Surgery

Subcuticular sutures or staples use in gastrointestinal surgery

Subcuticular sutures compared with staples have been associated with decreased wound complications and better cosmetic results in many areas of surgery. However, the use subcuticular sutures for wound closure in open gastrointestinal surgery have not been explored.

A 24-institution trial randomised patients to receive either staples or subcuticular sutures after elective gastrointestinal surgery. The incidence of wound complications within 30 days of surgery was the primary endpoint.

In the subcuticular group 382 and 172 patients underwent upper or lower gastrointestinal procedures respectively. Wound complications occurred in 8.4% of patients compared with 11.5% of patients with staples. The 413 patients receiving staples underwent upper gastrointestinal surgery and 101 underwent lower gastrointestinal. Overall, the rates of wound complications did not differ significantly between the two groups, odds ratio 0.709.

Subcuticular sutures, compared with staples do not significantly reduce wound complications in open gastrointestinal surgeries.

Tsujinaka T, Yamamoto K, Fujita J, et al. Subcuticular sutures versus staples for skin closure after open gastrointestinal surgery: a phase 3, multicentre, open-label, randomised controlled trial. *Lancet* 2013; 382: 1105–12.

The burden of adhesions in abdominal and pelvic surgery

Postoperative adhesions are the most common complication following abdominal and pelvic surgery. Not only associated with longer operation times, adhesions may also lead to further complications including bowel obstruction and infertility.

A systematic review and meta-analysis of 196 eligible papers was conducted to estimate the incidence of adhesive small bowel obstructions in patients with a history of peritoneal surgery. A random effects model was used to account for considerable study heterogeneity.

The incidence of small bowel obstruction by any cause after abdominal surgery was 9% and 2% for adhesive small bowel obstruction. Adhesions were the single most common cause of obstruction accounting for 56% of cases and in patients previously treated with surgery the operation was prolonged by a mean of 15 minutes. Pregnancy rates following surgical treatment for inflammatory bowel disease were significantly lower at 50% compared with 80% in patients treated medically.

Postsurgical adhesions complications are frequent with a detrimental impact on patients' health in addition to increasing workload in clinical practice.

Ten Broek R, Issa Y, van Santbrink E, et al. Burden of adhesions in abdominal and pelvic surgery: systematic review and met-analysis. *BMJ* 2013; 347: 5588.

Adipose stem cells in autologous fat grafts

Autologous fat grafting is used with increasing popularity in the treatment of a range of conditions. The use of autologous adipose stem cell (ASC) grafts has been investigated in animal studies with promising results, reporting increased graft volume and improved histological appearance compared with traditional lipofilling. However; results have not shown consistency in humans with resorption rates reported ranging from 25–80%.

A triple-blind study compared the survival of ASC fat grafts with non-enriched fat grafts. 10 participants underwent two liposuctions; one purified sample was enriched with ASC while the other served as a control. After 14 days the two samples were injected subcutaneously into the right and left posterior arm. Immediately after graft volumes were measured by MRI and again after 121 days prior to graft removal.

ASC-enriched graft residual volumes were significantly higher than in the control measuring 23.00 cm^3 and 4.66 cm^3 respectively. This corresponded to 80.9% of the initial volume in the ASC-enriched graft and 16.3% in the control.

ASC-enriched grafting is safe with excellent feasibility.

Kølle S, Fischer-Nielsen A, Mathiasen A, et al. Enrichment of autologous fat grafts with ex-vivo expanded adipose tissue-derived stem cells for graft survival: a randomised placebo-controlled trial. *Lancet* 2013; 382: 1113–20.

Infection

Treating foetal lower urinary tract obstruction

Foetal lower urinary tract obstruction (LUTO) is often caused by congenital abnormalities, often leading to abnormal renal development. LUTO is linked to high perinatal and long-term childhood mortality and morbidity.

A randomised trial assessed the effectiveness of vesicoamniotic shunting verses conservative treatment. Pregnant women whose male foetuses had been diagnosed with isolated LUTO were randomly assigned to receive the shunt or conservative management. The primary outcome was 28-day survival postnatally.

The study was closed early due to poor recruitment. A total of 16 women were assigned to the shunting group and 15 to the conservative management with 12 livebirths in each group. At 28 days survival was higher in the shunt group (eight babies) compared with four in the conservative group. Morbidity in the short and long term was high across both groups. Seven complications occurred in the shunt group resulting in four pregnancy losses.

Survival was higher in the vesicoamniotic shunting group.

Morris RK, Malin GL, Quinlan-Jones E, et al. Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. *Lancet* 2013; 382: 1496–506.

Antiretroviral therapy in infants

Interim results from the CHER trial (children with HIV early antiretroviral) have shown antiretroviral treatment (ART) to be lifesaving. This CHER trial reports the effects of early time-limited ART verses deferred ART.

CHER was a randomised trial of HIV-infected asymptomatic infants in South Africa (<12 weeks) with CD4-positive T lymphoctyes (CD4%) of ≥25%. A cohort of 377 infants was randomly allocated to receive deferred ART (def-ART), immediate ART for 40 weeks (ART-40W), or immediate ART for 96 weeks (ART-96W). First-line combination therapy consisted of lopinavir-ritonavir, zidovudine, and lamivudine. The primary end-point was failure of ART or death.

Proportions of follow-up time spent on ART were 81% in ART-def group, 70% in ART-40W group, and 69% in ART-96W group. The primary end-point was reached in 38% in ART-def group, 25% in ART-40W group, and 21% in ART-96W group. Significant hazard ratios relative to ART-def were calculated as 0.59 for ART-40W and 0.47 for ART-96W.

Early time-limited ART has better outcomes than deferred ART. Longer time on primary ART is marginally more effective.

Cotton MF, Violari A, Otwombe K, et al. Early time-limited antiretroviral therapy versus deferred therapy in South African infants infected with HIV: results from the children with HIV early antiretroviral (CHER) randomised trial. *Lancet* 2013; 382: 1555–63.

Identification and control of poliomyelitis outbreak in China

China was certified as a poliomyelitis-free region in 2000, 6 years after the last case of wild-type indigenous poliovirus was reported in 1994. In 2011, an outbreak of infection with imported wild-type poliovirus occurred in the province of Xinjiang.

A total of 21 cases of infection with wild-type poliovirus and 23 clinically compatible cases were identified in Southern Xinjiang resulting in the declaration of a public health emergency. Sequence analysis identified the source of the outbreak originated in Pakistan. Serologic and coverage surveys were created to assess viral propagation risk whilst surveillance for acute flaccid paralysis was enhanced. Five rounds of vaccination with live, attenuated oral poliovirus vaccine (OPV) were conducted among children and adults, with 43 million OPV doses administered. Trivalent OPV was used in three rounds, and monovalent OPV type 1 was used in two rounds. The outbreak was stopped within 1.5 months.

Poliomyelitis free countries remain at risk of outbreaks while poliovirus circulates elsewhere in the world.

Luo H-M, Zhang Y, Wang X-Q, et al. Identification and Control of a Poliomyelitis Outbreak in Xinjiang, China. *NEJM* 2013; 369: 1981–90.

Obs & Gyn

Caseload midwifery care verses standard maternity care

Caseload midwifery care involves allocating women a named midwife working within a midwifery group practice and thus ensuring continuity of care throughout and after a woman's pregnancy. Women with low-risk pregnancies benefit from caseload midwifery care but no data exist for women with identified risk factors.

An Australian randomised trial assigned women to receive caseload midwifery care or standard maternity care. Caseload care women received care from a named midwife while the controls received care from standard rostered care. The primary outcome measured the proportion of women who had a caesarean section.

A total of 871 women and 877 were assigned to caseload and standard care respectively. The proportion of caesarean sections did not differ significantly between the groups, however, the number of elective caesarean sections were significantly lower in the caseload care (8%) compared with the standard care (11%). Neonatal outcomes did not differ between the groups but the total cost per woman was AUS$566.74 less in the caseload care.

Caseload midwifery care is safe and cost-effective for women of any risk.

Tracy SK, Hartz DL, Tracy MB, et al. Caseload midwifery care versus standard maternity care for women of any risk: M@NGO, a randomised controlled trial. *Lancet* 2013; 382: 1723–32.

Pre-eclampsia rates in the United States

The prevalence of pre-eclampsia has shown variation over time, indicating population level risk factors may influence these trends. A retrospective population study of 120 million births between 1980 and 2010 measured trends in pre-eclampsia in relation to maternal age, year of delivery, and birth cohorts.

The overall rate of pre-eclampsia was 3.4% with women at the extremes of maternal age are at greatest risk. Women delivering in 1980 had a 6.7-fold increased risk of severe pre-eclampsia compared with those women delivering in 2003; however period effects have declined since 2003. Trends for severe pre-eclampsia showed a moderate birth cohort effect with women born in the 1970s at increased risk. The pattern was similar but attenuated in mild pre-eclampsia.

Changes in prevalence of obesity and smoking may partially explain these trends but changes in diagnostic criteria have also contributed to age-period-cohort effects.

Ananth C, Keyes K, Wapner R. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. *BMJ* 2013; 347: 6564.

Probiotic supplementation in pregnancy for the prevention of asthma and wheeze

The microflora hypothesis of allergic disease has been proposed to explain the rising incidence of asthma and other allergic disorders. Meta-analysis data showed that probiotic supplementation during pregnancy or infancy decreased incidence of atopic dermatitis by 21%. A recent systematic review and meta-analysis of 20 trials evaluated the association of probiotic supplementation during pregnancy or infancy with doctor diagnosed childhood asthma and wheeze.

The overall rate of asthma was 10.7% and 33.3% for wheeze, with lower respiratory tract infections (LRTI) occurring in 13.9% of children. The insignificant relative risk ratios for asthma and wheeze in women receiving probiotics were 0.99 and 0.97 respectively. The relative risk ratio of LRTI after probiotic supplementation was insignificant at 1.26.

There was no evidence to support the association between perinatal administration of probiotics and doctor diagnosed asthma or childhood wheeze.

Azad MB, Coneys JG, Kozyrskyj AL, et al. Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis. *BMJ* 2013; 347: 6471.

Rheumatology

New monoclonal antibody for treatment of ankylosing spondylitis

Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory condition. Interleukin 17 (IL-17) has been proposed as a key inflammatory mediator of the disease; therefore a recent trial assessed the efficacy and safety of the anti-IL-17A monoclonal antibody, secukinumab.

The double-blinded, proof-of-concept trial took place across eight European Centres. Patients were randomly assigned to receive intravenous secukinumab (2 x 10 mg/kg) (n=24) or a placebo (n=6) every 3 weeks. The primary end-point was the percentage of patients with a 20% response according to the Assessment of SpondyloArthritis international Society criteria for improvement (ASAS20) at 6 weeks. Safety was assessed up to week 28.

At week 6, ASAS response estimates were significant, a reduction of 59% in patients receiving secukinumab was observed versus 24% on placebo. One serious adverse event (subcutaneous *Staphylococcus Aureus* abscess) occurred in the secukinumab-treated group.

Secukinumab rapidly reduced clinical and biological signs of active AS and was well tolerated.

Baeten D, Baraliakos X, Braun J, et al. Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. *Lancet* 2013; 382: 1705–13.

Efficacy of interspinous process devices in treating lumbar spinal stenosis

The modest outcomes from conventional decompression surgery and increasing popularity of minimally invasive techniques has led to the development of interspinous process devices designed

to stabilise and increase interspinous distance whilst indirectly decompressing the nerve roots.

A multicentre, double-blinded trial assessed whether a interspinous process device implant or conventional surgical decompression was more effective in patients with intermittent neurogenic claudication due to lumbar spinal stenosis. A total of 80 patients received the device whilst 79 underwent spinal bony decompression. The primary outcome measured symptom severity, physical function, and patient satisfaction at 8 weeks and 1 year.

At 8 weeks, the success rate of the device group was not superior to that for the conventional group. No differences in disability or other parameters were observed during the first year. However, repeat surgeries were significant higher in the device group (n=21; 29%) compared with the conventional group (n=6; 8%).

There is no short-term advantage of the interspinous process device over conventional surgical decompression.

Moojen WA, Arts MP, Jacobs WCH, et al. Interspinous process device versus standard conventional surgical decompression for lumbar spinal stenosis: randomized controlled trial. *BMJ* 2013; 347: 6415.

Mortality rates in hip resurfacing and replacements

Total hip replacement (THR) is a highly successful treatment of symptomatic osteoarthritis, but metal-on-metal resurfacing is a common alternative in younger patients. However, there are little data on the mortality risks of these operations in the long term.

A retrospective cohort study compared 10-year mortality rates among patients with cemented THR (n=22311), uncemented THR (n=24303), and metal-on-metal resurfacing (n=8101). The primary outcome was all cause mortality at 10 years after surgery.

Ten-year rates of cumulative mortality were 3.6% for metal-on-metal hip resurfacing versus 6.1% for cemented THR, and 3.0% for metal-on-metal hip resurfacing versus 4.1% for uncemented THR. Survival probability was highest among the metal-on-metal resurfacing group (hazard ratio 0.51 for cemented THR; 0.55 for uncemented THR).

Metal-on-metal hip resurfacing has reduced mortality in the long term even after adjustment for confounding variables.

Kendal AR, Prieto-Alhambra D, Arden NK, Carr A, Judge A. Mortality rates at 10 years after metal-on-metal hip resurfacing compared with total hip replacement in England: retrospective cohort analysis of hospital episode statistics. *BMJ* 2013; 347: 6549.

Oncology

Autologous transplantation in non-Hodgkin's lymphoma

The efficacy of autologous stem-cell transplantation during the first remission in patients with diffuse, aggressive non-Hodgkin's lymphoma and a 5-year survival prediction of less than 50% (intermediate-high or high-risk patients) remains controversial and is untested since the introduction of rituximab therapy.

Intermediate-high or high-risk patients who had responded to chemotherapy were divided into an autologous stem-cell transplantation group (n=125) or a control group (n=128) who were given additional chemotherapy. The end-points included 2-year progression-free survival and overall survival.

The transplant group had a 2-year progression-free rate of 69% compared with the control group of 55%, giving a significant hazard ratio of 1.72. Overall 2-year survival hazard ratios were non-significant, however, in high-risk patients the 2-year survival rate was 82% in the transplant group and 64% in the control group.

Early stem-cell transplant improved progression free but overall survival with transplantation was not improved.

Stiff PJ, Unger JM, Cook JR, et al. Autologous Transplantation as Consolidation for Aggressive Non-Hodgkin's Lymphoma. *NEJM* 2013; 369: 1681–90.

Interventions for non-metastatic squamous cell carcinoma of the skin

Cutaneous squamous cell carcinoma (SCC) is the second most common type of non-melanoma skin cancer. Current guidelines recommend surgical excision, however, evidence of SCC treatment has not been rigorously studied. A systematic review of 118 observational studies aimed to assess the efficacies of different treatments.

Pooled estimates for the recurrence of SCC were lowest after cyrotherapy (0.8%) followed by curettage and electrodesiccation (both 1.7%) but these techniques were often used in treatment for small, low-risk lesions. After Mohs micrographic surgery, the estimate of local recurrence was 3%, which was non-significantly lower than after standard surgical excision (5.4%) and radiotherapy (6.4%). Pooled average recurrence was 26.4% after photodynamic therapy, whilst evidence was limited for laser, topical and systemic treatments.

Outcomes should be interpreted cautiously due to biases inherent in the types of studies included. Further evidence is needed to develop a prognostic model.

Lansbury L, Bath-Hextall F, Perkins W, Stanton W, and Leonardi-Bee J. Interventions for non-metastatic squamous cell carcinoma of the skin: systematic review and pooled analysis of observational studies. *BMJ* 2013; 347: 6153.

nab-Paclitaxel plus gemcitabine therapy for pancreatic cancer

Gemcitabine is the current standard first-line treatment for advanced pancreatic cancer. However, phase 1–2 trials of nab-paclitaxel plus gemcitabine have shown promising results. A phase 3 randomised controlled trial assessed the efficacy and safety of the combination therapy verses gemcitabine monotherapy.

Patients were randomly assigned to receive either gemcitabine monotherapy (n=430) or the combination therapy of gemcitabine plus *nab*-paclitaxel (n=431). End-points included overall survival and progression-free survival.

The median overall survival was 8.5 months in the *nab*-paclitaxel-gemcitabine group compared with 6.7 months in the gemcitabine group, yielding a significant hazard ratio of 0.72. At 1 year, the survival rate was 35% in the combination group verses 22% in the monotherapy group (9% verses 4% at 2 years). The proportion of serious adverse effects was higher in the combination therapy group (50%) than the monotherapy group (43%), the most common being neutropenia, fatigue, and neuropathy.

nab-Paclitaxel plus gemcitabine improved overall survival but rates of adverse effects were higher.

Von Hoff DD, Ervin T, Arena FP, et al. Increased Survival in Pancreatic Cancer with *nab*-Paclitaxel plus Gemcitabine. *NEJM* 2013; 369: 1691–703.

Critical Care

Induced hypothermia in severe bacterial meningitis

Despite advances in care, mortality and morbidity remains high in adults with acute bacterial meningitis. Therapeutic hypothermia is widely used in global cerebral hypoxia and evidence from animal models suggest moderate levels of hypothermia may have favourable effects for bacterial meningitis.

A multicentre randomised controlled trial assessed whether inducing hypothermia improves outcomes in severe

bacterial meningitis in 98 comatose patients. The intervention group received sufficient cold saline to reduce body temperature to between 32^{0}C and 34^{0}C for 48 hours. The control group received standard care. The outcome was measured using the Glasgow Outcome Scale (a score of 5 (favourable outcome) verses a score of 1–4 (unfavourable outcome) at 3 months.

The trial was stopped prematurely after concerns over excess mortality in the hypothermia group (51%) verses 31% in the control group, giving a significant relative risk of 1.99. At 3 months, 86% of the hypothermia group had an unfavourable outcome compared with 74% of the control group.

Moderate hypothermia did not improve the outcome in patients and may be harmful.

Mourvillier B, Tubach F, van de Beek D, et al. Induced hypothermia in severe bacterial meningitis: A randomized clinical trial. *JAMA* 2013; 310: 2174–83.

Colloids or crystalloids in hypovolaemic shock?

Uncertainties still remain over whether use of colloids or crystalloid solutions pare superior for the management of hypovolaemic shock. Therefore the multinational randomised controlled trial, CRISTAL, compared mortality rates at 28 days and 90 days in patients admitted to the intensive care unit (ICU) with hypovolaemic shock. Overall, 1414 patients received various colloids while 1443 patients were administered colloids.

At 28 days, the number of deaths did not significantly differ between the two groups. A mortality rate of 25.4% in the colloid group was observed compared with 27.0% in the crystalloids group. The 90-day mortality among the colloids group had significantly lower (30.7%) than in the crystalloid group (34.2%) (relative risk, 0.92).

The use of crystalloids or colloids did not have a significant difference on the 28-day mortality. However, at 90 days the mortality was lower in the colloid group.

Annane D, Siami S, Jaber S, et al. Effects of fluid resuscitation with colloids vs crystalloids on mortality in critically ill patients presenting with hypovolemic shock: The cristal randomized trial. *JAMA* 2013; 310: 1809–17.

Beta-blocker therapy usage in severe septic shock

Noradrenaline is the mainstay treatment for sepsis related hypotension but it is known that adrenergic stress can have multiple adverse effects. The use of β-Blocker therapy may control heart rate and attenuate adrenergic stimulation but treating tachycardia in septic shock is controversial.

An open-label randomised controlled trial tested the effects of short-acting β-blocker, esmolol, in patients with severe septic shock and a heart rate of above 95/min requiring noradrenaline. The primary outcome was to maintain a rate between 80/min and 94/min over 96 hours. The control group received standard care.

Target heart rate reductions (mean reduction, 28/min) were achieved in all patients in the esmolol group verses the control group (mean reduction, 6/min). Compared with the control group, the esmolol group also increased stroke volume, maintained mean arterial pressure, and reduced noradrenaline requirements. The 28-day mortality in the esmolol group was 49.4% compared with 80.5% in the control group yielding a significant adjusted hazard ration of 0.39.

Esmolol was associated with reductions in heart rates without increased adverse effects.

Morelli A, Ertmer C, Westphal M, et al. Effect of heart rate control with esmolol on hemodynamic and clinical outcomes in patients with septic shock: A randomized clinical trial. *JAMA* 2013; 310: 1683–91.

Psychiatry

Premature mortality in epilepsy

Premature mortality is substantial in epilepsy, however, the contribution of psychiatric comorbidity is unknown but clarification may help suicide prevention strategies.

A Swedish population study aimed to assess the prevalence and risks of premature mortality from external causes such as suicide, accidents, and assaults in epileptic patients, with and without psychiatric comorbidities. Risks and premature mortality rates were recorded in diagnosed epileptic patients (n=69 995) and were age and sex-matched to a general population control group (n=660 869) and unaffected siblings (n=81 396).

Premature mortality was substantially elevated, with adjusted odds ratio (aOR) being significant at 11.1 compared with the general population and 11.4 for unaffected siblings. Non-vehicle accidents aOR was significantly higher in the epilepsy group (5.5) while the aOR for suicide was 3.7 when compared with the general population. Of the epileptic patients that died from external causes 75.2% had comorbid psychiatric disorders, with strong associations to co-occuring depression (aOR, 13) and substance misuse (22.4) compared with patients with no epilepsy and no psychiatric comorbidity.

Psychiatric comorbidity plays a substantial role in premature mortality in epilepsy.

Fazel S, Wolf A, Långström N, Newton CR, and Lichtenstein P. Premature mortality in epilepsy and the role of psychiatric comorbidity: a total population study. *Lancet* 2013; 382: 1646–54.

The global burden of mental and substance use disorders

Historically, mental and substance use disorders were not a global health priority; however, international efforts to improve mental health of global populations are now underway.

Using the GBD data, estimation of the burden of disease attributable to mental and substance use disorders was calculated in terms of disability-adjusted life years (DALYs), years of life lost to premature mortality (YLL), and years lived with disability (YLD).

In 2010, mental and substance use disorders accounted for 183.9 million DALYs, 7.4% of all DALYs worldwide. Globally the total number of YLLs calculated was 8.6 million (0.4% of all YLL) and 175.3 million YLDs (22.9% of all YLDs) with mental and substance use disorders were the leading cause of YLDs worldwide. Depressive disorders accounted for 40.5% of DALYs caused by mental and substance use disorders, followed by anxiety disorders (14.6%), and illicit drug use disorders (10.9%). Mental and substance use disorders have increased by 37.6% between 1990 and 2010.

Mental and substance use disorders make up a significant proportion of the global burden of disease and is increasing.

Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013; 382: 1575–86.

The global burden of illicit drug use

No systematic reviews have attempted to establish the worldwide burden of illicit drug use and dependence. Therefore, the GBD conducted the first review to estimate the global prevalence of amphetamine, cannabis, cocaine, and opioid dependence whilst quantifying their burden using DALYs.

Illicit drug dependence directly accounted for 20 million DALYs in 2010, accounting for 0.8% of global all-cause DALYs. Global dependence was highest for opioids and amphetamines, with opioids accounting for 9.2 million DALYs. There was increased proportion of burden in countries with the highest incomes. Injecting drug use as a risk factor for HIV accounted for 2.1 million DALYs and as a risk factor for hepatitis C it accounted for 502 000 DALYs. Suicide as a risk of amphetamine dependence accounted for 854 000 DALYs, and as a risk of opioid dependence for 671 000 DALYs.

Illicit drug use is an important contributor to the global burden of disease.

Degenhardt L, Whiteford HA, Ferrari AJ, et al. Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010. *Lancet* 2013; 382: 1564–74.

Paediatrics

The duration of respiratory tract infections in children

Respiratory tract infections (RTIs) in children are common and often self-limiting but account for over a third of paediatric consultations in the United Kingdom and the United States. Estimates of the expected time courses of common RTIs are highly variable and not consistently evidence based.

A systematic review of randomised controlled trials and observational studies of children with acute RTIs aimed to determine the duration of symptoms including: earache, sore throat, cough (acute cough, bronchiolitis, and croup), and the common cold.

In 90% of children, earache was resolved by 7 to 8 days, sore throat between 2 and 7 days, and croup by 2 days. Bronchiolitis was resolved by 21 days in 90% of children, common cold in 15 days, and non-specific RTI symptoms in 18 days.

The duration of earache and common colds are longer than current guidelines in the United Kingdom and the United States.

Thompson M, Vodicka T, Blair P, et al. Duration of symptoms of respiratory tract infections in children: systematic review. *BMJ* 2013; 347: 7027.

Thalidomide for paediatric-onset Crohn's disease

Paediatric-onset Crohn's disease is more aggressive than adult-onset disease; it is often drug-resistant and without adequate treatment children may suffer permanent impairments. Observational studies assessing thalidomide treatment have reported remission rates of 40% to 70% in patients with Crohn's disease.

A multicentre randomised controlled trial evaluated the use of thalidomide (1.5 to 5.5 mg/kg per day) in patients with active Crohn's disease despite immunosuppressive treatment. The primary outcome measured clinical remission at week 8.

A total of 13 of 28 patients in the thalidomide group reached clinical remission compared with 3 of 26 in the placebo group (significant relative risk, 4.0). Responses at 4 weeks were not different, but greater improvement was observed at 8 weeks in the thalidomide group. Mean duration of clinical remission was 181.1 weeks in the thalidomide group verses 6.3 weeks in the placebo. The cumulative incidence of severe adverse effects was 2.1 per 1000 patient weeks, with peripheral neuropathy being the most frequent.

Thalidomide improved clinical remission at 8 weeks in aggressive paediatric-onset Crohn disease.

Lazzerini M, Martelossi S, Magazzù G, et al. Effect of thalidomide on clinical remission in children and adolescents with refractory crohn disease: A randomized clinical trial. *JAMA* 2013; 310: 2164–73.

Vaccine for prevention of influenza in children

Routine vaccination of children against influenza is recommended in the United States despite limited evidence. Commonly used trivalent vaccines contain one influenza B virus lineage but may be ineffective against other B lineage viruses. A recent study evaluated the efficacy of inactivated quadrivalent influenza vaccine (QIV) for the prevention of influenza A or B in children.

Children were randomised to receive the QIV (n=2379) and 2398 children received a control vaccine, hepatitis A vaccine. The primary end-point was confirmed real-time polymerase chain reaction (rt-PCR) influenza A or B.

A total of 62 children in the QIV group (2.4%) and 148 in the control group (5.73%) had influenza, representing a significant QIV efficacy of 59.1%. For moderate-to-severe influenza the attack rate was 0.62% in the QIV group and 2.36% in the control, giving a significant QIV efficacy of 74.2%. Serious adverse effects were observed in 1.4% of the QIV group (0.9% in the control).

The QIV was efficacious in preventing influenza in children.

Jain VK, Rivera L, Zaman K, et al. Vaccine for prevention of mild and moderate-to-severe influenza in children. *NEJM* 2013 (online). DOI: 10.1056/NEJMoa1215817.