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Subdirección General de Planificación, Calidad e Investigación

1. **ARTÍCULO Nº: 4573**

Bates ER. ***Evolution from fibrinolytic therapy to a fibrinolytic strategy for patients with ST-segment-elevation myocardial infarction.*** Circulation. 2014; 130(14): 1133-1135.

2. **ARTÍCULO Nº: 4574**

Sinnaeve PR, Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Lambert Y et al. ***ST-segment-elevation myocardial infarction patients randomized to a pharmaco-invasive strategy or primary percutaneous coronary intervention: Strategic Reperfusion Early After Myocardial Infarction (STREAM) 1-year mortality follow-up.*** Circulation. 2014; 130(14): 1139-1145.

BACKGROUND: In the Strategic Reperfusion Early After Myocardial Infarction (STREAM) trial, a pharmaco-invasive (PI) strategy was compared with primary percutaneous coronary intervention (pPCI) in ST-segment-elevation myocardial infarction patients presenting within 3 hours after symptom onset but unable to undergo pPCI within 1 hour. At 30 days, the PI approach was associated with a nominally but nonstatistically significant lower incidence of the composite primary end point of death, shock, congestive heart failure, and reinfarction when compared with pPCI. The aim of the present study was to determine the effect of these strategies on 1-year mortality. METHODS AND RESULTS: Vital status at 1 year was available in 936 of 944 (99.2%) and 941 of 948 (99.3%) patients in the PI and pPCI arm, respectively. At 1 year, all-cause mortality rates (6.7% versus 5.9%) were similar for PI and pPCI-treated patients (P=0.49; risk ratio, 1.13; 95% confidence interval, 0.79-1.62). Cardiac mortality rates were similar as well (4.0% versus 4.1%, P=0.93; risk ratio, 0.98; 95% confidence interval, 0.62-1.54). Overall, only 34 patients died between day 30 and 1 year, 20 in the PI arm and 14 in the pPCI arm, of whom 20 died of noncardiac reasons (13 in the PI and 7 in the pPCI arm). There was no significant difference in 1-year all-cause mortality between the 2 groups among the prespecified key subgroups. CONCLUSIONS: At 1 year, mortality rates in the PI and pPCI arms were similar in ST-segment-elevation myocardial infarction patients presenting within 3 hours after symptom onset and unable to undergo pPCI within 1 hour. CLINICAL TRIAL REGISTRATION URL: http://www.clinicaltrials.gov. Unique identifier: NCT00623623.

3. **ARTÍCULO Nº: 4575**

Jacobs AK, Anderson JL, Halperin JL, Anderson JL, Halperin JL, Albert NM et al. ***The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines.*** Circulation. 2014; 130(14): 1208-1217.

4. **ARTÍCULO Nº: 4576**

Quiles J, Miralles-Vicedo B. ***Secondary Prevention Strategies for Acute Coronary Syndrome***. Rev.Esp.Cardiol. 2014;

Cardiovascular disease is the main health problem in Europe and the rest of the world and is the leading cause of death and health care expenditure. By reducing mortality and ischemic event recurrence, prevention strategies play a fundamental role in patients who have had an acute coronary syndrome. Although these prevention strategies have focused with great success on high-risk individuals, they should also be used in the general population, which is showing an increase in the prevalence of obesity, diabetes mellitus, and other comorbidities that may reverse this trend toward reduced mortality. The present article consists of an up-to-date review of the main cardiovascular prevention measures, particularly the new developments of the last year, as well as the particularities of these measures when they are targeted at patients with a prior acute coronary syndrome. Full English text available from: www.revespcardiol.org/en.

5. **ARTÍCULO Nº: 4577**

da Costa BR, Hilfiker R, Egger M. ***PEDro's bias: summary quality scores should not be used in meta-analysis***. J.Clin.Epidemiol. 2013; 66(1): 75-77.

6. **ARTÍCULO Nº: 4578**

Kulik DM, Uleryk EM, Maguire JL. ***Does this child have appendicitis? A systematic review of clinical prediction rules for children with acute abdominal pain***. J.Clin.Epidemiol. 2013; 66(1): 95-104.

OBJECTIVES: To systematically identify clinical prediction rules (CPRs) for children with suspected appendicitis and compare their methodological quality and performance. STUDY DESIGN AND SETTING: Included studies involved children aged 0-18 years with suspected appendicitis identified through MEDLINE and EMBASE from 1950 to 2012. The quality was assessed using 17 previously published items. The performance was evaluated using the sensitivity, negative likelihood ratio, and predicted frequency of appendicitis diagnosis that would result if the rule was used. RESULTS: Twelve studies fulfilled the inclusion criteria describing the derivation or validation of six unique CPRs involving 4,201 children with suspected appendicitis. Migratory pain, nausea or vomiting, and right lower quadrant tenderness were common predictors to all rules. Methodological quality varied widely. The most poorly addressed quality items were the predictor and outcome assessor blinding, predictor description, and reproducibility of predictor assessment. The most well-validated CPRs were the Pediatric Appendicitis Score (PAS) and MANTRELS (Migration, Anorexia, Nausea/vomiting, Tenderness in the right lower quadrant, Rebound pain, Elevation in temperature, Leukocytosis, Shift to the left)/Alvarado Score. Overall, the PAS validation studies outperformed the Alvarado validation studies. CONCLUSION: The PAS and Alvarado scores were the most well validated but neither met the current performance benchmarks. A high quality, well validated, and consistently high-performing CPR was not identified. Further research is needed before a CPR for children with suspected appendicitis can be used in routine practice.

7. **ARTÍCULO Nº: 4579**

Golder S, Loke YK, Zorzela L. ***Some improvements are apparent in identifying adverse effects in systematic reviews from 1994 to 2011***. J.Clin.Epidemiol. 2013; 66(3): 253-260.

OBJECTIVE: An increasing amount of research and guidelines has been published on search methodology and the reporting of search strategies in systematic reviews. This research assessed whether this has lead to any improvements in the reporting and quality of searching in systematic reviews of adverse effects. STUDY DESIGN AND SETTING: All records within Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects were scanned for systematic reviews of adverse effects. Data were then extracted on the methods used for information retrieval in these reviews and a descriptive analysis conducted by publication year. RESULTS: A total of 849 reviews published from 1994 to 2011 met the inclusion criteria. There has been a significant increase (P<0.001) in the number of adverse effects reviews per year from 1994 (n=5) to 2010 (n=104). Some improvements were apparent, such as an increase in the number of databases searched and fewer date and language restrictions applied. However, there has been an increase in reviews limited to data from randomized controlled trials, whereas the reporting of search strategies could still be improved further, with only 9% (74/849) of the reviews reporting reproducible searches. CONCLUSION: Some improvements in searching systematic reviews of adverse effects are apparent; however, poor reporting of search strategies remains a great obstacle to readers.

8. **ARTÍCULO Nº: 4580**

Kotz D, Cals JW, Tugwell P, Knottnerus JA. ***Introducing a new series on effective writing and publishing of scientific papers.*** J.Clin.Epidemiol. 2013; 66(4): 359-360.

9. **ARTÍCULO Nº: 4581**

Prasad V, Jorgenson J, Ioannidis JP, Cifu A. ***Observational studies often make clinical practice recommendations: an empirical evaluation of authors' attitudes.*** J.Clin.Epidemiol. 2013; 66(4): 361-366.

OBJECTIVES: Although observational studies provide useful descriptive and correlative information, their role in the evaluation of medical interventions remains contentious. There has been no systematic evaluation of authors' attitudes toward their own nonrandomized studies and how often they recommend specific medical practices. STUDY DESIGN AND SETTING: We reviewed all original articles of nonrandomized studies published in 2010 in New England Journal of Medicine, Lancet, Journal of the American Medical Association, and Annals of Internal Medicine. We classified articles based on whether authors recommend a medical practice and whether they state that a randomized trial is needed to support their recommendation. We also examined the types of logical extrapolations used by authors who did advance recommendations. RESULTS: Of the 631 original articles published in 2010, 298 (47%) articles were eligible observational studies. In 167 (56%) of 298 studies, authors recommended a medical practice based on their results. Only 24 (14%) of 167 studies stated that a randomized controlled trial (RCT) should be done to validate the recommendation, whereas the other 143 articles made a total of 149 logical extrapolations to recommend specific medical practices. Recommendations without a call for a randomized trial were most common in studies of modifiable factors (59%), but they were also common in studies reporting incidence or prevalence (51%), studies examining novel tests (41%), and association studies of nonmodifiable factors (32%). CONCLUSION: The authors of observational studies often extrapolate their results to make recommendations concerning a medical practice, typically without first calling for a RCT.

10. **ARTÍCULO Nº: 4582**

Kotz D, Cals JW. ***Effective writing and publishing scientific papers--part I: how to get started.*** J.Clin.Epidemiol. 2013; 66(4): 397

11. **ARTÍCULO Nº: 4583**
Tugwell P, Knottnerus JA, Idzerda L. ***Methods for setting priorities in systematic reviews***. J.Clin.Epidemiol. 2013; 66(5): 467-468.

12. **ARTÍCULO Nº: 4584**
Cals JW, Kotz D. ***Effective writing and publishing scientific papers, part II: title and abstract***. J.Clin.Epidemiol. 2013; 66(6): 585

13. **ARTÍCULO Nº: 4585**
Cals JW, Kotz D. ***Effective writing and publishing scientific papers, part III: introduction***. J.Clin.Epidemiol. 2013; 66(7): 702

14. **ARTÍCULO Nº: 4586**
Kotz D, Cals JW. ***Effective writing and publishing scientific papers, part IV: methods***. J.Clin.Epidemiol. 2013; 66(8): 817

15. **ARTÍCULO Nº: 4587**
Morrow E, Cotterell P, Robert G, Grocott P, Ross F. ***Mechanisms can help to use patients' experiences of chronic disease in research and practice: an interpretive synthesis***. J.Clin.Epidemiol. 2013; 66(8): 856-864.

OBJECTIVE: To identify and examine mechanisms through which patients' experiences of chronic disease can be accessed, understood, and used to improve outcomes, health care costs, and quality of life for individual patients. STUDY DESIGN AND SETTING: Interpretive synthesis of the research literature on chronic disease and associated areas of clinical practice and service development. Searches of electronic databases (MEDLINE, EMBASE, and British Nursing Index), Internet searches, and snowballing techniques identified 66 relevant publications. The analysis focused on identifying mechanisms; their strengths, weaknesses, and impact. RESULTS: Ten mechanisms were identified, each with differing potential to access and reach patients; involve patients in decisions about what information is important; enable patients to share experiences/expertise and validate their knowledge; allow professionals and patients to deliberate and build understanding; support shared decision-making, continuity/partnership development, and potential to use patients' experiences. The extent to which patients' experiences led to improved outcomes, health care costs, or quality of life related to the aims of individual studies. CONCLUSION: Patients can contribute to improving the design and delivery of chronic disease health care and research if appropriate mechanisms are in place. There is a need for future research about optimal configurations of mechanisms and links between mechanisms across health care and research.

16. **ARTÍCULO Nº: 4588**
Macia F, Pumarega J, Gallen M, Porta M. ***Time from (clinical or certainty) diagnosis to treatment onset in cancer patients: the choice of diagnostic date strongly influences differences in therapeutic delay by tumor site and stage***. J.Clin.Epidemiol. 2013; 66(8): 928-939.

OBJECTIVES: To analyze whether differences between the interval from suspicion or clinical diagnosis to treatment onset (IClinDT) and the interval from certainty diagnosis to treatment onset (ICertDT) varied by tumor site, stage, and mode of hospital admission. STUDY DESIGN AND SETTING: From our hospital cancer registry, we selected all 8,814 patients with breast, colorectal, lung, prostate, or cervical cancer diagnosed between 1992 and 2006. We compared IClinDT and ICertDT with density

plots and logistic regression. RESULTS: IClinDT was up to three times higher than ICertDT. There were very large differences among stages and within each stage in IClinDT and ICertDT. Tumor stage significantly influenced the difference between the two intervals in three of the five locations (breast, lung, and prostate cancer); as stage worsened, the difference between IClinDT and ICertDT became smaller. In all tumor sites, the difference was larger in scheduled than in emergency admissions. Overall, therapeutic delays--even when measured by ICertDT--were disturbingly common for important subgroups of patients. CONCLUSION: The difference between IClinDT and ICertDT varied highly by tumor site, stage, and mode of hospital admission. More standardized definitions and procedures to calculate time intervals between cancer diagnosis and treatment onset are needed.

17. **ARTÍCULO Nº: 4589**

Schneeweiss S, Seeger JD, Jackson JW, Smith SR. ***Methods for comparative effectiveness research/patient-centered outcomes research: from efficacy to effectiveness***. J.Clin.Epidemiol. 2013; 66(8 Suppl): S1-S4.

18. **ARTÍCULO Nº: 4590**

Kotz D, Cals JW. ***Effective writing and publishing scientific papers, part V: results***. J.Clin.Epidemiol. 2013; 66(9): 945

19. **ARTÍCULO Nº: 4591**

Smulders YM. ***A two-step manuscript submission process can reduce publication bias***. J.Clin.Epidemiol. 2013; 66(9): 946-947.

Much of what is researched is never published. This would not be of great concern if the selection of what we read would occur irrespective of study outcomes. Unfortunately, the reverse is the case: "positive" studies have a much larger chance of acceptance after editorial and peer review than "negative" ones. Several solutions to this problem of publication bias have been discussed or implemented, but none seem to be very effective. In this article, the approach of implementing an editorial and peer-review procedure that is blinded to study outcomes is discussed. This would require a two-step submission procedure of manuscripts: first a version including just the introduction and methods and in some cases followed by a second submission including results and discussion. The pros and cons of such an approach are discussed.

20. **ARTÍCULO Nº: 4592**

Hartling L, Hamm MP, Milne A, Vandermeer B, Santaguida PL, Ansari M et al. ***Testing the risk of bias tool showed low reliability between individual reviewers and across consensus assessments of reviewer pairs***. J.Clin.Epidemiol. 2013; 66(9): 973-981.

OBJECTIVES: To assess the reliability of the Cochrane Risk of Bias (ROB) tool between individual raters and across consensus agreements of pairs of reviewers and examine the impact of study-level factors on reliability. STUDY DESIGN AND SETTING: Two reviewers assessed risk of bias for 154 randomized controlled trials (RCTs). For 30 RCTs, two reviewers from each of four centers assessed risk of bias and reached consensus. We assessed interrater agreement using kappas and the impact of study-level factors through subgroup analyses. RESULTS: Reliability between two reviewers was fair for most domains (kappa=0.24-0.37), except sequence generation (kappa=0.79, substantial). Reliability results across reviewer pairs: sequence generation, moderate (kappa=0.60); allocation concealment and "other sources of bias," fair (kappa=0.37-0.27); and other domains, slight (kappa=0.05-0.09). Reliability was influenced by the nature of the outcome, nature of the intervention, study design, trial

hypothesis, and funding source. Variability resulted from different interpretation of the tool rather than different information identified in the study reports. CONCLUSION: Low agreement has implications for interpreting systematic reviews. These findings suggest the need for detailed guidance in assessing the risk of bias.

21. **ARTÍCULO Nº: 4593**

Hartling L, Milne A, Hamm MP, Vandermeer B, Ansari M, Tsertsvadze A et al. ***Testing the Newcastle Ottawa Scale showed low reliability between individual reviewers.*** J.Clin.Epidemiol. 2013; 66(9): 982-993.

OBJECTIVES: To assess inter-rater reliability and validity of the Newcastle Ottawa Scale (NOS) used for methodological quality assessment of cohort studies included in systematic reviews. STUDY DESIGN AND SETTING: Two reviewers independently applied the NOS to 131 cohort studies included in eight meta-analyses. Inter-rater reliability was calculated using kappa (kappa) statistics. To assess validity, within each meta-analysis, we generated a ratio of pooled estimates for each quality domain. Using a random-effects model, the ratios of odds ratios for each meta-analysis were combined to give an overall estimate of differences in effect estimates. RESULTS: Inter-rater reliability varied from substantial for length of follow-up (kappa = 0.68, 95% confidence interval [CI] = 0.47, 0.89) to poor for selection of the nonexposed cohort and demonstration that the outcome was not present at the outset of the study (kappa = -0.03, 95% CI = -0.06, 0.00; kappa = -0.06, 95% CI = -0.20, 0.07). Reliability for overall score was fair (kappa = 0.29, 95% CI = 0.10, 0.47). In general, reviewers found the tool difficult to use and the decision rules vague even with additional information provided as part of this study. We found no association between individual items or overall score and effect estimates. CONCLUSION: Variable agreement and lack of evidence that the NOS can identify studies with biased results underscore the need for revisions and more detailed guidance for systematic reviewers using the NOS.

22. **ARTÍCULO Nº: 4594**

Knottnerus JA, Tugwell P. ***The potential impact of unpublished results.*** J.Clin.Epidemiol. 2013; 66(10): 1061-1063.

23. **ARTÍCULO Nº: 4595**

Cals JW, Kotz D. ***Effective writing and publishing scientific papers, part VI: discussion.*** J.Clin.Epidemiol. 2013; 66(10): 1064

24. **ARTÍCULO Nº: 4596**

Sun GH, Aliu O, Hayward RA. ***Open-access electronic case report journals: the rationale for case report guidelines.*** J.Clin.Epidemiol. 2013; 66(10): 1065-1070.

25. **ARTÍCULO Nº: 4597**

McDonagh MS, Peterson K, Balshem H, Helfand M. ***US Food and Drug Administration documents can provide unpublished evidence relevant to systematic reviews.*** J.Clin.Epidemiol. 2013; 66(10): 1071-1081.

OBJECTIVES: A key systematic review (SR) methodology is comprehensive searching. The Drug Effectiveness Review Project (DERP) SRs search US Food and Drug Administration (FDA) documents to identify unpublished evidence. This study evaluates the success of those efforts. STUDY DESIGN AND SETTING: We examined DERP reports published since 2003 for the use of FDA preapproval and

postmarketing documents. We categorized evidence as (1) unique unpublished studies, (2) supplemental unpublished data, or (3) FDA postmarketing data analysis. Three reviewers independently assigned predetermined impact categories (e.g., qualitative or quantitative usage, fills gaps, confirms findings, and alters conclusions), resolving disagreements through consensus. RESULTS: Among 114 DERP reports, 19% included unpublished studies and/or supplemental data and 10% included postmarketing analyses. From 175 preapproval documents, 14% provided eligible unpublished studies and 4.0% supplemental unpublished data that helped confirm previous findings, identify important harms, and fill gaps in knowledge about understudied subpopulations, outcomes, and comparisons. Report conclusion statements changed in 9 of 33 instances of premarketing documents compared with 4 of 12 postmarketing analyses. CONCLUSIONS: The FDA documents can provide important unpublished evidence for SRs, although in a small proportion of cases. Future research should identify attributes that predict which reviews may benefit most from review of FDA documents.

26. **ARTÍCULO Nº: 4598**

Whiting PF, Rutjes AW, Westwood ME, Mallett S. ***A systematic review classifies sources of bias and variation in diagnostic test accuracy studies***. J.Clin.Epidemiol. 2013; 66(10): 1093-1104.

OBJECTIVE: To classify the sources of bias and variation and to provide an updated summary of the evidence of the effects of each source of bias and variation. STUDY DESIGN AND SETTING: We conducted a systematic review of studies of any design with the main objective of addressing bias or variation in the results of diagnostic accuracy studies. We searched MEDLINE, EMBASE, BIOSIS, the Cochrane Methodology Register, and Database of Abstracts of Reviews of Effects (DARE) from 2001 to October 2011. Citation searches based on three key papers were conducted, and studies from our previous review (search to 2001) were eligible. One reviewer extracted data on the study design, objective, sources of bias and/or variation, and results. A second reviewer checked the extraction. RESULTS: We summarized the number of studies providing evidence of an effect arising from each source of bias and variation on the estimates of sensitivity, specificity, and overall accuracy. CONCLUSIONS: We found consistent evidence for the effects of case-control design, observer variability, availability of clinical information, reference standard, partial and differential verification bias, demographic features, and disease prevalence and severity. Effects were generally stronger for sensitivity than for specificity. Evidence for other sources of bias and variation was limited.

27. **ARTÍCULO Nº: 4599**

Berkman ND, Lohr KN, Morgan LC, Kuo TM, Morton SC. ***Interrater reliability of grading strength of evidence varies with the complexity of the evidence in systematic reviews***. J.Clin.Epidemiol. 2013; 66(10): 1105-1117.

OBJECTIVES: To examine consistency (interrater reliability) of applying guidance for grading strength of evidence in systematic reviews for the Agency for Healthcare Research and Quality Evidence-based Practice Center program. STUDY DESIGN AND SETTING: Using data from two systematic reviews, authors tested the main components of the approach: (1) scoring evidence on the four required domains (risk of bias, consistency, directness, and precision) separately for randomized controlled trials (RCTs) and observational studies and (2) developing an overall strength of evidence grade, given the scores for each of these domains. RESULTS: Conclusions about overall strength of evidence reached by experienced systematic reviewers based on the same evidence can differ greatly, especially for complex bodies of evidence. Current instructions may be sufficient for straightforward quantitative evaluations that use meta-analysis for summarizing RCT findings. In contrast, agreement

suffered when evaluations did not lend themselves to meta-analysis and reviewers needed to rely on their own qualitative judgment. Three areas raised particular concern: (1) evidence from a combination of RCTs and observational studies, (2) outcomes with differing measurement, and (3) evidence that appeared to show no differences in outcomes. CONCLUSION: Interrater reliability was highly variable for scoring strength of evidence domains and combining scores to reach overall strength of evidence grades. Future research can help in establishing improved methods for evaluating these complex bodies of evidence.

28. **ARTÍCULO Nº: 4600**

Struik FM, Kerstjens HA, Bladder G, Sprooten R, Zijnen M, Asin J et al. ***The Severe Respiratory Insufficiency Questionnaire scored best in the assessment of health-related quality of life in chronic obstructive pulmonary disease.*** J.Clin.Epidemiol. 2013; 66(10): 1166-1174.

OBJECTIVE: There are limited data on health-related quality of life (HRQL) in chronic obstructive pulmonary disease (COPD) patients with chronic hypercapnic respiratory failure during an admission requiring ventilatory support. The aim was to assess and compare the reliability and validity of the Clinical COPD Questionnaire (CCQ), Chronic Respiratory Questionnaire (CRQ), Maugeri Respiratory Failure-28 (MRF-28) Questionnaire, and Severe Respiratory Insufficiency (SRI) Questionnaire in patients with very severe COPD. STUDY DESIGN AND SETTING: One hundred eighty hospitalized patients filled out the CCQ, CRQ, MRF-28, SRI, Groningen Activity Restriction Scale (GARS), Hospital Anxiety and Depression Scale (HADS), and the Medical Research Council Dyspnea Scale (MRC). Reliability was examined by assessing distribution of total scores, floor and ceiling effects, and internal consistency (using Cronbach alpha coefficient). Construct validity between questionnaires and also the other measurements were tested with Spearman rho. RESULTS: All four questionnaires were feasible in this setting and had reasonable characteristics for distribution of total scores, floor and ceiling effects, internal consistency, and construct validity. On balance, the SRI scored best. Additionally, the SRI had a remarkable high explained variance by HADS, GARS, and MRC (73%). CONCLUSION: The SRI performed slightly better than the CCQ, CRQ, and MRF-28, which renders it the preferred questionnaire for scoring HRQL in patients with very severe COPD.

29. **ARTÍCULO Nº: 4601**

Kotz D, Cals JW. ***Effective writing and publishing scientific papers, part VII: tables and figures.*** J.Clin.Epidemiol. 2013; 66(11): 1197

30. **ARTÍCULO Nº: 4602**

Cals JW, Kotz D. ***Effective writing and publishing scientific papers, part VIII: references.*** J.Clin.Epidemiol. 2013; 66(11): 1198

31. **ARTÍCULO Nº: 4603**

Tharyan P. ***Introducing conceptual and analytical clarity on dimensions of complexity in systematic reviews of complex interventions.*** J.Clin.Epidemiol. 2013; 66(11): 1202-1204.

32. **ARTÍCULO Nº: 4604**

Anderson LM, Petticrew M, Chandler J, Grimshaw J, Tugwell P, O'Neill J et al. ***Introducing a series of methodological articles on considering complexity in systematic reviews of interventions.*** J.Clin.Epidemiol. 2013; 66(11): 1205-1208.

33. **ARTÍCULO Nº: 4605**

Petticrew M, Anderson L, Elder R, Grimshaw J, Hopkins D, Hahn R et al. ***Complex interventions and their implications for systematic reviews: a pragmatic approach***. J.Clin.Epidemiol. 2013; 66(11): 1209-1214.

Complex interventions present unique challenges for systematic reviews. Current debates tend to center around describing complexity, rather than providing guidance on what to do about it. At a series of meetings during 2009-2012, we met to review the challenges and practical steps reviewer could take to incorporate a complexity perspective into systematic reviews. Based on this, we outline a pragmatic approach to dealing with complexity, beginning, as for any review, with clearly defining the research question(s). We argue that reviews of complex interventions can themselves be simple or complex, depending on the question to be answered. In systematic reviews and evaluations of complex interventions, it will be helpful to start by identifying the sources of complexity, then mapping aspects of complexity in the intervention onto the appropriate sources of evidence (such as specific types of quantitative or qualitative study). Although we focus on systematic reviews, the general approach is also applicable to primary research that is aimed at evaluating complex interventions. Although the examples are drawn from health care, the approach may also be applied to other sectors (e.g., social policy or international development). We end by concluding that systematic reviews should follow the principle of Occam's razor: explanations should be as complex as they need to be and no more.

34. **ARTÍCULO Nº: 4606**

Squires JE, Valentine JC, Grimshaw JM. ***Systematic reviews of complex interventions: framing the review question***. J.Clin.Epidemiol. 2013; 66(11): 1215-1222.

The first and most important decision in preparing any systematic review is to clearly frame the question the review team seeks to answer. However, this is not always straightforward, particularly if synthesis teams are interested in the effects of complex interventions. In this article, we discuss how to formulate good systematic review questions of complex interventions. We describe the rationale for developing well-formulated review questions and review the existing guidance on formulating review questions. We discuss that complex interventions can contain a mix of effective and ineffective (or even harmful) actions, which may interact synergistically or dysynergistically or be interdependent, and how these interactions and interdependencies need to be considered when formulating systematic review questions. We discuss complexity specifically in terms of how it relates to the type of question, the scope of the review (i.e., lumping vs. splitting debate), and specification of the intervention. We offer several recommendations to assist review authors in developing a definition for their complex intervention of interest, which is an essential first step in formulating the review question. We end by identifying areas in which future methodological research aimed at improving question formulation, especially as it relates to complex interventions, is needed.

35. **ARTÍCULO Nº: 4607**

Anderson LM, Oliver SR, Michie S, Rehfuess E, Noyes J, Shemilt I. ***Investigating complexity in systematic reviews of interventions by using a spectrum of methods***. J.Clin.Epidemiol. 2013; 66(11): 1223-1229.

Systematic reviews framed by PICOS (Populations, Interventions, Comparisons, Outcomes, and Study designs) have been valuable for synthesizing evidence about the effects of interventions. However, this framework is limited in its utility for exploring the influence of variations within populations or

interventions, or about the mechanisms of action or causal pathways thought to mediate outcomes, other contextual factors that might similarly moderate outcomes, or how and when these mechanisms and elements interact. Valuable insights into these issues come from configurative as well as aggregative methods of synthesis. This article considers the range of evidence that can be used in systematic reviews of interventions to investigate complexity in terms of potential sources of variation in interventions and their effects, and presents a continuum of purposes for, and approaches to, evidence synthesis. Choosing an appropriate synthesis method takes into account whether the purpose of the synthesis is to generate, explore, or test theories. Taking complexity into account in a synthesis of economic evidence similarly shifts emphasis from evidence synthesis strategies focused on aggregation toward configurative strategies that aim to develop, explore, and refine (in advance of testing) theories or explanations of how and why interventions are more or less resource intensive, costly or cost-effective in different settings, or when implemented in different ways.

36. **ARTÍCULO Nº: 4608**

Petticrew M, Rehfuess E, Noyes J, Higgins JP, Mayhew A, Pantoja T et al. ***Synthesizing evidence on complex interventions: how meta-analytical, qualitative, and mixed-method approaches can contribute*** . J.Clin.Epidemiol. 2013; 66(11): 1230-1243.

OBJECTIVES: Although there is increasing interest in the evaluation of complex interventions, there is little guidance on how evidence from complex interventions may be reviewed and synthesized, and the relevance of the plethora of evidence synthesis methods to complexity is unclear. This article aims to explore how different meta-analytical approaches can be used to examine aspects of complexity; describe the contribution of various narrative, tabular, and graphical approaches to synthesis; and give an overview of the potential choice of selected qualitative and mixed-method evidence synthesis approaches. STUDY DESIGN AND SETTING: The methodological discussions presented here build on a 2-day workshop held in Montebello, Canada, in January 2012, involving methodological experts from the Campbell and Cochrane Collaborations and from other international review centers (Anderson L, Petticrew M, Chandler J, et al. INTRODUCTION: systematic reviews of complex interventions. In press). These systematic review methodologists discussed the broad range of existing methods and considered the relevance of these methods to reviews of complex interventions. RESULTS: The evidence from primary studies of complex interventions may be qualitative or quantitative. There is a wide range of methodological options for reviewing and presenting this evidence. Specific contributions of statistical approaches include the use of meta-analysis, meta-regression, and Bayesian methods, whereas narrative summary approaches provide valuable precursors or alternatives to these. Qualitative and mixed-method approaches include thematic synthesis, framework synthesis, and realist synthesis. A suitable combination of these approaches allows synthesis of evidence for understanding complex interventions. CONCLUSION: Reviewers need to consider which aspects of complex interventions should be a focus of their review and what types of quantitative and/or qualitative studies they will be including, and this will inform their choice of review methods. These may range from standard meta-analysis through to more complex mixed-method synthesis and synthesis approaches that incorporate theory and/or user's perspectives.

37. **ARTÍCULO Nº: 4609**

Pigott T, Shepperd S. ***Identifying, documenting, and examining heterogeneity in systematic reviews of complex interventions.*** J.Clin.Epidemiol. 2013; 66(11): 1244-1250.

This article describes approaches for planning, dealing, and analyzing heterogeneity in a systematic review of complex interventions. Approaches aim to generate a priori hypotheses of the mechanism

of action of a complex intervention to identify the key variables that might contribute to variation among studies and guide statistical analysis. In addition to characteristics related to the population, intervention, and outcomes, we describe study-related variables, such as the way the interventions have been implemented and the context and conduct of studies. These approaches will guide reviewers planning a meta-analysis and provide a rationale for not meta-analyzing data if there is too much variability. Potential difficulties in applying meta-analytical techniques to examine statistical association among study results and sources of potential heterogeneity are described; these include the selection of a fixed or random-effects model, the risk of multiple testing and confounding when studies include different aspects of a complex intervention or different subsamples of the intended participant pool.

38. **ARTÍCULO Nº: 4610**

Burford B, Lewin S, Welch V, Rehfuess E, Waters E. ***Assessing the applicability of findings in systematic reviews of complex interventions can enhance the utility of reviews for decision making***. J.Clin.Epidemiol. 2013; 66(11): 1251-1261.

Assessment of applicability is an essential part of the systematic review process. In the context of systematic reviews of the effects of interventions, applicability is an assessment of whether the findings of a review can be applied in a particular context or population. For more complex interventions, assessing applicability can be challenging because of greater diversity of, and interactions within and between, the intended population, intervention components, comparison conditions, and outcomes as well as a range of further considerations related to intervention context and theoretical basis. We recommend that review authors plan and conduct analyses to explain variations in effect and answer questions about mechanisms of action and influence of different settings, contexts, and populations. We also recommend that review authors provide rich descriptions of the setting, implementation details, resource use, and contexts of included studies and assess applicability for at least one target population, setting, and context. This should facilitate applicability assessments by end users. Consensus on terminology is needed and guidance should be developed for the synthesis of implementation information within reviews as well as the documentation of applicability judgments by review authors.

39. **ARTÍCULO Nº: 4611**

Noyes J, Gough D, Lewin S, Mayhew A, Michie S, Pantoja T et al. ***A research and development agenda for systematic reviews that ask complex questions about complex interventions***. J.Clin.Epidemiol. 2013; 66(11): 1262-1270.

OBJECTIVES: This article outlines a research and development agenda for systematic reviews that ask complex questions about interventions varying in degree and type of complexity. STUDY DESIGN AND SETTING: Consensus development by key authors of articles on methodological challenges in systematic reviews of complex interventions, based on a 2-day workshop in Montebello, Canada, January 2012. RESULTS: There is an urgent need for a more precise and consistently applied lexicon and language to disaggregate several conceptually distinct dimensions of "complexity." Selected current evidence synthesis methods have potential application in reviews where complexity is important. There is a lack of evaluation of methods to better understand the nature of complex interventions and the optimal processes of synthesizing and interpreting evidence from these systematic reviews. Gaps in methods, knowledge, and know-how exist, and there is a need for additional guidance. CONCLUSION: Understanding how complexity can impact on findings of systematic reviews is critical. Experience in applying methods that have been developed to facilitate

this understanding is limited, and the degree to which these approaches improve the systematic review process or transparency is only partially understood. Future research should concentrate on the impact of complexity on the systematic review process and findings and on further methodological development.

40. **ARTÍCULO Nº: 4612**

Shaw RJ, McDuffie JR, Hendrix CC, Edie A, Lindsey-Davis L, Nagi A et al. ***Effects of nurse-managed protocols in the outpatient management of adults with chronic conditions: a systematic review and meta-analysis***. Ann.Intern.Med. 2014; 161(2): 113-121.

BACKGROUND: Changes in federal health policy are providing more access to medical care for persons with chronic disease. Providing quality care may require a team approach, which the American College of Physicians calls the "medical home." One new model may involve nurse-managed protocols. PURPOSE: To determine whether nurse-managed protocols are effective for outpatient management of adults with diabetes, hypertension, and hyperlipidemia. DATA SOURCES: MEDLINE, Cochrane Central Register of Controlled Trials, EMBASE, and CINAHL from January 1980 through January 2014. STUDY SELECTION: Two reviewers used eligibility criteria to assess all titles, abstracts, and full texts and resolved disagreements by discussion or by consulting a third reviewer. DATA EXTRACTION: One reviewer did data abstractions and quality assessments, which were confirmed by a second reviewer. DATA SYNTHESIS: From 2954 studies, 18 were included. All studies used a registered nurse or equivalent who titrated medications by following a protocol. In a meta-analysis, hemoglobin A1c level decreased by 0.4% (95% CI, 0.1% to 0.7%) (n = 8); systolic and diastolic blood pressure decreased by 3.68 mm Hg (CI, 1.05 to 6.31 mm Hg) and 1.56 mm Hg (CI, 0.36 to 2.76 mm Hg), respectively (n = 12); total cholesterol level decreased by 0.24 mmol/L (9.37 mg/dL) (CI, 0.54-mmol/L decrease to 0.05-mmol/L increase [20.77-mg/dL decrease to 2.02-mg/dL increase]) (n = 9); and low-density-lipoprotein cholesterol level decreased by 0.31 mmol/L (12.07 mg/dL) (CI, 0.73-mmol/L decrease to 0.11-mmol/L increase [28.27-mg/dL decrease to 4.13-mg/dL increase]) (n = 6). LIMITATION: Studies had limited descriptions of the interventions and protocols used. CONCLUSION: A team approach that uses nurse-managed protocols may have positive effects on the outpatient management of adults with chronic conditions, such as diabetes, hypertension, and hyperlipidemia. PRIMARY FUNDING SOURCE: U.S. Department of Veterans Affairs.

41. **ARTÍCULO Nº: 4613**

Centor RM, Fleming DA, Moyer DV. ***Maintenance of certification: beauty is in the eyes of the beholder***. Ann.Intern.Med. 2014; 161(3): 226-227.

42. **ARTÍCULO Nº: 4614**

Koltov MK, Damle NS. ***Health policy basics: physician quality reporting system***. Ann.Intern.Med. 2014; 161(5): 365-367.

The U.S. health care system is in the midst of transforming from a fee-for-service system to a value-based system that delivers high-quality and cost-effective care. Quality reporting programs and increasing transparency of performance are meant to encourage physicians and hospitals to invest in improving the delivery of care. In 2006, the Centers for Medicare & Medicaid Services implemented the Physician Quality Reporting System (PQRS). The PQRS is an incentive and penalty payment program for eligible professionals who report data on quality measures for covered professional services furnished to Medicare beneficiaries. The program gives eligible professionals the opportunity to assess the quality of care they are providing to their patients and compare their performance on a

given measure with that of their peers. This article discusses the history of PQRS, the 2014 PQRS, and how it affects other quality programs.

43. **ARTÍCULO Nº: 4615**

Fernandez-Liz E, Romero Suau MR. ***[Nonsteroidal antiinflammatory drugs and cardiovascular risk: Implications for clinical practice]***. Aten.Primaria. 2014; 46(7): 323-325.

44. **ARTÍCULO Nº: 4616**

Bernabeu-Wittel M, onso-Coello P, Rico-Blazquez M, Rotaeche del CR, Sanchez GS, Casariego VE. ***[Development of clinical practice guidelines for patients with comorbidity and multiple diseases]***. Aten.Primaria. 2014; 46(7): 385-392.

The management of patients with comorbidity and polypathology represents a challenge for all healthcare systems. Clinical practice guidelines (CPGs) have limitations when applied to this population. The aim of this study is to propose the terminology and methodology for optimally approach comorbidity and polypathology in the CPGs. Based on a literature review, we suggest a number of proposals for the approach in different phases of CPG preparation, with special attention to the inclusion of clusters of comorbidity in the initial questions the implementation of indirect evidence, the burden of disease management for patients and their environment, when establishing recommendations, as well as the strategies of dissemination and implementation. These proposals should be developed in greater depth with the implication of more agents in order to have valid and useful tools for this population.

45. **ARTÍCULO Nº: 4617**

Gracia BR, Garcia AM, Martinez N, I, Galvan LF. ***[Positioning of scientific societies and working groups reviews: statement on conflicts of interest and need for transparency]***. Aten.Primaria. 2014; 46(7): 396

46. **ARTÍCULO Nº: 4618**

Dewa CS, Loong D, Bonato S, Thanh NX, Jacobs P. ***How does burnout affect physician productivity? A systematic literature review***. BMC.Health Serv.Res. 2014; 14: 325

BACKGROUND: Interest in the well-being of physicians has increased because of their contributions to the healthcare system quality. There is growing recognition that physicians are exposed to workplace factors that increase the risk of work stress. Long-term exposure to high work stress can result in burnout. Reports from around the world suggest that about one-third to one-half of physicians experience burnout. Understanding the outcomes associated with burnout is critical to understanding its affects on the healthcare system. Productivity outcomes are among those that could have the most immediate effects on the healthcare system. This systematic literature review is one of the first to explore the evidence for the types of physician productivity outcomes associated with physician burnout. It answers the question, "How does burnout affect physician productivity?" METHODS: A systematic search was performed of: Medline Current, Medline in process, PsycInfo, Embase and Web of Science. The search period covered 2002 to 2012. The searches identified articles about practicing physicians working in civilian settings. Articles that primarily looked only at residents or medical students were excluded. Productivity was captured by hours worked, patients seen, sick leave, leaving the profession, retirement, workload and presenteeism. Studies also were excluded if: (1) the study sample was not comprised of at least 50% physicians, (2) the study did not examine the relationship between burnout and productivity or (3) a validated measure of burnout was not used. RESULTS: The

search identified 870 unique citations; 5 met the inclusion/exclusion criteria. This review indicates that globally there is recognition of the potential impact of physician burnout on productivity. Productivity was examined using: number of sick leave days, work ability, intent to either continue practicing or change jobs. The majority of the studies indicate there is a negative relationship between burnout and productivity. However, there is variation depending on the type of productivity outcome examined. CONCLUSIONS: There is evidence that burnout is associated with decreased productivity. However, this line of inquiry is still developing. A number of gaps are yet to be filled including understanding how to quantify the changes in productivity related to burnout.

47. **ARTÍCULO Nº: 4619**

Vogl M, Wilkesmann R, Lausmann C, Plotz W. ***The impact of preoperative patient characteristics on the cost-effectiveness of total hip replacement: a cohort study***. BMC.Health Serv.Res. 2014; 14: 342

BACKGROUND: To facilitate the discussion on the increasing number of total hip replacements (THR) and their effectiveness, we apply a joint evaluation of hospital case costs and health outcomes at the patient level to enable comparative effectiveness research (CER) based on the preoperative health state. METHODS: In 2012, 292 patients from a German orthopedic hospital participated in health state evaluation before and 6 months after THR, where health-related quality of life (HRQoL) and disease specific pain and dysfunction were analyzed using EQ-5D and WOMAC scores. Costs were measured with a patient-based DRG costing scheme in a prospective observation of a cohort. Costs per quality-adjusted life year (QALY) were calculated based on the preoperative WOMAC score, as preoperative health states were found to be the best predictors of QALY gains in multivariate linear regressions. RESULTS: Mean inpatient costs of THR were 6,310 Euros for primary replacement and 7,730 Euros for inpatient lifetime costs including revisions. QALYs gained using the U.K. population preference-weighted index were 5.95. Lifetime costs per QALY were 1,300 Euros. CONCLUSIONS: The WOMAC score and the EQ-5D score before operation were the most important predictors of QALY gains. The poorer the WOMAC score or the EQ-5D score before operation, the higher the patient benefit. Costs per QALY were far below common thresholds in all preoperative utility score groups and with all underlying calculation methodologies.

48. **ARTÍCULO Nº: 4620**

Eldh AC, Fredriksson M, Halford C, Wallin L, Dahlstrom T, Vengberg S et al. ***Facilitators and barriers to applying a national quality registry for quality improvement in stroke care***. BMC.Health Serv.Res. 2014; 14: 354

BACKGROUND: National quality registries (NQRs) purportedly facilitate quality improvement, while neither the extent nor the mechanisms of such a relationship are fully known. The aim of this case study is to describe the experiences of local stakeholders to determine those elements that facilitate and hinder clinical quality improvement in relation to participation in a well-known and established NQR on stroke in Sweden. METHODS: A strategic sample was drawn of 8 hospitals in 4 county councils, representing a variety of settings and outcomes according to the NQR's criteria. Semi-structured telephone interviews were conducted with 25 managers, physicians in charge of the Riks-Stroke, and registered nurses registering local data at the hospitals. Interviews, including aspects of barriers and facilitators within the NQR and the local context, were analysed with content analysis. RESULTS: An NQR can provide vital aspects for facilitating evidence-based practice, for example, local data drawn from national guidelines which can be used for comparisons over time within the organisation or with other hospitals. Major effort is required to ensure that data entries are accurate and valid, and thus the trustworthiness of local data output competes with resources needed for

everyday clinical stroke care and quality improvement initiatives. Local stakeholders with knowledge of and interest in both the medical area (in this case stroke) and quality improvement can apply the NQR data to effectively initiate, carry out, and evaluate quality improvement, if supported by managers and co-workers, a common stroke care process and an operational management system that embraces and engages with the NQR data.
CONCLUSION: While quality registries are assumed to support adherence to evidence-based guidelines around the world, this study proposes that a NQR can facilitate improvement of care but neither the registry itself nor the reporting of data initiates quality improvement. Rather, the local and general evidence provided by the NQR must be considered relevant and must be applied in the local context. Further, the quality improvement process needs to be facilitated by stakeholders collaborating within and outside the context, who know how to initiate, perform, and evaluate quality improvement, and who have the resources to do so.

49. **ARTÍCULO Nº: 4621**

Panagioti M, Richardson G, Small N, Murray E, Rogers A, Kennedy A et al. ***Self-management support interventions to reduce health care utilisation without compromising outcomes: a systematic review and meta-analysis***. BMC.Health Serv.Res. 2014; 14: 356

BACKGROUND: There is increasing interest in the role of 'self-management' interventions to support the management of long-term conditions in health service settings. Self-management may include patient education, support for decision-making, self-monitoring and psychological and social support. Self-management support has potential to improve the efficiency of health services by reducing other forms of utilisation (such as primary care or hospital use), but a shift to self-management may lead to negative outcomes, such as patients who feel more anxious about their health, are less able to cope, or who receive worse quality of care, all of which may impact on their health and quality of life. We sought to determine which models of self-management support are associated with significant reductions in health services utilisation without compromising outcomes among patients with long-term conditions.
METHODS: We used systematic review with meta-analysis. We included randomised controlled trials in patients with long-term conditions which included self-management support interventions and reported measures of service utilisation or costs, as well as measures of health outcomes (standardized disease specific quality of life, generic quality of life, or depression/anxiety).We searched multiple databases (CENTRAL, CINAHL, Econlit, EMBASE, HEED, MEDLINE, NHS EED and PsycINFO) and the reference lists of published reviews. We calculated effects sizes for both outcomes and costs, and presented the results in permutation plots, as well as conventional meta-analyses.
RESULTS: We included 184 studies. Self-management support was associated with small but significant improvements in health outcomes, with the best evidence of effectiveness in patients with diabetic, respiratory, cardiovascular and mental health conditions. Only a minority of self-management support interventions reported reductions in health care utilisation in association with decrements in health. Evidence for reductions in utilisation associated with self-management support was strongest in respiratory and cardiovascular problems. Studies at higher risk of bias were more likely to report benefits.
CONCLUSIONS: Self-management support interventions can reduce health service utilization without compromising patient health outcomes, although effects were generally small, and the evidence was strongest in respiratory and cardiovascular disorders. Further work is needed to determine which components of self-management support are most effective.

50. **ARTÍCULO Nº: 4622**

Clay-Williams R, Nosrati H, Cunningham FC, Hillman K, Braithwaite J. ***Do large-scale hospital- and system-wide interventions improve patient outcomes: a systematic review***. BMC.Health Serv.Res. 2014; 14(1): 369

BACKGROUND: While health care services are beginning to implement system-wide patient safety interventions, evidence on the efficacy of these interventions is sparse. We know that uptake can be variable, but we do not know the factors that affect uptake or how the interventions establish change and, in particular, whether they influence patient outcomes. We conducted a systematic review to identify how organisational and cultural factors mediate or are mediated by hospital-wide interventions, and to assess the effects of those factors on patient outcomes. METHODS: A systematic review was conducted and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Database searches were conducted using MEDLINE from 1946, CINAHL from 1991, EMBASE from 1947, Web of Science from 1934, PsycINFO from 1967, and Global Health from 1910 to September 2012. The Lancet, JAMA, BMJ, BMJ Quality and Safety, The New England Journal of Medicine and Implementation Science were also hand searched for relevant studies published over the last 5 years. Eligible studies were required to focus on organisational determinants of hospital- and system-wide interventions, and to provide patient outcome data before and after implementation of the intervention. Empirical, peer-reviewed studies reporting randomised and non-randomised controlled trials, observational, and controlled before and after studies were included in the review. RESULTS: Six studies met the inclusion criteria. Improved outcomes were observed for studies where outcomes were measured at least two years after the intervention. Associations between organisational factors, intervention success and patient outcomes were undetermined: organisational culture and patient outcomes were rarely measured together, and measures for culture and outcome were not standardised. CONCLUSIONS: Common findings show the difficulty of introducing large-scale interventions, and that effective leadership and clinical champions, adequate financial and educational resources, and dedicated promotional activities appear to be common factors in successful system-wide change.The protocol has been registered in the international prospective register of systematic reviews, PROSPERO (Registration No. CRD42103003050).

51. **ARTÍCULO Nº: 4623**

van Riet PJ, Vernooij-Dassen M, Droes RM, Radbruch L, Vissers K, Engels Y. ***Consensus on quality indicators to assess the organisation of palliative cancer and dementia care applicable across national healthcare systems and selected by international experts***. BMC.Health Serv.Res. 2014; 14: 396

BACKGROUND: Large numbers of vulnerable patients are in need of palliative cancer and dementia care. However, a wide gap exists between the knowledge of best practices in palliative care and their use in everyday clinical practice. As part of a European policy improvement program, quality indicators (QIs) have been developed to monitor and improve the organisation of palliative care for patients with cancer and those with dementia in various settings in different European countries. METHOD: A multidisciplinary, international panel of professionals participated in a modified RAND Delphi procedure to compose a set of palliative care QIs based on existing sets of QIs on the organisation of palliative care. Panellists participated in three written rounds, one feedback round and one meeting. The panel's median votes were used to identify the final set of QIs. RESULTS: The Delphi procedure

resulted in 23 useful QIs. These QIs represent key elements of the organisation of good clinical practice, such as the availability of palliative care teams, the availability of special facilities to provide palliative care for patients and their relatives, and the presence of educational interventions for professionals. The final set also includes QIs that are related to the process of palliative care, such as documentation of pain and other symptoms, communication with patients in need of palliative care and their relatives, and end-of-life decisions. CONCLUSION: International experts selected a set of 23 QIs for the organisation of palliative care. Although we particularly focused on the organisation of cancer and dementia palliative care, most QIs are generic and are applicable for other types of diseases as well.

52. **ARTÍCULO Nº: 4624**

Bradshaw PJ, Trafalski S, Hung J, Briffa TG, Einarsdottir K. ***Outcomes after first percutaneous coronary intervention for acute myocardial infarction according to patient funding source.*** BMC.Health Serv.Res. 2014; 14: 405

BACKGROUND: Disparities in the use of invasive coronary artery revascularisation procedures to manage acute myocardial infarction (AMI) have been found in several developed economies. Factors such as socio-economic status, income and funding source may influence the use of invasive procedures and have also been associated with ongoing care. The objectives of this study were to determine whether outcomes for patients at one and five years after AMI treated with first-ever percutaneous coronary intervention (PCI) were the same for public and privately funded patients. METHODS: Retrospective, population-based cohort study using linked data to identify 30-day survivors of AMI treated with PCI in the index admission between 1995 and 2008 in Western Australian hospitals. The main outcome measures were admission for another PCI, re-AMI, and all-cause and cardiac mortality at one and five years. RESULTS: At one year, private patients were at greater adjusted risk for another PCI (HR 1.62 [1.36 - 1.94]; $p < 0.001$) than public patients, and more likely to have an additional revascularisation procedure from 90 days to 5 years (HR 1.33 [1.11 - 1.58]; $p < 0.001$). They were at less risk for all-cause death within five years (HR 0.69 [0.62-0.91]; $p = 0.01$) with a trend to reduced risk for cardiac death and re-AMI. CONCLUSIONS: Treatment as a private patient for AMI with first PCI is associated with an increased likelihood of additional coronary revascularisation procedure within 12 months and to five years, and a reduced risk for all-cause mortality to 5 years. While additional procedures were not associated with poorer outcomes, there was no clear relationship between better outcomes and additional procedures. Other lifestyle and health care factors may contribute to the significant reduction in all-cause mortality and the trends to reduced hazard for AMI and cardiac death among private patients.

53. **ARTÍCULO Nº: 4625**

Greening NJ, Williams JE, Hussain SF, Harvey-Dunstan TC, Bankart MJ, Chaplin EJ et al. ***An early rehabilitation intervention to enhance recovery during hospital admission for an exacerbation of chronic respiratory disease: randomised controlled trial.*** BMJ. 2014; 349: g4315

OBJECTIVE: To investigate whether an early rehabilitation intervention initiated during acute admission for exacerbations of chronic respiratory disease reduces the risk of readmission over 12 months and ameliorates the negative effects of the episode on physical performance and health status. DESIGN: Prospective, randomised controlled trial. SETTING: An acute cardiorespiratory unit in a teaching hospital and an acute medical unit in an affiliated teaching district general hospital, United Kingdom. PARTICIPANTS: 389 patients aged between 45 and 93 who within 48 hours of admission to hospital with an exacerbation of chronic respiratory disease were randomised to an early

rehabilitation intervention (n=196) or to usual care (n=193). MAIN OUTCOME MEASURES: The primary outcome was readmission rate at 12 months. Secondary outcomes included number of hospital days, mortality, physical performance, and health status. The primary analysis was by intention to treat, with prespecified per protocol analysis as a secondary outcome. INTERVENTIONS: Participants in the early rehabilitation group received a six week intervention, started within 48 hours of admission. The intervention comprised prescribed, progressive aerobic, resistance, and neuromuscular electrical stimulation training. Patients also received a self management and education package. RESULTS: Of the 389 participants, 320 (82%) had a primary diagnosis of chronic obstructive pulmonary disease. 233 (60%) were readmitted at least once in the following year (62% in the intervention group and 58% in the control group). No significant difference between groups was found (hazard ratio 1.1, 95% confidence interval 0.86 to 1.43, P=0.4). An increase in mortality was seen in the intervention group at one year (odds ratio 1.74, 95% confidence interval 1.05 to 2.88, P=0.03). Significant recovery in physical performance and health status was seen after discharge in both groups, with no significant difference between groups at one year. CONCLUSION: Early rehabilitation during hospital admission for chronic respiratory disease did not reduce the risk of subsequent readmission or enhance recovery of physical function following the event over 12 months. Mortality at 12 months was higher in the intervention group. The results suggest that beyond current standard physiotherapy practice, progressive exercise rehabilitation should not be started during the early stages of the acute illness.Trial registration Current Controlled Trials ISRCTN05557928.

54. **ARTÍCULO Nº: 4626**

Rabar S, Harker M, O'Flynn N, Wierzbicki AS. ***Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance***. BMJ. 2014; 349: g4356

55. **ARTÍCULO Nº: 4627**

Carville S, Wonderling D, Stevens P. ***Early identification and management of chronic kidney disease in adults: summary of updated NICE guidance***. BMJ. 2014; 349: g4507

56. **ARTÍCULO Nº: 4628**

Morris S, Hunter RM, Ramsay AI, Boaden R, McKevitt C, Perry C et al. ***Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis***. BMJ. 2014; 349: g4757

OBJECTIVE: To investigate whether centralisation of acute stroke services in two metropolitan areas of England was associated with changes in mortality and length of hospital stay. DESIGN: Analysis of difference-in-differences between regions with patient level data from the hospital episode statistics database linked to mortality data supplied by the Office for National Statistics. SETTING: Acute stroke services in Greater Manchester and London, England. PARTICIPANTS: 258,915 patients with stroke living in urban areas and admitted to hospital in January 2008 to March 2012. INTERVENTIONS: "Hub and spoke" model for acute stroke care. In London hyperacute care was provided to all patients with stroke. In Greater Manchester hyperacute care was provided to patients presenting within four hours of developing symptoms of stroke. MAIN OUTCOME MEASURES: Mortality from any cause and at any place at 3, 30, and 90 days after hospital admission; length of hospital stay. RESULTS: In London there was a significant decline in risk adjusted mortality at 3, 30, and 90 days after admission. At 90 days the absolute reduction was -1.1% (95% confidence interval -2.1 to -0.1; relative reduction 5%), indicating 168 fewer deaths (95% confidence interval 19 to 316) during the 21 month period after reconfiguration in London. In both areas there was a significant decline in risk adjusted length of

hospital stay: -2.0 days in Greater Manchester (95% confidence interval -2.8 to -1.2; 9%) and -1.4 days in London (-2.3 to -0.5; 7%). Reductions in mortality and length of hospital stay were largely seen among patients with ischaemic stroke. CONCLUSIONS: A centralised model of acute stroke care, in which hyperacute care is provided to all patients with stroke across an entire metropolitan area, can reduce mortality and length of hospital stay.

57. **ARTÍCULO Nº: 4629**

Nieuwenhuijse MJ, Nelissen RG, Schoones JW, Sedrakyan A. ***Appraisal of evidence base for introduction of new implants in hip and knee replacement: a systematic review of five widely used device technologies***. BMJ. 2014; 349: g5133

OBJECTIVE: To determine the evidence of effectiveness and safety for introduction of five recent and ostensibly high value implantable devices in major joint replacement to illustrate the need for change and inform guidance on evidence based introduction of new implants into healthcare. DESIGN: Systematic review of clinical trials, comparative observational studies, and registries for comparative effectiveness and safety of five implantable device innovations. DATA SOURCES: PubMed (Medline), Embase, Web of Science, Cochrane, CINAHL, reference lists of articles, annual reports of major registries, summaries of safety and effectiveness for pre-market application and mandated post-market studies at the US Food and Drug Administration. STUDY SELECTION: The five selected innovations comprised three in total hip replacement (ceramic-on-ceramic bearings, modular femoral necks, and uncemented monoblock cups) and two in total knee replacement (high flexion knee replacement and gender specific knee replacement). All clinical studies of primary total hip or knee replacement for symptomatic osteoarthritis in adults that compared at least one of the clinical outcomes of interest (patient centred outcomes or complications, or both) in the new implant group and control implant group were considered. Data searching, abstraction, and analysis were independently performed and confirmed by at least two authors. Quantitative data syntheses were performed when feasible. RESULTS: After assessment of 10,557 search hits, 118 studies (94 unique study cohorts) met the inclusion criteria and reported data related to 15,384 implants in 13,164 patients. Comparative evidence per device innovation varied from four low to moderate quality retrospective studies (modular femoral necks) to 56 studies of varying quality including seven high quality (randomised) studies (high flexion knee replacement). None of the five device innovations was found to improve functional or patient reported outcomes. National registries reported two to 12 year follow-up for revision occurrence related to more than 200,000 of these implants. Reported comparative data with well established alternative devices (over 1,200,000 implants) did not show improved device survival. Moreover, we found higher revision occurrence associated with modular femoral necks (hazard ratio 1.9) and ceramic-on-ceramic bearings (hazard ratio 1.0-1.6) in hip replacement and with high flexion knee implants (hazard ratio 1.0-1.8). CONCLUSION: We did not find convincing high quality evidence supporting the use of five substantial, well known, and already implemented device innovations in orthopaedics. Moreover, existing devices may be safer to use in total hip or knee replacement. Improved regulation and professional society oversight are necessary to prevent patients from being further exposed to these and future innovations introduced without proper evidence of improved clinical efficacy and safety.

58. **ARTÍCULO Nº: 4630**

Grau J, Castells A. ***[Early colorectal cancer detection programs: an integration and quality healthcare challenge]***. Rev.Calid.Asist. 2014; 29(4): 185-187.

59. **ARTÍCULO Nº: 4631**

Rabunal-Alvarez MT, Calvin-Lamas M, Feal-Cortizas B, Martinez-Lopez LM, Pedreira-Vazquez I, Martin-Herranz MI. ***[Quality indicators in the storage and dispensing process in a Hospital Pharmacy]***. Rev.Calid.Asist. 2014; 29(4): 204-211.

OBJECTIVE: To establish indicators for the evaluation of the quality of the storage and dispensing processes related to semiautomatic vertical (SAVCS) and horizontal (SAHCS) carousel systems.
MATERIAL AND METHODS: Descriptive observational study conducted between January-December 2012. Definition of quality indicators, a target value is established and an obtained value is calculated for 2012.
RESULTS: Five quality indicators in the process of storage and dispensing of drugs were defined and calculated: indicator 1, error filling unidose trolleys: target (<1.67%), obtained (1.03%); indicator 2, filling accuracy unidose trolleys by using an SAVCS: target (<15%), obtained (11.5%); indicator 3, reliability of drug inventory in the process of drug entries using an SAHCS: target (<15%), obtained (6.53%); indicator 4, reliability of drug inventory in the picking process of orders replacement stock of clinical units using an SAHCS: target (<10%), obtained (1.97%); indicator 5, accuracy of the picking process of drug orders using an SAHCS: target (<10%), obtained (10.41%).
CONCLUSIONS: Establishing indicators has allowed the quality in terms of safety, precision and reliability of semiautomatic systems for storage and dispensing drugs to be assessed.

60. **ARTÍCULO Nº: 4632**

de Andres GB, Salazar de la Guerra RM, Ferrer AC, Revuelta ZM, Ayuso MD, Gonzalez SJ. ***[An approach to care indicators benchmarking. Learning to improve patient safety]***. Rev.Calid.Asist. 2014; 29(4): 212-219.

Improvements in clinical safety can be achieved by promoting a safety culture, professional training, and learning through benchmarking. The aim of this study was to identify areas for improvement after analysing the safety indicators in two public Hospitals in North-West Madrid Region.
MATERIAL AND METHODS: Descriptive study performed during 2011 in Hospital Universitario Puerta de Hierro Majadahonda (HUPHM) and Hospital de Guadarrama (HG). The variables under study were 40 indicators on nursing care related to patient safety. Nineteen of them were defined in the SENECA project as care quality standards in order to improve patient safety in the hospitals. The data collected were clinical history, Madrid Health Service assessment reports, care procedures, and direct observation
RESULTS: Within the 40 indicators: 22 of them were structured (procedures), HUPHM had 86%, and HG 95% 14 process indicators (training and protocols compliance) with similar results in both hospitals, apart from the care continuity reports and training in hand hygiene. The 4 results indicators (pressure ulcer, falls and pain) showed different results.
CONCLUSIONS: The analysis of the indicators allowed the following actions to be taken: to identify improvements to be made in each hospital, to develop joint safety recommendations in nursing care protocols in prevention and treatment of chronic wound, to establish systematic pain assessments, and to prepare continuity care reports on all patients transferred from HUPHM to HG.

61. **ARTÍCULO Nº: 4633**

Cantero MJ. ***[More on the Royal Decree-law 16/2012 and its urgent measures to guarantee the sustainability of the National Health System in Spain]***. Gac.Sanit. 2014; 28(5): 351-353.

62. **ARTÍCULO Nº: 4634**

Safavi KC, Dai F, Gilbertsen TA, Schonberger RB. ***Variation in surgical quality measure adherence within hospital referral regions: do publicly reported surgical quality measures distinguish among hospitals that patients are likely to compare?*** Health Serv.Res. 2014; 49(4): 1108-1120.

OBJECTIVE: To determine whether surgical quality measures that Medicare publicly reports provide a basis for patients to choose a hospital from within their geographic region. DATA SOURCE: The Department of Health and Human Services' public reporting website, http://www.medicare.gov/hospitalcompare. STUDY DESIGN: We identified hospitals (n = 2,953) reporting adherence rates to the quality measures intended to reduce surgical site infections (Surgical Care Improvement Project, 1-3) in 2012. We defined regions within which patients were likely to compare hospitals using the hospital referral regions (HRRs) from the Dartmouth Atlas of Health Care Project. We described distributions of reported SCIP adherence within each HRR, including medians, interquartile ranges (IQRs), skewness, and outliers. PRINCIPAL FINDINGS: Ninety-seven percent of HRRs had median SCIP-1 scores >/=95 percent. In 93 percent of HRRs, half of the hospitals in the HRR were within 5 percent of the median hospital's score. In 62 percent of HRRs, hospitals were skewed toward the higher rates (negative skewness). Seven percent of HRRs demonstrated positive skewness. Only 1 percent had a positive outlier. SCIP-2 and SCIP-3 demonstrated similar distributions. CONCLUSIONS: Publicly reported quality measures for surgical site infection prevention do not distinguish the majority of hospitals that patients are likely to choose from when selecting a surgical provider. More studies are needed to improve public reporting's ability to positively impact patient decision making.

63. **ARTÍCULO Nº: 4635**

DuGoff EH, Bekelman JE, Stuart EA, Armstrong K, Pollack CE. ***Surgical quality is more than volume: the association between changing urologists and complications for patients with localized prostate cancer.*** Health Serv.Res. 2014; 49(4): 1165-1183.

OBJECTIVES: To examine the association of changing urologists on surgical complications in men with prostate cancer. DATA SOURCES/STUDY SETTING: Registry and administrative claims data from the Surveillance, Epidemiology, and End Results-Medicare database from 1995 to 2005. STUDY DESIGN: A cross-sectional observational study of men with prostate cancer who underwent radical prostatectomy. METHODS: Subjects were classified as having "changed urologists" if they had a different urologist who diagnosed their cancer from the one who performed their surgery. "Doubly robust" propensity score weighted multivariable logistic regression models were used to investigate the effect of changing urologists on 30-day surgical complications, late urinary complications, and long-term incontinence. PRINCIPAL FINDINGS: Men who changed urologists between diagnosis and treatment had significantly lower odds of 30-day surgical complications compared with men who did not change urologists (odds ratio: 0.82; 95 percent confidence interval: 0.76-0.89), after adjustment. Changing urologists was associated with lower risks of 30-day complications for both black and white men compared with staying with the same urologist for their diagnosis and surgical treatment. CONCLUSIONS: Urologist changing is associated with the observed variation in complications following radical prostatectomy. This may suggest that patients are responding to aspects of surgical quality not captured in surgical volume.

64. **ARTÍCULO Nº: 4636**

randa-Gallardo M, Morales-Asencio JM, Canca-Sanchez JC, Toribio-Montero JC. ***Circumstances and causes of falls by patients at a Spanish acute care hospital.*** J.Eval.Clin.Pract. 2014; 20(5): 631-637.

RATIONALE, AIMS AND OBJECTIVES: A major problem in hospitals is that of falls, which can seriously reduce patients' quality of life. Fall rates vary considerably depending on health care practices, the hospital environment and the measurement method used. The aim of this study was to determine the characteristics of hospitalized acute patients who suffer falls, by analysing the distribution and the profile of these patients. METHODS: This is an analytic cross-sectional study conducted at a Spanish hospital. All patients who suffered a fall during hospitalization in 2011 were studied by analysing the computerized register of falls. Downton index, circumstances and consequences of falls were analysed. Descriptive statistics, bivariate analysis and logistic regression analysis were performed. RESULTS: The frequency of falls was 0.64%. The rate of falls increased with age (mean age: 71.06 years). The highest percentage occurred among patients in the medical care area (63.7%). The probability of suffering a fall was 1.33 times higher among men than women. Differences in age, type of risk of fall and circumstances were found, depending on the type of hospitalization. Multivariate analysis revealed that patients in the medical care area suffered more falls with consequences: 7.01 [95% confidence interval (CI): 1.34-36.79], as did the patients classified as 'low risk': 2.40 (CI 95%: 1.02-5.65). CONCLUSIONS: Falls have diverse causes. Determining these circumstances can contribute to promoting a culture of prevention and to reducing the injuries provoked by falls. Notification procedures should be standardized in order to enable comparisons among different environments.

65. **ARTÍCULO Nº: 4637**

Kristensen SR, Meacock R, Turner AJ, Boaden R, McDonald R, Roland M et al. ***Long-term effect of hospital pay for performance on mortality in England***. N.Engl.J.Med. 2014; 371(6): 540-548.

BACKGROUND: A pay-for-performance program based on the Hospital Quality Incentive Demonstration was introduced in all hospitals in the northwest region of England in 2008 and was associated with a short-term (18-month) reduction in mortality. We analyzed the long-term effects of this program, called Advancing Quality.
METHODS: We analyzed 30-day in-hospital mortality among 1,825,518 hospital admissions for eight conditions, three of which were covered by the financial-incentive program. The hospitals studied included the 24 hospitals in the northwest region that were participating in the program and 137 elsewhere in England that were not participating. We used difference-in-differences regression analysis to compare risk-adjusted mortality for an 18-month period before the program was introduced with subsequent mortality in the short term (the first 18 months of the program) and the longer term (the next 24 months).
RESULTS: Throughout the short-term and the long-term periods, the performance of hospitals in the incentive program continued to improve and mortality for the three conditions covered by the program continued to fall. However, the reduction in mortality among patients with these conditions was greater in the control hospitals (those not participating in the program) than in the hospitals that were participating in the program (by 0.7 percentage points; 95% confidence interval [CI], 0.3 to 1.2). By the end of the 42-month follow-up period, the reduced mortality in the participating hospitals was no longer significant (-0.1 percentage points; 95% CI, -0.6 to 0.3). From the short term to the longer term, the mortality for conditions not covered by the program fell more in the participating hospitals than in the control hospitals (by 1.2 percentage points; 95% CI, 0.4 to 2.0), raising the possibility of a positive spillover effect on care for conditions not covered by the program.
CONCLUSIONS: Short-term relative reductions in mortality for conditions linked to financial incentives in hospitals participating in a pay-for-performance program in England were not maintained.

66. **ARTÍCULO Nº: 4638**

Neumann PJ, Cohen JT, Weinstein MC. ***Updating cost-effectiveness--the curious resilience of the $50,000-per-QALY threshold.*** N.Engl.J.Med. 2014; 371(9): 796-797.

67. **ARTÍCULO Nº: 4639**

Lieberman D. ***Colon-polyp surveillance--do patients benefit?*** N.Engl.J.Med. 2014; 371(9): 860-861.

68. **ARTÍCULO Nº: 4640**

Footman K, Garthwaite K, Bambra C, McKee M. ***Quality check: Does it matter for quality how you organize and pay for health care? A review of the international evidence.*** Int.J.Health Serv. 2014; 44(3): 479-505.

Health systems in high-income countries have experienced significant organizational and financial reforms over the last 25 years. The implications of these changes for the effectiveness of health care systems need to be examined, particularly in relation to their effects on the quality of health services (a pertinent issue in the United Kingdom in light of the Francis Report). Systematic review methodology was used to locate and evaluate published systematic reviews of quantitative intervention studies (experimental and observational) on the effects of health system organizational and financial reforms (system financing, funding allocations, direct purchasing arrangements, organization of service provision, and service integration) on quality of care in high-income countries. Nineteen systematic reviews were identified. The evidence on the payment of providers and purchaser-provider splits was inconclusive. In contrast, there is some evidence that greater integration of services can benefit patients. There were no relevant studies located relating to funding allocation reforms or direct purchasing arrangements. The systematic review-level evidence base suggests that the privatization and marketization of health care systems does not improve quality, with most financial and organizational reforms having either inconclusive or negative effects.

69. **ARTÍCULO Nº: 4641**

Weinick RM, Quigley DD, Mayer LA, Sellers CD. ***Use of CAHPS patient experience surveys to assess the impact of health care innovations.*** Jt.Comm J.Qual.Patient.Saf. 2014; 40(9): 418-427.

BACKGROUND: The Consumer Assessment of Healthcare Providers and Systems (CAHPS) surveys are the standard for collecting information about patient experience of care in the United States. However, despite their widespread use, including in pay-for-performance and public reporting efforts and various provisions of the Affordable Care Act, knowledge about the use of CAHPS in assessing the impact of quality improvement efforts is limited. A study was conducted to examine the use of patient experience surveys in assessing the impact of innovations implemented in health care settings. METHODS: Innovation profiles identified on the Agency for Healthcare Research and Quality (AHRQ) Health Care Innovations Exchange website that included patient experience (including patient satisfaction) as an outcome (N = 201), were analyzed with a variety of qualitative analysis methods. RESULTS: Fewer than half of the innovations used a patient experience measure, most commonly employing global measures such as an overall rating. Most innovations assessed patient experience at a single time point, with only one third using techniques such as pre-post comparisons, time trends, or comparisons to control groups. Ten domains of measures addressed reports of patient experience, all of which could be assessed by existing CAHPS instruments. Similarly, CAHPS measures are available to assess all of the organizational processes that are addressed by innovations in the profiles and for which patients are the best source of information. While 120 of the innovations that use patient experience measures report using surveys to collect these data, only 6 reported using a CAHPS

measure. CONCLUSIONS: Although innovations targeting quality improvement are often evaluated using surveys, there is considerable untapped potential for using CAHPS measures or surveys to assess their effectiveness.

70. **ARTÍCULO Nº: 4642**

Kontis V, Mathers CD, Rehm J, Stevens GA, Shield KD, Bonita R et al. ***Contribution of six risk factors to achieving the 25x25 non-communicable disease mortality reduction target: a modelling study***. Lancet. 2014; 384(9941): 427-437.

BACKGROUND: Countries have agreed to reduce premature mortality (defined as the probability of dying between the ages of 30 years and 70 years) from four main non-communicable diseases (NCDs)--cardiovascular diseases, chronic respiratory diseases, cancers, and diabetes--by 25% from 2010 levels by 2025 (referred to as 25x25 target). Targets for selected NCD risk factors have also been agreed on. We estimated the contribution of achieving six risk factor targets towards meeting the 25x25 mortality target. METHODS: We estimated the impact of achieving the targets for six risk factors (tobacco and alcohol use, salt intake, obesity, and raised blood pressure and glucose) on NCD mortality between 2010 and 2025. Our methods accounted for multi-causality of NCDs and for the fact that when risk factor exposure increases or decreases, the harmful or beneficial effects on NCDs accumulate gradually. We used data for risk factor and mortality trends from systematic analyses of available country data. Relative risks for the effects of individual and multiple risks, and for change in risk after decreases or increases in exposure, were from re-analyses and meta-analyses of epidemiological studies. FINDINGS: If risk factor targets are achieved, the probability of dying from the four main NCDs between the ages of 30 years and 70 years will decrease by 22% in men and by 19% in women between 2010 and 2025, compared with a decrease of 11% in men and 10% in women under the so-called business-as-usual trends (ie, projections based on current trends with no additional action). Achieving the risk factor targets will delay or prevent more than 37 million deaths (16 million in people aged 30-69 years and 21 million in people aged 70 years or older) from the main NCDs over these 15 years compared with a situation of rising or stagnating risk factor trends. Most of the benefits of achieving the risk factor targets, including 31 million of the delayed or prevented deaths, will be in low-income and middle-income countries, and will help to reduce the global inequality in premature NCD mortality. A more ambitious target on tobacco use (a 50% reduction) will almost reach the target in men (>24% reduction in the probability of death), and enhance the benefits to a 20% reduction in women. INTERPRETATION: If the agreed risk factor targets are met, premature mortality from the four main NCDs will decrease to levels that are close to the 25x25 target, with most of these benefits seen in low-income and middle-income countries. On the basis of mortality benefits and feasibility, a more ambitious target than currently agreed should be adopted for tobacco use. FUNDING: UK MRC.

71. **ARTÍCULO Nº: 4643**

Ridker PM. ***LDL cholesterol: controversies and future therapeutic directions***. Lancet. 2014; 384(9943): 607-617.

Lifelong exposure to raised concentrations of LDL cholesterol increases cardiovascular event rates, and the use of statin therapy as an adjunct to diet, exercise, and smoking cessation has proven highly effective in reducing the population burden associated with hyperlipidaemia. Yet, despite consistent biological, genetic, and epidemiological data, and evidence from randomised trials, there is controversy among national guidelines and clinical practice with regard to LDL cholesterol, its measurement, the usefulness of population-based screening, the net benefit-to-risk ratio for different

LDL-lowering drugs, the benefit of treatment targets, and whether aggressive lowering of LDL is safe. Several novel therapies have been introduced for the treatment of people with genetic defects that result in loss of function within the LDL receptor, a major determinant of inherited hyperlipidaemias. Moreover, the usefulness of monoclonal antibodies that extend the LDL-receptor lifecycle (and thus result in substantial lowering of LDL cholesterol below the levels achieved with statins alone) is being assessed in phase 3 trials that will enrol more than 60,000 at-risk patients worldwide. These trials represent an exceptionally rapid translation of genetic observations into clinical practice and will address core questions of how low LDL cholesterol can be safely reduced, whether the mechanism of LDL-cholesterol lowering matters, and whether ever more aggressive lipid-lowering provides a safe, long-term mechanism to prevent atherothrombotic complications.

72. **ARTÍCULO Nº: 4644**

Nordestgaard BG, Varbo A. ***Triglycerides and cardiovascular disease***. Lancet. 2014; 384(9943): 626-635.

After the introduction of statins, clinical emphasis first focussed on LDL cholesterol-lowering, then on the potential for raising HDL cholesterol, with less focus on lowering triglycerides. However, the understanding from genetic studies and negative results from randomised trials that low HDL cholesterol might not cause cardiovascular disease as originally thought has now generated renewed interest in raised concentrations of triglycerides. This renewed interest has also been driven by epidemiological and genetic evidence supporting raised triglycerides, remnant cholesterol, or triglyceride-rich lipoproteins as an additional cause of cardiovascular disease and all-cause mortality. Triglycerides can be measured in the non-fasting or fasting states, with concentrations of 2-10 mmol/L conferring increased risk of cardiovascular disease, and concentrations greater than 10 mmol/L conferring increased risk of acute pancreatitis and possibly cardiovascular disease. Although randomised trials showing cardiovascular benefit of triglyceride reduction are scarce, new triglyceride-lowering drugs are being developed, and large-scale trials have been initiated that will hopefully provide conclusive evidence as to whether lowering triglycerides reduces the risk of cardiovascular disease.