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BMJ (21 April 2018, Vol. 361, No. 8149)

Use of haloperidol versus atypical antipsychotics and risk of in-hospital death in patients with acute myocardial infarction: Cohort study
Yoonyoung Park, Brian T Bateman, Dae Hyun Kim, et al.
BMJ 2018; 360 (Published 28 March 2018)
https://www.bmj.com/content/360/bmj.k1218

Abstract
Objective To compare the risk of in-hospital mortality associated with haloperidol compared with atypical antipsychotics in patients admitted to hospital with acute myocardial infarction.
Design Cohort study using a healthcare database.
Setting Nationwide sample of patient data from more than 700 hospitals across the United States.
Participants 6578 medical patients aged more than 18 years who initiated oral haloperidol or oral atypical antipsychotics (olanzapine, quetiapine, risperidone) during a hospital admission with a primary diagnosis of acute myocardial infarction between 2003 and 2014.
Main outcome measure In-hospital mortality during seven days of follow-up from treatment initiation.
Results Among 6578 patients (mean age 75.2 years) treated with an oral antipsychotic drug, 1668 (25.4%) initiated haloperidol and 4910 (74.6%) initiated atypical antipsychotics. The mean time from admission to start of treatment (5.3 *v* 5.6 days) and length of stay (12.5 *v* 13.6 days) were similar, but the mean treatment duration was shorter in patients using haloperidol compared with those using atypical antipsychotics (2.4 *v* 3.9 days). 1:1 propensity score matching was used to adjust for confounding. In intention to treat analyses with the matched cohort, the absolute rate of death per 100 person days was 1.7 for haloperidol (129 deaths) and 1.1 for atypical antipsychotics (92 deaths) during seven days of follow-up from treatment initiation. The survival probability was 0.93 in patients using haloperidol and 0.94 in those using atypical antipsychotics at day 7, accounting for the loss of follow-up due to hospital discharge. The unadjusted and adjusted hazard ratios of death were 1.51 (95% confidence interval 1.22 to 1.85) and 1.50 (1.14 to 1.96), respectively. The association was strongest during the first four days of follow-up and

decreased over time. By day 5, the increased risk was no longer evident (1.12, 0.79 to 1.59). In the as-treated analyses, the unadjusted and adjusted hazard ratios were 1.90 (1.43 to 2.53) and 1.93 (1.34 to 2.76), respectively.
Conclusion The results suggest a small increased risk of death within seven days of initiating haloperidol compared with initiating an atypical antipsychotic in patients with acute myocardial infarction. Although residual confounding cannot be excluded, this finding deserves consideration when haloperidol is used for patients admitted to hospital with cardiac morbidity.

Artificial pancreas treatment for outpatients with type 1 diabetes: Systematic review and meta-analysis

Eleni Bekiari, Konstantinos Kitsios, Hood Thabit, et al.
BMJ 2018; 361 (Published 18 April 2018)
https://www.bmj.com/content/361/bmj.k1310

Abstract
Objective To evaluate the efficacy and safety of artificial pancreas treatment in non-pregnant outpatients with type 1 diabetes.
Design Systematic review and meta-analysis of randomised controlled trials.
Data sources Medline, Embase, Cochrane Library, and grey literature up to 2 February 2018.
Eligibility criteria for selecting studies Randomised controlled trials in non-pregnant outpatients with type 1 diabetes that compared the use of any artificial pancreas system with any type of insulin based treatment. Primary outcome was proportion (%) of time that sensor glucose level was within the near normoglycaemic range (3.9-10 mmol/L). Secondary outcomes included proportion (%) of time that sensor glucose level was above 10 mmol/L or below 3.9 mmol/L, low blood glucose index overnight, mean sensor glucose level, total daily insulin needs, and glycated haemoglobin. The Cochrane Collaboration risk of bias tool was used to assess study quality.
Results 40 studies (1027 participants with data for 44 comparisons) were included in the meta-analysis. 35 comparisons assessed a single hormone artificial pancreas system, whereas nine comparisons assessed a dual hormone system. Only nine studies were at low risk of bias. Proportion of time in the near normoglycaemic range (3.9-10.0 mmol/L) was significantly higher with artificial pancreas use, both overnight (weighted mean difference 15.15%, 95% confidence interval 12.21% to 18.09%) and over a 24 hour period (9.62%, 7.54% to 11.7%). Artificial pancreas systems had a favourable effect on the proportion of time with sensor glucose level above 10 mmol/L (−8.52%, −11.14% to −5.9%) or below 3.9 mmol/L (−1.49%, −1.86% to −1.11%) over 24 hours, compared with control treatment. Robustness of findings for the primary outcome was verified in sensitivity analyses, by including only trials at low risk of bias (11.64%, 9.1% to 14.18%) or trials under unsupervised, normal living conditions (10.42%, 8.63% to 12.2%). Results were consistent in a subgroup analysis both for single hormone and dual hormone artificial pancreas systems.
Conclusions Artificial pancreas systems are an efficacious and safe approach for treating outpatients with type 1 diabetes. The main limitations of current research evidence on artificial pancreas systems are related to inconsistency in outcome reporting, small sample size, and short follow-up duration of individual trials.

Differences in rates of switchbacks after switching from branded to authorized generic and branded to generic drug products: Cohort study
Rishi J Desai, Ameet Sarpatwari, Sara Dejene, et al.
BMJ 2018; 361 (Published 03 April 2018)
https://www.bmj.com/content/361/bmj.k1180

Abstract
Objectives To compare rates of switchbacks to branded drug products for patients switched from branded to authorized generic drug products, which have the same active ingredients, appearance, and excipients as the branded product, with patients switched from branded to generic drug products, which have the same active ingredients as the branded product but may differ in appearance and excipients.
Design Observational cohort study.
Setting Private (a large commercial health plan) and public (Medicaid) insurance programs in the US.
Participants Beneficiaries of a large US commercial health insurer between 2004 and 2013 (primary cohort) and Medicaid beneficiaries between 2000 and 2010 (replication cohort).
Main outcome measures Patients taking branded products for one of the study drugs (alendronate tablets, amlodipine tablets, amlodipine-benazepril capsules, calcitonin salmon nasal spray, escitalopram tablets, glipizide extended release tablets, quinapril tablets, and sertraline tablets) were identified when they switched to an authorized generic or a generic drug product after the date of market entry of generic drug products. These patients were followed for switchbacks to the branded drug product in the year after their switch to an authorized generic or a generic drug product. Cox proportional hazard models were used to estimate hazard ratios and 95% confidence intervals after adjusting for demographics, including age, sex, and calendar year. Inverse variance meta-analysis was used to pool adjusted hazard ratios across all drug products.
Results A total of 94 909 patients switched from branded to authorized generic drug products and 116 017 patients switched from branded to generic drug products and contributed to the switchback analysis. Unadjusted incidence rates of switchback varied across drug products, ranging from a low of 3.8 per 100 person years (for alendronate tablets) to a high of 17.8 per 100 person years (for amlodipine-benazepril capsules), with an overall rate of 8.2 per 100 person years across all drug products. Adjusted switchback rates were consistently lower for patients who switched from branded to authorized generic drug products compared with branded to generic drug products in the primary cohort (pooled hazard ratio 0.72, 95% confidence interval 0.64 to 0.81). Similar results (0.75, 0.62 to 0.91) were observed in the replication cohort.
Conclusion Switching from branded to authorized generic drug products was associated with lower switchback rates compared with switching from branded to generic drug products.

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JAMA: Journal of the American Medical Association (24 April 2018, Vol. 319, No. 16)

Effect of a Home-Based Exercise Intervention of Wearable Technology and Telephone Coaching on Walking Performance in Peripheral Artery Disease: The HONOR Randomized Clinical Trial
Mary M. McDermott, Bonnie Spring, Jeffrey S. Berger, et al
JAMA. 2018; 319 (16): 1665-1676.

https://jamanetwork.com/journals/jama/article-abstract/2679277?redirect=true

Abstract

Importance Clinical practice guidelines support home-based exercise for patients with peripheral artery disease (PAD), but no randomized trials have tested whether an exercise intervention without periodic medical center visits improves walking performance.

Objective To determine whether a home-based exercise intervention consisting of a wearable activity monitor and telephone coaching improves walking ability over 9 months in patients with PAD.

Design, Setting, and Participants Randomized clinical trial conducted at 3 US medical centers. Patients with PAD were randomized between June 18, 2015, and April 4, 2017, to home-based exercise vs usual care for 9 months. Final follow-up was on December 5, 2017.

Interventions The exercise intervention group (n = 99) received 4 weekly medical center visits during the first month followed by 8 months of a wearable activity monitor and telephone coaching. The usual care group (n = 101) received no onsite sessions, active exercise, or coaching intervention.

Main Outcomes and Measures The primary outcome was change in 6-minute walk distance at 9-month follow-up (minimal clinically important difference [MCID], 20 m). Secondary outcomes included 9-month change in subcomponents of the Walking Impairment Questionnaire (WIQ) (0-100 score; 100, best), SF-36 physical functioning score, Patient-Reported Outcomes Measurement Information System (PROMIS) mobility questionnaire (higher = better; MCID, 2 points), PROMIS satisfaction with social roles questionnaire, PROMIS pain interference questionnaire (lower = better; MCID range, 3.5-4.5 points), and objectively measured physical activity.

Results Among 200 randomized participants (mean [SD] age, 70.2 [10.4] years; 105 [52.5%] women), 182 (91%) completed 9-month follow-up. The mean change from baseline to 9-month follow-up in the 6-minute walk distance was 5.5 m in the intervention group vs 14.4 m in the usual care group (difference, −8.9 m; 95% CI, −26.0 to 8.2 m; *P* = .31). The exercise intervention worsened the PROMIS pain interference score, mean change from baseline to 9 months was 0.7 in the intervention group vs −2.8 in the usual care group (difference, 3.5; 95% CI, 1.3 to 5.8; *P* = .002). There were no significant between-group differences in the WIQ score, the SF-36 physical functioning score, or the PROMIS mobility or satisfaction with social roles scores.

Conclusions and Relevance Among patients with PAD, a home-based exercise intervention consisting of a wearable activity monitor and telephone coaching, compared with usual care, did not improve walking performance at 9-month follow-up. These results do not support home-based exercise interventions of wearable devices and telephone counseling without periodic onsite visits to improve walking performance in patients with PAD.

Effect of Ticagrelor Plus Aspirin, Ticagrelor Alone, or Aspirin Alone on Saphenous Vein Graft Patency 1 Year After Coronary Artery Bypass Grafting: A Randomized Clinical Trial

Qiang Zhao, Yunpeng Zhu, Zhiyun Xu, et al

JAMA. 2018; 319 (16): 1677-1686.

https://jamanetwork.com/journals/jama/article-abstract/2679276?redirect=true

Abstract

Importance The effect of ticagrelor with or without aspirin on saphenous vein graft patency in patients undergoing coronary artery bypass grafting (CABG) is unknown.
Objective To compare the effect of ticagrelor + aspirin or ticagrelor alone vs aspirin alone on saphenous vein graft patency 1 year after CABG.
Design, Setting, and Participants Randomized, multicenter, open-label, clinical trial among 6 tertiary hospitals in China. Eligible patients were aged 18 to 80 years with indications for elective CABG. Patients requiring urgent revascularization, concomitant cardiac surgery, dual antiplatelet or vitamin K antagonist therapy post-CABG, and who were at risk of serious bleeding were excluded. From July 2014 until November 2015, 1256 patients were identified and 500 were enrolled. Follow-up was completed in January 2017.
Interventions Patients were randomized (1:1:1) to start ticagrelor (90 mg twice daily) + aspirin (100 mg once daily) (n = 168), ticagrelor (90 mg twice daily) (n = 166), or aspirin (100 mg once daily) (n = 166) within 24 hours post-CABG. Neither patients nor treating physicians were blinded to allocation.
Main Outcomes and Measures Primary outcome was saphenous vein graft patency 1 year after CABG (FitzGibbon grade A) adjudicated independently by a committee blinded to allocation. Saphenous vein graft patency was assessed by multislice computed tomographic angiography or coronary angiography.
Results Among 500 randomized patients (mean age, 63.6 years; women, 91 [18.2%]), 461 (92.2%) completed the trial. Saphenous vein graft patency rates 1 year post-CABG were 88.7% (432 of 487 vein grafts) with ticagrelor + aspirin; 82.8% (404 of 488 vein grafts) with ticagrelor alone; and 76.5% (371 of 485 vein grafts) with aspirin alone. The difference between ticagrelor + aspirin vs aspirin alone was statistically significant (12.2% [95% CI, 5.2% to 19.2%]; $P < .001$), whereas the difference between ticagrelor alone vs aspirin alone was not statistically significant (6.3% [95% CI, –1.1% to 13.7%]; $P = .10$). Five major bleeding episodes occurred during 1 year of follow-up (3 with ticagrelor + aspirin; 2 with ticagrelor alone).
Conclusions and Relevance Among patients undergoing elective CABG with saphenous vein grafting, ticagrelor + aspirin significantly increased graft patency after 1 year vs aspirin alone; there was no significant difference between ticagrelor alone and aspirin alone. Further research with more patients is needed to assess comparative bleeding risks.

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The Lancet (21 April 2018, Vol. 391, No. 10130)

Effectiveness of a long-lasting piperonyl butoxide-treated insecticidal net and indoor residual spray interventions, separately and together, against malaria transmitted by pyrethroid-resistant mosquitoes: A cluster, randomised controlled, two-by-two factorial design trial

Natacha Protopopoff, Jacklin F Mosha, Eliud Lukole, et al.

The Lancet: Volume 391, No. 10130, p1577–1588, 21 April 2018
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30427-6/fulltext

Summary
Background
Progress in malaria control is under threat by wide-scale insecticide resistance in malaria vectors. Two recent vector control products have been developed: a long-lasting insecticidal net that incorporates a synergist piperonyl butoxide (PBO) and a long-lasting

indoor residual spraying formulation of the insecticide pirimiphos-methyl. We evaluated the effectiveness of PBO long-lasting insecticidal nets versus standard long-lasting insecticidal nets as single interventions and in combination with the indoor residual spraying of pirimiphos-methyl.

Methods

We did a four-group cluster randomised controlled trial using a two-by-two factorial design of 48 clusters derived from 40 villages in Muleba (Kagera, Tanzania). We randomly assigned these clusters using restricted randomisation to four groups: standard long-lasting insecticidal nets, PBO long-lasting insecticidal nets, standard long-lasting insecticidal nets plus indoor residual spraying, or PBO long-lasting insecticidal nets plus indoor residual spraying. Both standard and PBO nets were distributed in 2015. Indoor residual spraying was applied only once in 2015. We masked the inhabitants of each cluster to the type of nets received, as well as field staff who took blood samples. Neither the investigators nor the participants were masked to indoor residual spraying. The primary outcome was the prevalence of malaria infection in children aged 6 months to 14 years assessed by cross-sectional surveys at 4, 9, 16, and 21 months after intervention. The endpoint for assessment of indoor residual spraying was 9 months and PBO long-lasting insecticidal nets was 21 months. This trial is registered with ClinicalTrials.gov, number NCT02288637.

Findings

7184 (68·0%) of 10 560 households were selected for post-intervention survey, and 15 469 (89·0%) of 17 377 eligible children from the four surveys were included in the intention-to-treat analysis. Of the 878 households visited in the two indoor residual spraying groups, 827 (94%) had been sprayed. Reported use of long-lasting insecticidal nets, across all groups, was 15 341 (77·3%) of 19 852 residents after 1 year, decreasing to 12 503 (59·2%) of 21 105 in the second year. Malaria infection prevalence after 9 months was lower in the two groups that received PBO long-lasting insecticidal nets than in the two groups that received standard long-lasting insecticidal nets (531 [29%] of 1852 children *vs* 767 [42%] of 1809; odds ratio [OR] 0·37, 95% CI 0·21–0·65; p=0·0011). At the same timepoint, malaria prevalence in the two groups that received indoor residual spraying was lower than in groups that did not receive indoor residual spraying (508 [28%] of 1846 children *vs* 790 [44%] of 1815; OR 0·33, 95% CI 0·19–0·55; p<0·0001) and there was evidence of an interaction between PBO long-lasting insecticidal nets and indoor residual spraying (OR 2·43, 95% CI 1·19–4·97; p=0·0158), indicating redundancy when combined. The PBO long-lasting insecticidal net effect was sustained after 21 months with a lower malaria prevalence than the standard long-lasting insecticidal net (865 [45%] of 1930 children *vs* 1255 [62%] of 2034; OR 0·40, 0·20–0·81; p=0·0122).

Interpretation

The PBO long-lasting insecticidal net and non-pyrethroid indoor residual spraying interventions showed improved control of malaria transmission compared with standard long-lasting insecticidal nets where pyrethroid resistance is prevalent and either intervention could be deployed to good effect. As a result, WHO has since recommended to increase coverage of PBO long-lasting insecticidal nets. Combining indoor residual spraying with pirimiphos-methyl and PBO long-lasting insecticidal nets provided no additional benefit compared with PBO long-lasting insecticidal nets alone or standard long-lasting insecticidal nets plus indoor residual spraying.

Perioperative patient outcomes in the African Surgical Outcomes Study: A 7-day prospective observational cohort study

Bruce M Biccard, Thandinkosi E Madiba, Hyla-Louise Kluyts, et al. on behalf of the African Surgical Outcomes Study (ASOS) Investigators
The Lancet: Volume 391, No. 10130, p1589–1598, 21 April 2018
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30001-1/fulltext

Summary

Background

There is a need to increase access to surgical treatments in African countries, but perioperative complications represent a major global health-care burden. There are few studies describing surgical outcomes in Africa.

Methods

We did a 7-day, international, prospective, observational cohort study of patients aged 18 years and older undergoing any inpatient surgery in 25 countries in Africa (the African Surgical Outcomes Study). We aimed to recruit as many hospitals as possible using a convenience sampling survey, and required data from at least ten hospitals per country (or half the surgical centres if there were fewer than ten hospitals) and data for at least 90% of eligible patients from each site. Each country selected one recruitment week between February and May, 2016. The primary outcome was in-hospital postoperative complications, assessed according to predefined criteria and graded as mild, moderate, or severe. Data were presented as median (IQR), mean (SD), or n (%), and compared using *t* tests. This study is registered on the South African National Health Research Database (KZ_2015RP7_22) and ClinicalTrials.gov (NCT03044899).

Findings

We recruited 11 422 patients (median 29 [IQR 10–70]) from 247 hospitals during the national cohort weeks. Hospitals served a median population of 810 000 people (IQR 200 000–2 000 000), with a combined number of specialist surgeons, obstetricians, and anaesthetists totalling 0·7 (0·2–1·9) per 100 000 population. Hospitals did a median of 212 (IQR 65–578) surgical procedures per 100 000 population each year. Patients were younger (mean age 38·5 years [SD 16·1]), with a lower risk profile (American Society of Anesthesiologists median score 1 [IQR 1–2]) than reported in high-income countries. 1253 (11%) patients were infected with HIV, 6504 procedures (57%) were urgent or emergent, and the most common procedure was caesarean delivery (3792 patients, 33%). Postoperative complications occurred in 1977 (18·2%, 95% CI 17·4–18·9]) of 10 885 patients. 239 (2·1%) of 11 193 patients died, 225 (94·1%) after the day of surgery. Infection was the most common complication (1156 [10·2%] of 10 970 patients), of whom 112 (9·7%) died.

Interpretation

Despite a low-risk profile and few postoperative complications, patients in Africa were twice as likely to die after surgery when compared with the global average for postoperative deaths. Initiatives to increase access to surgical treatments in Africa therefore should be coupled with improved surveillance for deteriorating physiology in patients who develop postoperative complications, and the resources necessary to achieve this objective.

Re-emergence of yaws after single mass azithromycin treatment followed by targeted treatment: A longitudinal study

Oriol Mitjà, Charmie Godornes, Wendy Houinei, et al.
The Lancet: Volume 391, No. 10130, p1599–1607, 21 April 2018
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30204-6/fulltext

Summary
Background
Yaws is a substantial cause of chronic disfiguring ulcers in children in at least 14 countries in the tropics. WHO's newly adopted strategy for yaws eradication uses a single round of mass azithromycin treatment followed by targeted treatment programmes, and data from pilot studies have shown a short-term significant reduction of yaws. We assessed the long-term efficacy of the WHO strategy for yaws eradication.
Methods
Between April 15, 2013, and Oct 24, 2016, we did a longitudinal study on a Papua New Guinea island (Lihir; 16 092 population) in which yaws was endemic. In the initial study, the participants were followed for 12 months; in this extended follow-up study, clinical, serological, and PCR surveys were continued every 6 months for 42 months. We used genotyping and travel history to identify importation events. Active yaws confirmed by PCR specific for *Treponema pallidum* was the primary outcome indicator. The study is registered with ClinicalTrials.gov, number NCT01955252.
Findings
Mass azithromycin treatment (coverage rate of 84%) followed by targeted treatment programmes reduced the prevalence of active yaws from 1·8% to a minimum of 0·1% at 18 months (difference from baseline −1·7%, 95% CI, −1·9 to −1·4; p<0·0001), but the infection began to re-emerge after 24 months with a significant increase to 0·4% at 42 months (difference from 18 months 0·3%, 95% CI 0·1 to 0·4; p<0·0001). At each timepoint after baseline, more than 70% of the total community burden of yaws was found in individuals who had not had the mass treatment or as new infections in non-travelling residents. At months 36 and 42, five cases of active yaws, all from the same village, showed clinical failure following azithromycin treatment, with PCR-detected mutations in the 23S ribosomal RNA genes conferring resistance to azithromycin. A sustained decrease in the prevalence of high-titre latent yaws from 13·7% to <1·5% in asymptomatic children aged 1–5 years old and of genetic diversity of yaws strains from 0·139 to less than 0·046 between months 24 and 42 indicated a reduction in transmission of infection.
Interpretation
The implementation of the WHO strategy did not, in the long-term, achieve elimination in a high-endemic community mainly due to the individuals who were absent at the time of mass treatment in whom yaws reactivated; repeated mass treatment might be necessary to eliminate yaws. To our knowledge, this is the first report of the emergence of azithromycin-resistant *T p pertenue* and spread within one village. Communities' surveillance should be strengthened to detect any possible treatment failure and biological markers of resistance.

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The New England Journal of Medicine (19 April 2018, Vol. 378, No. 16)

Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia
Alexis A. Thompson, Mark C. Walters, Janet Kwiatkowski, et al.
N Engl J Med 2018; 378:1479-1493 April 19, 2018
http://www.nejm.org/doi/full/10.1056/NEJMoa1705342

Abstract
Background
Donor availability and transplantation-related risks limit the broad use of allogeneic hematopoietic-cell transplantation in patients with transfusion-dependent β-thalassemia.

After previously establishing that lentiviral transfer of a marked β-globin (βA-T87Q) gene could substitute for long-term red-cell transfusions in a patient with β-thalassemia, we wanted to evaluate the safety and efficacy of such gene therapy in patients with transfusion-dependent β-thalassemia.

Methods

In two phase 1–2 studies, we obtained mobilized autologous CD34+ cells from 22 patients (12 to 35 years of age) with transfusion-dependent β-thalassemia and transduced the cells ex vivo with LentiGlobin BB305 vector, which encodes adult hemoglobin (HbA) with a T87Q amino acid substitution (HbAT87Q). The cells were then reinfused after the patients had undergone myeloablative busulfan conditioning. We subsequently monitored adverse events, vector integration, and levels of replication-competent lentivirus. Efficacy assessments included levels of total hemoglobin and HbAT87Q, transfusion requirements, and average vector copy number.

Results

At a median of 26 months (range, 15 to 42) after infusion of the gene-modified cells, all but 1 of the 13 patients who had a non–β0/β0 genotype had stopped receiving red-cell transfusions; the levels of HbAT87Q ranged from 3.4 to 10.0 g per deciliter, and the levels of total hemoglobin ranged from 8.2 to 13.7 g per deciliter. Correction of biologic markers of dyserythropoiesis was achieved in evaluated patients with hemoglobin levels near normal ranges. In 9 patients with a β0/β0 genotype or two copies of the IVS1-110 mutation, the median annualized transfusion volume was decreased by 73%, and red-cell transfusions were discontinued in 3 patients. Treatment-related adverse events were typical of those associated with autologous stem-cell transplantation. No clonal dominance related to vector integration was observed.

Conclusions

Gene therapy with autologous CD34+ cells transduced with the BB305 vector reduced or eliminated the need for long-term red-cell transfusions in 22 patients with severe β-thalassemia without serious adverse events related to the drug product.

Education Outcomes in a Duty-Hour Flexibility Trial in Internal Medicine

Sanjay V. Desai, David A. Asch, Lisa M. Bellini, et al. for the iCOMPARE Research Group

N Engl J Med 2018; 378:1494-1508 April 19, 2018
http://www.nejm.org/doi/full/10.1056/NEJMoa1800965

Abstract

Background

Concern persists that inflexible duty-hour rules in medical residency programs may adversely affect the training of physicians.

Methods

We randomly assigned 63 internal medicine residency programs in the United States to be governed by standard duty-hour policies of the 2011 Accreditation Council for Graduate Medical Education (ACGME) or by more flexible policies that did not specify limits on shift length or mandatory time off between shifts. Measures of educational experience included observations of the activities of interns (first-year residents), surveys of trainees (both interns and residents) and faculty, and intern examination scores.

Results

There were no significant between-group differences in the mean percentages of time that interns spent in direct patient care and education nor in trainees' perceptions of an appropriate balance between clinical demands and education (primary outcome for trainee satisfaction with education; response rate, 91%) or in the assessments by program

directors and faculty of whether trainees' workload exceeded their capacity (primary outcome for faculty satisfaction with education; response rate, 90%). Another survey of interns (response rate, 49%) revealed that those in flexible programs were more likely to report dissatisfaction with multiple aspects of training, including educational quality (odds ratio, 1.67; 95% confidence interval [CI], 1.02 to 2.73) and overall well-being (odds ratio, 2.47; 95% CI, 1.67 to 3.65). In contrast, directors of flexible programs were less likely to report dissatisfaction with multiple educational processes, including time for bedside teaching (response rate, 98%; odds ratio, 0.13; 95% CI, 0.03 to 0.49). Average scores (percent correct answers) on in-training examinations were 68.9% in flexible programs and 69.4% in standard programs; the difference did not meet the noninferiority margin of 2 percentage points (difference, −0.43; 95% CI, −2.38 to 1.52; P=0.06 for noninferiority).

Conclusions

There was no significant difference in the proportion of time that medical interns spent on direct patient care and education between programs with standard duty-hour policies and programs with more flexible policies. Interns in flexible programs were less satisfied with their educational experience than were their peers in standard programs, but program directors were more satisfied.

Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality

José R. Banegas, Luis M. Ruilope, Alejandro de la Sierra, et al.

N Engl J Med 2018; 378:1509-1520 April 19, 2018
http://www.nejm.org/doi/full/10.1056/NEJMoa1712231

Abstract

Background

Evidence for the influence of ambulatory blood pressure on prognosis derives mainly from population-based studies and a few relatively small clinical investigations. This study examined the associations of blood pressure measured in the clinic (clinic blood pressure) and 24-hour ambulatory blood pressure with all-cause and cardiovascular mortality in a large cohort of patients in primary care.

Methods

We analyzed data from a registry-based, multicenter, national cohort that included 63,910 adults recruited from 2004 through 2014 in Spain. Clinic and 24-hour ambulatory blood-pressure data were examined in the following categories: sustained hypertension (elevated clinic and elevated 24-hour ambulatory blood pressure), "white-coat" hypertension (elevated clinic and normal 24-hour ambulatory blood pressure), masked hypertension (normal clinic and elevated 24-hour ambulatory blood pressure), and normotension (normal clinic and normal 24-hour ambulatory blood pressure). Analyses were conducted with Cox regression models, adjusted for clinic and 24-hour ambulatory blood pressures and for confounders.

Results

During a median follow-up of 4.7 years, 3808 patients died from any cause, and 1295 of these patients died from cardiovascular causes. In a model that included both 24-hour and clinic measurements, 24-hour systolic pressure was more strongly associated with all-cause mortality (hazard ratio, 1.58 per 1-SD increase in pressure; 95% confidence interval [CI], 1.56 to 1.60, after adjustment for clinic blood pressure) than the clinic systolic pressure (hazard ratio, 1.02; 95% CI, 1.00 to 1.04, after adjustment for 24-hour blood pressure). Corresponding hazard ratios per 1-SD increase in pressure were 1.55 (95% CI, 1.53 to 1.57, after adjustment for clinic and daytime blood pressures) for nighttime

ambulatory systolic pressure and 1.54 (95% CI, 1.52 to 1.56, after adjustment for clinic and nighttime blood pressures) for daytime ambulatory systolic pressure. These relationships were consistent across subgroups of age, sex, and status with respect to obesity, diabetes, cardiovascular disease, and antihypertensive treatment. Masked hypertension was more strongly associated with all-cause mortality (hazard ratio, 2.83; 95% CI, 2.12 to 3.79) than sustained hypertension (hazard ratio, 1.80; 95% CI, 1.41 to 2.31) or white-coat hypertension (hazard ratio, 1.79; 95% CI, 1.38 to 2.32). Results for cardiovascular mortality were similar to those for all-cause mortality.

Conclusions

Ambulatory blood-pressure measurements were a stronger predictor of all-cause and cardiovascular mortality than clinic blood-pressure measurements. White-coat hypertension was not benign, and masked hypertension was associated with a greater risk of death than sustained hypertension.

Evaluation of Intussusception after Monovalent Rotavirus Vaccination in Africa

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Abstract

Background

Postlicensure evaluations have identified an association between rotavirus vaccination and intussusception in several high- and middle-income countries. We assessed the association between monovalent human rotavirus vaccine and intussusception in lower-income sub-Saharan African countries.

Methods

Using active surveillance, we enrolled patients from seven countries (Ethiopia, Ghana, Kenya, Malawi, Tanzania, Zambia, and Zimbabwe) who had intussusception that met international (Brighton Collaboration level 1) criteria. Rotavirus vaccination status was confirmed by review of the vaccine card or clinic records. The risk of intussusception within 1 to 7 days and 8 to 21 days after vaccination among infants 28 to 245 days of age was assessed by means of the self-controlled case-series method.

Results

Data on 717 infants who had intussusception and confirmed vaccination status were analyzed. One case occurred in the 1 to 7 days after dose 1, and 6 cases occurred in the 8 to 21 days after dose 1. Five cases and 16 cases occurred in the 1 to 7 days and 8 to 21 days, respectively, after dose 2. The risk of intussusception in the 1 to 7 days after dose 1 was not higher than the background risk of intussusception (relative incidence [i.e., the incidence during the risk window vs. all other times], 0.25; 95% confidence interval [CI], <0.001 to 1.16); findings were similar for the 1 to 7 days after dose 2 (relative incidence, 0.76; 95% CI, 0.16 to 1.87). In addition, the risk of intussusception in the 8 to 21 days or 1 to 21 days after either dose was not found to be higher than the background risk.

Conclusions

The risk of intussusception after administration of monovalent human rotavirus vaccine was not higher than the background risk of intussusception in seven lower-income sub-Saharan African countries.

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Sources

BMJ: British Medical Journal	http://www.bmj.com/theBMJ
JAMA: The Journal of the American Medical Association	http://jama.ama-assn.org/
The Lancet	www.thelancet.com
The New England Journal of Medicine	http://content.nejm.org/
The British Medical Journal (BMJ), JAMA and the New England Journal of Medicine (NEJM) can be accessed in full-text through your NHS Athens account. Unfortunately the national subscription to The Lancet has been cancelled.	https://www.evidence.nhs.uk/nhs-evidence-content/journals-and-databases or http://www.openathens.net/
If you have not already registered for an NHS Athens Account, please register at: NB: It is recommended that you register on a Trust (NHS) PC for speedy confirmation of your username and password. Once registered, your account can be accessed from any device with online access.	https://openathens.nice.org.uk/

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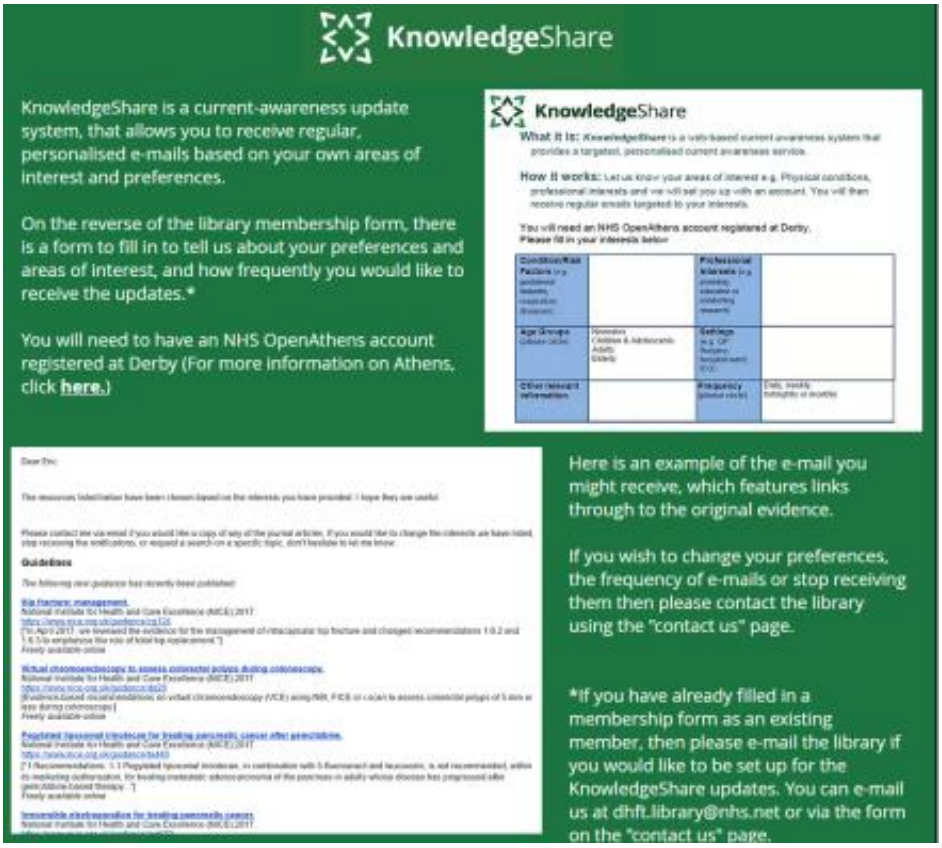

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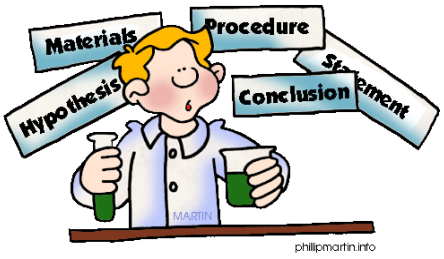

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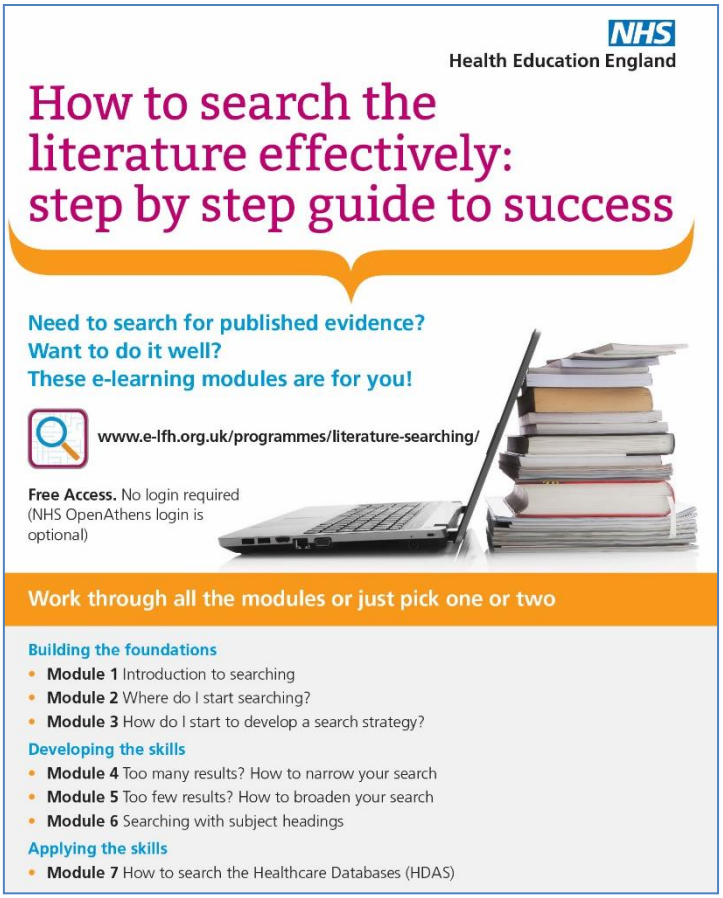

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