

Care bundle reduces deaths from emergency abdominal surgery

Adopting a 'care bundle' devised by patient safety specialists has led to a decrease in the overall death rate for patients undergoing emergency abdominal surgery from 16% to 10% – a

Dr Nial Quiney, Consultant in Anaesthesia and Intensive Care Medicine, Royal Surrey County Hospital, Guildford



38% reduction in the death rate (Huddart et al, 2014).

The care bundle was developed at the Royal Surrey County Hospital in Guildford and implemented in the Royal United Hospital Bath, Torbay Hospital and the Royal Devon and Exeter Hospital. The results were analysed by academics at the University of Bradford.

The care bundle included five elements: an initial assessment with early warning scores; delivery of early antibiotics; a maximum of 6 hours between the decision to operate and surgery; goal-directed fluid therapy; and postoperative intensive care.

Dr Nial Quiney, Consultant in Anaesthesia and Intensive

Care Medicine at the Royal Surrey County Hospital, said: 'Although we have relatively good outcomes from elective surgery, we've known for a long time that emergency surgical admissions have poor outcomes. This is caused by a range of factors, including multi organ failure and sepsis. Often these emergency cases are elderly patients with additional pre-existing conditions.

He continued: 'The quality of care following emergency surgery needs to draw level with what is offered following elective surgery. Implementing this care bundle in four hospitals goes a long way towards achieving that. The results

we've achieved with this project have been remarkable: around 50 000 of these operations are carried out in the UK each year. We estimate that the improvements we've made could enable hospitals to save an additional 2–3 000 lives.'

The researchers are planning to work with other hospitals in England to implement the care bundle, with the goal of seeing it adopted as a standardized model of care across the UK.

Huddart S, Peden CJ, Swart M et al, and the ELPQuiC Collaborator Group (2014) Use of a pathway quality improvement care bundle to reduce mortality after emergency laparotomy. *Br J Surg* (doi: 10.1002/bjs.9658)

Preterm and low birth weight increases risk of hip arthroplasty

Researchers from Australia (Hussain et al, 2014) report that low birth weight and preterm birth are linked to increased risk of osteoarthritis-related hip replacements in adulthood, although this change in risk was not seen for knee arthroplasty.

The study used data from 3604 participants of the Australian Diabetes, Obesity and Lifestyle Study who were 40 years of age or older at the time data on joint replacement surgeries were collected. Participants provided information about their weight at birth and if they were prematurely delivered.

The participants' records were then linked to data on knee and hip replacements as a result of osteoarthritis (2002–11) from the

Australian Orthopaedic Association National Joint Replacement Registry.

Of the participants, 116 had knee replacement surgery and 75 underwent hip arthroplasty for osteoarthritis. Low birth weight and preterm birth were linked to increased incidence of hip arthroplasty independent of age, sex, body mass index, education level, hypertension, diabetes, smoking and physical activity. Researchers found no significant association between low birth weight or preterm birth and knee replacement surgery.

Hussain SM, Wang Y, Wluka AE, Shaw JE, Magliano DJ, Graves S, Cicuttini FM (2014) Association of low birth weight and preterm birth with the incidence of knee and hip arthroplasty for osteoarthritis. *Arthritis Care Res* (doi: 10.1002/acr.22475)

Women receive dialysis treatment less often than men

Regular haemodialysis or a kidney transplant are often the only way to keep patients with chronic kidney disease, alive. A group at the MedUni Vienna and the Arbor Research Collaborative for Health (Ann Arbor, Michigan, USA) has used patient data to show that women receive dialysis treatment much less often than men, despite statistics showing that women suffer from kidney disease more frequently than men.

Patient data have been collected in the Dialysis Outcomes and Practice Patterns Study since 1996 and subjected to scientific analysis. These data, from over 206 000 patients, were investigated for gender differences.

In all twelve countries involved in the analysis (Australia, Belgium, Canada, France, Germany, Italy, Japan,

Spain, Sweden, the UK and the USA), more men were treated with dialysis. The percentage distribution averaged 59% men to 41% women, with further differences noted between individual countries.

Looking to explain these differences, Alexandra Kautzky-Willer from the MedUni Vienna said: 'There are likely fewer biological reasons than socio-economic ones that are causing this discrepancy.'

In individual countries, different access modalities as well as social imbalances between the genders may make this discrepancy even greater.

Hecking M, Bieber BA, Ethier J et al (2014) Sex-Specific Differences in Hemodialysis Prevalence and Practices and the Male-to-Female Mortality Rate: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *PLoS Med* 11(10): e1001750 (doi: 10.1371/journal.pmed.1001750)

Fewer than half of amputation patients had good care, says NCEPOD report

More than 5000 people in England, Wales and Northern Ireland undergo a major amputation each year, but fewer than half (44%, 229/519) of patients who needed leg amputation received good care because of poorly coordinated care and a lack of multidisciplinary team working. So says the latest report from the National Confidential Enquiry into Patient Outcome and Death (NCEPOD), which also highlights concerns about the growth in diabetes which is increasingly leading to amputation.

Lead report author and consultant vascular surgeon, Professor Michael Gough, stated that: 'A significant improve-

ment is needed in the care of amputation patients given that fewer than half received good care, and that the mortality rate of 12.4% for the procedure was higher than has been reported in the US (9.6%).

He continued: 'Having a limb removed is a life-changing experience and patients need to be supported by a wide range of health professionals, other than just the surgeon. Good multidisciplinary care from the outset is required to ensure that these patients, who often have multiple medical problems, receive the best possible treatment, including treatment of diabetes and heart

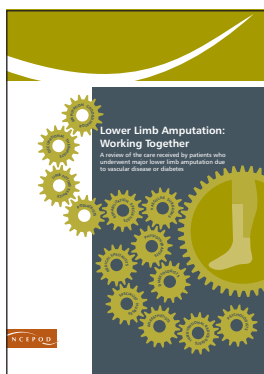
problems, physio-

therapy, rehabilitation and a properly planned discharge.'

Professor Gough added: 'Many amputations are performed in the emergency operating theatre and are often subject to last minute cancellation. These are high-risk patients and they should be given the benefit of surgery in normal working hours where senior doctors can oversee their care.'

Key findings in *Lower limb amputation: working together* also showed that more than half of the patients included in the study had diabetes (55.6%), but there had been little involvement in their care by diabetes specialists.

National Confidential Enquiry into Patient Outcome and Death (2014) *Lower limb amputation: working together*. www.ncepod.org.uk/2014report2/downloads/Working%20Together_FullReport.pdf (accessed 24 November 2014)



Research highlights unseen dangers of pelvic fracture

A new study (pii: afu123) has found pelvic fracture mortality rates to be equivalent to those for hip fracture. The collaboration between the Queen Elizabeth Hospital in Gateshead and Newcastle University included pelvic fracture patients aged 60 years or over, and showed an inpatient mortality rate of 9% and an all-cause mortality rate within 3 months of 13%.

Frailty increases kidney transplant recipients' risk of dying prematurely

Regardless of age, frailty is a strong risk factor for dying prematurely after a kidney transplant (doi: 10.1111/ajt.12992). These findings suggest that patients should be screened for frailty before kidney transplantation, and that those who are identified as frail should be closely monitored after the procedure.

NHS needs more clinical pharmacologists

The British Pharmacological Society has called for an increase in the number of clinical pharmacologists across the four UK nations, to help the NHS surmount its financial challenges.

Combination allows effective, safe and cheap treatment for early rheumatoid arthritis

A new drug combination for rheumatoid arthritis treats the disease just as well as other intensive treatment strategies but with less medication and fewer side effects at a significantly lower cost, found a study from Belgium (Verschuere et al, 2014).

In the 2-year CareRA study, researchers and clinicians in the rheumatology unit at University Hospitals Leuven examined various therapies for early rheumatoid arthritis. Their goal was to find the optimal combination and dosage of three commonly prescribed antirheumatic drugs (methotrexate, sulfasalazine

and leflunomide) in combination with glucocorticoids.

The researchers divided 290 early rheumatoid arthritis patients into three treatment groups. Each group received a different combination therapy: 'COBRA Classic' (methotrexate, sulfasalazine and a high first dose of glucocorticoids), 'COBRA Slim' (methotrexate and a moderate dose of glucocorticoids) or 'COBRA Avant-Garde' (methotrexate, leflunomide and a moderate dose of glucocorticoids).

All three strategies showed a similarly high efficacy: disease remission was achieved in 7 in 10 patients after 16 weeks of

treatment, but they varied significantly when it came to side effects.

The COBRA Slim strategy, which calls for the least amount of medication, had half as many side effects as the two other strategies and was just as effective. It would also be easier to implement in daily practice because it is less complicated.

Verschuere P, De Cock D, Corluy L et al (2014) Methotrexate in combination with other DMARDs is not superior to methotrexate alone for remission induction with moderate-to-high-dose glucocorticoid bridging in early rheumatoid arthritis after 16 weeks of treatment: the CareRA trial. *Ann Rheum Dis* (doi:10.1136/annrheumdis-2014-205489)

Trial confirms 'lower is better' for LDL cholesterol

Lowering low density lipoprotein (LDL) cholesterol levels to below 1.8 mmol/litre, by adding the cholesterol absorption inhibitor ezetimibe to simvastatin, significantly reduces major cardiovascular events in high-risk patients who have suffered an acute coronary syndrome compared to simvastatin alone, according to results from the international IMPROVE-IT study reported at the American Heart Association 2014 Scientific Sessions.

The study randomized 18 144 high-risk patients who had suffered an acute coronary syndrome, including unstable angina, non-ST segment elevation acute myocardial infarction and ST segment elevation acute myocardial infarction, in the previous 10 days to lipid-lowering therapy with either ezetimibe (10 mg) plus simvas-

tatin (40 mg) or simvastatin alone (40 mg).

All patients were considered at high risk for further events and had an initial low density lipoprotein cholesterol level of 3.2 mmol/litre or lower if not previously treated with lipid-lowering therapy on prescription or <2.6 mmol/litre if they had been on prescribed lipid-lowering treatment.

Results showed that patients treated with ezetimibe plus simvastatin combination therapy had a 6.4% lower risk of major cardiovascular events at 7 years compared to those treated with simvastatin alone (hazard ratio 0.936, $P=0.016$). Of these high-risk patients taking ezetimibe/simvastatin 32.7% suffered a major cardiovascular event compared to 34.7% of patients taking simvastatin alone.

'The results provide a real step forward in our under-

standing or the role of low density lipoprotein cholesterol reduction in preventing cardiovascular disease. This is the first trial showing clinical benefit when adding a non-statin agent – ezetimibe – to a statin. And results show that lower is better, in terms of lowering cholesterol to reduce cardiovascular events,' said Dr Mark Signy, consultant cardiologist at Western Sussex NHS Trust and an investigator on the IMPROVE-IT study.

Dr Signy noted that the lower low density lipoprotein cholesterol level in patients treated with ezetimibe/simvastatin (mean level of 1.37 mmol/litre at 1 year) compared to those on simvastatin alone (mean of 1.8 mmol/litre) reaffirmed the low density lipoprotein hypothesis that lowering low density lipoprotein cholesterol reduces cardiovas-

cular events. 'We have previously not had the evidence that going this low further reduces cardiovascular events,' he said.

There were no significant differences between the two treatment groups in adverse events of particular interest, including myopathy and rhabdomyolysis, and gallbladder adverse events. Myopathy was reported in 0.2% of patients treated with ezetimibe/simvastatin and in 0.1% of those randomized to simvastatin alone.

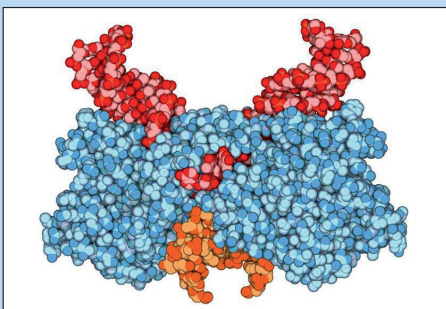
'We now have outcome data to show that low density lipoprotein cholesterol reduction with a combination of ezetimibe plus simvastatin, in comparison with a statin alone, has a significant and well-tolerated further cardiovascular benefit in high-risk patients, even those with relatively low baseline cholesterol levels,' Dr Signy concluded.

Susan Mayor

HIV virulence depends on where virus inserts itself into host DNA

The human immunodeficiency virus (HIV) can insert itself at different locations in the DNA of its human host – and this integration site determines how quickly the disease progresses (Demeulemeester et al, 2014).

The HIV protein integrase (blue) can insert viral DNA (red) at different locations in the DNA of its human host (orange) via two of the more than 200 amino acids that make up integrase's structure.



The HIV protein integrase plays a key role in HIV reprogramming hijacked cells to make new HIV particles: it recognizes a short segment in the DNA of its host and catalyzes the process by which viral DNA is inserted in host DNA.

Integrase can insert viral DNA at various places in human DNA, but how the virus selects its insertion points has puzzled virologists for over 20 years.

A team of researchers has discovered that the answer lies in two amino acids. Dr

Jonas Demeulemeester, first author, explains: 'HIV integrase is made up of a chain of more than 200 amino acids folded into a structure. By modelling this structure, we found two positions in the protein that make direct contact with the DNA of the host. These two amino acids determine the integration site.'

In a second phase of the study, the researchers were able to manipulate the integration site choice of HIV, explains Professor Rik Gijsbers. 'We changed the specific HIV integrase amino acids for those of animal-borne viruses and found that the viral DNA integrated in the host DNA at locations where the animal-

borne virus normally would have done so.'

The team studied the impact of these viral variants on progression towards AIDS in a cohort of African patients who have HIV. The disease progressed more quickly when the integration site was changed.

This insight increases their knowledge of the disease and opens new perspectives. By retargeting the integration site to a 'safer' part of the host DNA, they hope to eventually develop new therapies.

Demeulemeester J, Vets S, Schrijvers R et al (2014) HIV-1 integrase variants retarget viral integration and are associated with disease progression in a chronic infection cohort. *Cell Host Microbe* 16(5): 651–62 (doi: 10.1016/j.chom.2014.09.016)

Only half of patients take their medications as prescribed, but we still do not know which interventions will help them

The cost of patients not taking their medications as prescribed can be substantial in terms of their health. Although a large amount of research evidence has tried to address this problem, there are no well-established approaches to help them, according to a new systematic review (Nieuwlaat et al, 2014).

The authors of the review examined data testing different approaches to increasing medication adherence and patient health. Even though the review included a significant number of the best studies to date, in most cases, problems with the design of the trials made it hard

to determine which approaches actually worked.

Only about half of all patients who are prescribed medication that they must administer themselves actually take their medication as prescribed. Many stop taking medication all together and others do not follow the instructions for taking it properly. However, when researchers in the field have tried to draw together evidence on this, they have found it unreliable and inconsistent.

The researchers looked at data from 182 trials, having added 109 trials published after the previous version of this

review in 2007. The trials studied a wide range of medical conditions and trialled many different interventions for increasing adherence to medication. They revealed wide-ranging effects on adherence and patient health, measured using a large variety of methods, making it very difficult for the researchers to come to firm conclusions about whether any of the interventions worked well.

'The studies varied so much in terms of their design and their results that it would have been misleading to try to come up with general conclusions,' said lead researcher, Dr Robby

Nieuwlaat of the Department of Clinical Epidemiology and Biostatistics at McMaster University, in Hamilton, Canada. 'Based on this evidence, it is uncertain how adherence to medication can be consistently improved. We need to see larger and higher quality trials, which better take in account individual patient's problems with adherence.'

Most trials were unreliable, casting doubt on the validity of the results. Only 17 were of high quality and each of these tested combinations of several different approaches, such as support from family members or pharmacists, education and counselling. Only five of these 17 showed improvements in health outcomes for patients as well as in medication adherence.

The authors have now turned to the research community to help understand the issues. They have created a database of the relevant trials and made this available to other researchers in the field to encourage collaboration and more in-depth analyses on smaller groups of trials.

'By making our comprehensive database available for sharing we hope to contribute to the design of better trials and interventions for medication adherence,' said Dr Nieuwlaat. 'We need to avoid repeating the painful lessons of adherence research to date and begin with interventions that have shown some promise, or at least have not produced repeatedly negative results.'

Nieuwlaat R, Wilczynski N, Navarro T et al (2014) Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 11: CD000011 (doi: 10.1002/14651858.CD000011.pub3)

Non-clinical factors may affect use of intensive procedures at the end of life

A retrospective cohort study was undertaken to examine individual and regional factors associated with the use of intensive medical procedures in the last 6 months of life (Tschirhart et al, 2014).

The Health and Retirement Study, a American longitudinal nationally representative cohort of older adults, included 3069 decedents aged 66 years and older.

Multivariable logistic regression was used to evaluate associations between individual and regional factors and receipt of five intensive procedures: intubation and mechanical ventilation, tracheostomy, gastrostomy tube insertion, enteral and parenteral nutrition, or cardiopulmonary resuscitation in the last 6 months of life.

Approximately 18% of subjects ($n = 546$) underwent at

least one intensive procedure in the last 6 months of life. Characteristics significantly associated with lower odds of an intensive procedure included aged 85–94 years, having Alzheimer's disease or cancer, being a nursing home resident, and having an advance directive. In contrast, living in a region with higher hospital care intensity and black race each doubled the patient's odds of undergoing an intensive procedure.

Individual characteristics and regional practice patterns are important determinants of intensive procedure use in the last 6 months of life. The effect of non-clinical factors highlights the need to better align treatments with individual preferences.

First author Evan Tschirhart commented: 'It's pretty striking the extent to which non-clini-

cal factors – such as where you live and what race you are – appear to influence your chance of undergoing an invasive and potentially uncomfortable procedure at the end of life.'

Tschirhart EC, Du Q, Kelley AS (2014) Factors influencing the use of intensive procedures at the end of life. *J Am Geriatr Soc* 62(11): 2088–94 (doi: 10.1111/jgs.13104)

Evan Tschirhart, fourth year medical student, Icahn School of Medicine, Mount Sinai, New York

