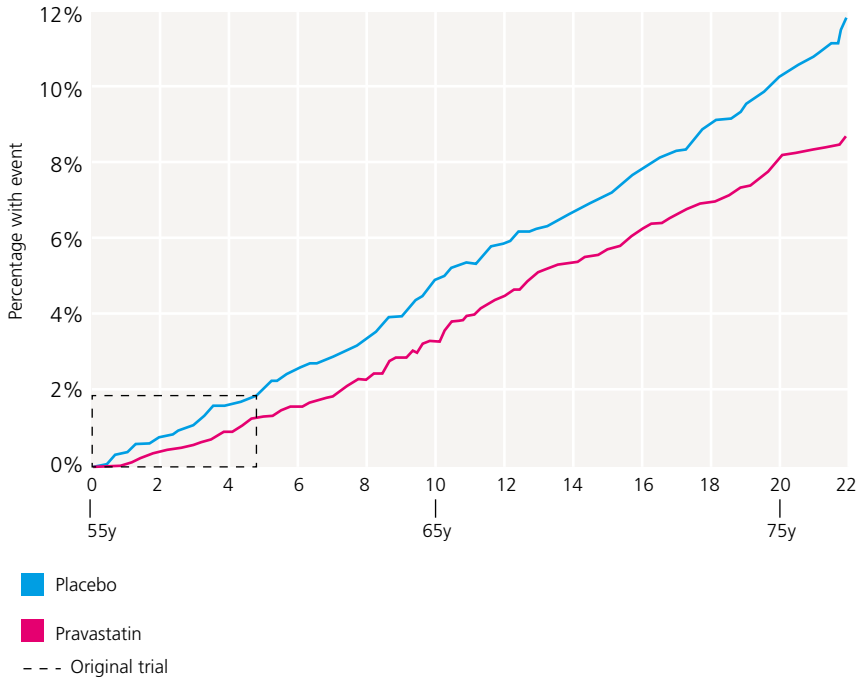
Researchers: Pell and team

Global adoption of statins for cardiovascular disease prevention

University of Glasgow

More than half of UK adults aged over 45 years have high cholesterol levels, the major modifiable risk factor for cardiovascular disease (CVD). Current estimates suggest that more than 7,000 European and US adults die of CVD each day. Internationally recognised clinical trials conducted by the University of Glasgow have provided the cornerstone of the evidence base supporting lipid lowering as a strategy to reduce CVD risk.

Long term follow up in statin studies: WOSCOPS 20-year experience CHD mortality
27% risk reduction over entire period P<0.001



This landmark research drove the global adoption of statins as the first-line medical option for prevention of CVD and continues to shape modern day lipid-lowering guidance and practice worldwide, with associated benefits for patients and healthcare systems. Statins offer major benefits for patient outcomes, including reduction in mortality and major CVD events.

The ground-breaking West of Scotland Coronary Prevention Study (WOSCOPS) was a clinically driven primary prevention randomised controlled trial (RCT): the researchers purposely targeted individuals with no history of heart attack who were apparently healthy yet were at a high risk of having a heart attack in the near future based on their cholesterol levels. The team randomised 6,595 men (aged 45–64 years) with raised low-density lipoprotein cholesterol levels to treatment with pravastatin or placebo and participants were followed for an average of five years. Pravastatin reduced the risk of a first-time heart attack (myocardial infarction, MI) or death from coronary heart disease (CHD) by 31% and was well tolerated. WOSCOPS therefore set the stage for statins as a safe primary prevention therapy for reducing CHD risk and provided conclusive evidence in support of the hypothesis that a raised blood cholesterol level is a modifiable risk factor for CVD.

The University of Glasgow led/steering committee involvement in RCTs on lipid lowering dominates the evidence base in current, high profile clinical guidelines on lipid lowering. 2011 ESC/EAS guidelines on the management of dyslipidaemias state that 'not only should those at high risk be identified and managed; those at moderate risk should also receive professional advice regarding lifestyle changes, and in some cases drug therapy will be needed to control their plasma lipids'. The guidelines also underscore the need to promote primary prevention efforts. Adults with a 20% chance of developing CVD within a 10-year timespan should be offered a statin for primary prevention. Furthermore, statins are unequivocally recommended for individuals considered to be at very high risk; namely, patients with diabetes (if aged over 40 years), chronic kidney disease or peripheral arterial disease, as well as those who have previously experienced a CVD event.

WOSCOPS continues to impact prevention strategies with the recently announced 20-year follow up (presented at the American Heart Association 2014) showing clear long-term efficacy and safety. This evidence lays to rest many current concerns concerning the widespread use of these drugs in the population.

Researchers: Shepherd and team

Landmark advances in outcomes for patients with heart failure

University of Glasgow

Heart failure is a complex syndrome in which the heart is unable to pump sufficient blood to meet the demands of the body. The incidence of heart failure increases with age, and the condition progressively leads to a significant debilitation of physical capacity and quality of life. Heart failure is associated with high mortality and more than 50% of patients die within five years of diagnosis. The condition represents a substantial economic burden to health services, with nearly 17 million people living with a heart failure diagnosis in the UK, USA and Europe. In 2010/2011 the cost of heart failure management in the NHS was in excess of £2 billion; approximately 70% of this expenditure was due to hospitalisation costs. Drugs can limit progression of the disease and patients are typically treated with multiple drugs that are prescribed for the rest of their lives.

Researchers at the University of Glasgow have made seminal contributions to the understanding of the causes, epidemiology, diagnosis and treatment of heart failure. Glasgow investigators conducted some of the first studies of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) in patients, studies showing non-ACE generation of angiotensin II and a proof of concept study for using a mineralocorticoid receptor antagonist (MRA) in mild heart failure. This crucial background work resulted in their leadership roles on large-scale randomised clinical trials demonstrating the value of each of the effective drug treatments for heart failure: beta-blockers, ACE inhibitors, ARBs and MRAs. The studies have provided the evidence base for current clinical recommendations for the management of heart failure which employ combinations of these drugs.

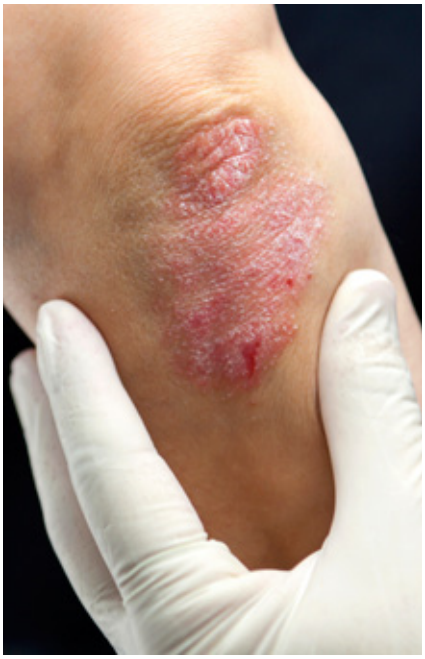
The landmark demonstration of the lifesaving benefits of the MRA, eplerenone in patients with heart failure is the biggest breakthrough in the drug management of heart failure since that of beta-blockers, and is the most recent change in these new international guidelines.

The reach of the recommendations based on University of Glasgow research impacts the clinical management of heart failure worldwide. These have contributed to the reduction in mortality and hospitalisation rates (by approximately 25% and 40% respectively) recorded in the past two decades, with mortality rates post 2008 continuing to follow this trend.

Researchers: **Cleland, McMurray, Dargie, Ford, McDonagh**

Towards a new, safe, oral treatment for psoriasis and psoriatic arthritis

University of Glasgow



Psoriasis is a chronic inflammatory skin disorder affecting up to 2.5% of the world's population, approximately 30% of whom eventually develop psoriatic arthritis, which can lead to debilitating long-term health problems. To date, therapies have been limited owing to side effects or reductions in efficacy.

Researchers at the University of Glasgow developed internationally recognised research to identify focused drug targets that would alleviate the symptoms of inflammatory skin conditions. To do this, they undertook a comprehensive study of the mechanisms underpinning disease development through a period that spanned 25 years. The work of the group worked on the identification of new targets in a messenger pathway termed 'cAMP signalling'. The researchers focused on the compound PDE4 family of cAMP regulators, which are important molecules involved in cell signalling and are predominantly expressed in pro-inflammatory conditions such as psoriasis and other inflammatory skin conditions. The research led directly to the identification that different PDE4 forms would function differently in different parts of the cells and could be targeted to affect disease process.

Working with US biotech company Celgene, which had identified compounds developed to treat cancer that modified PDE4 related inflammatory activity, the Glasgow researchers demonstrated the significant anti-inflammatory potential of these molecules. They identified the lead compounds and assays to screen for potential therapeutics for the treatment of psoriasis and psoriatic arthritis to facilitate their clinical development. This process led to the identification of a lead compound (apremilast), which was subsequently developed by Celgene. Between 2010 and 2013, phase 3 trials on apremilast validated it as a safe and clinically effective when given orally.

On the basis of this work apremilast was submitted for regulatory approval of its use in patients with psoriatic arthritis to the health authorities of the USA and Canada in March 2013. In 2010 the market for psoriasis treatment alone was valued at $3.9 billion. Further submissions to health authorities in the USA and Europe are expected to seek regulatory approval of apremilast for moderate to severe plaque psoriasis and for psoriatic arthritis and psoriasis in the near future.

Researchers: **Houslay and team**

Reducing violence to improve health, in the UK and internationally

University of St Andrews

The Public Health and Health Policy group at St Andrews University was established in 2008 and has become a leading centre in Violence Reduction Research. Its work includes evaluations of interventions and the study of factors that facilitate or prevent the adoption of effective violence prevention policies in the UK and internationally.

The team started by evaluating a gang member rehabilitation and violence reduction initiative, the Community Initiative to Reduce Violence (CIRV), in Glasgow in 2008. Motivations for positive change among gang members were explored and gaining work experience and obtaining and holding on to employment were identified as being particularly important. A detailed quantitative evaluation then demonstrated a fall of 52% in violent acts and a fall of 84% in knife carriage amongst those engaged in the programme.

Across 2009–2011 the group set about understanding factors that may underlie or precipitate violence, and they were able to show that young prisoners in Scotland have an excess of symptoms related to ADHD. It was found that the presence of these symptoms is predictive of violent breaches of prison discipline. An innovative trans-dermal alcohol monitoring technology was piloted, allowing continual sobriety monitoring, as a possible means to reduce levels of alcohol-related violent reoffending.

Since the start of the 2008 evaluation and the publication of the 2011 results, we have changed police and social work in terms of attitudes, policy and tactics, substantially altering what these professional groups think is possible in dealing with violent young men. This work has changed the way social workers practise and how they are managed, and the Prime Minister and national newspapers cited it as a solution after the London riots. Its impact is a positive change in young people's lives, transforming their prospects from those of a lifetime of intermittent imprisonment to one of useful and meaningful societal involvement and contribution.

Researchers: **Donnelly and team**

A new psychological intervention for cancer patients to alleviate heightened fears of recurrence

University of St Andrews

Fear of recurrence is a major concern for many cancer patients. Cancer survival has improved to the extent that many health commentators now regard it as a chronic disease. This has strengthened the field of cancer survivorship to the extent that services are being developed to address patient concerns more closely. Recurrence fears are related to psychological variables not clinical factors, such as the severity of the treated disease.

Over a third of patients find the prospect of a recurrence troubling and anxiety-provoking to the extent that longer-term rumination of this concern results in mood change and depressive symptomology. The effects are insidious and can feature many years after active treatment. Patients respond to high fear of recurrence by demanding multiple health checks and avoiding making future plans. The AFTERc (Adjustment of Fear, Threat or Expectation of a Recurrence of cancer) intervention creates a completely new approach based upon a cognitive behavioural theory which predicts that patients regard every unusual physical sensation as a signal for cancer return. The novel feature of AFTERc is that it makes this process explicit and encourages patients to reflect on other possibilities and how characteristic behaviours can be modified and communicated to close family members and the clinical team. Other inaccuracies in thinking are elucidated in a personal approach to planning incremental changes. Fears are exposed, discussed and managed using therapeutic techniques that are built upon clinical skills of rapport building, reinforcement, sharing of concerns within a family context and explicitly engaged to change behaviour and management of anxiety and potential mood change.

A new AFTER intervention built upon the original to include detailed supervisory notes, aide memoires for specialist staff in the 'field' (in clinics) with source materials referenced to explicit therapeutic procedures is being launched shortly on the St Andrews Medical School website. A Mini-AFTER version for use by specialist cancer nurses via the telephone is currently being feasibility tested. Initial results are promising with a large effect size reported.

This has resulted in a new readily attainable measure of fear of recurrence, as well as the delivery of training and implementation of the AFTER intervention into clinical practice, resulting in improvement in the quality of patient care.

Researcher: Humphris

For more on medical research in the UK as a whole, see *Health of the Nation: The impact of UK medical schools' research,* available at www.medschools.ac.uk

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