

Julio 2014

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*TRATAMIENTO DE LA MALARIA -- UN RETO CONTINUO*

## ACADEMIC MEDICINE

[S24826861](#)

Patients frequently do not receive recommended therapies because performance expectations are often unclear. Clinical guidelines provide exhaustive details and recommendations, but this information is not formatted in a way that supports decision making or bedside translation of therapies. When performance expectations are unclear, it is difficult for clinicians to assess their own or others' competence. Checklists offer hope because they codify interventions, remove ambiguity, and increase reliability of care processes. Schmutz and colleagues developed a robust methodology to create a checklist for evaluating clinical performance, which is described in this issue of Academic Medicine. In this commentary, the authors offer several points to consider as checklists become more prevalent in medical education and clinical practice. First, culture is a much larger part of the equation than the checklist; understanding what all stakeholders expect to gain will help engage checklist use. Second, the construction, validation, and maintenance of checklist evaluation tools is labor intensive, requiring innovative dissemination approaches to ensure maximum access and use of checklists. Third, integrated systems that evaluate technically specified and adaptive performance are needed because some aspects of clinical performance cannot be captured on a checklist. Fourth, checklists provide an opportunity to evaluate and improve an individual's performance concurrently with the context in which it is delivered. A tighter connection between education and training activities and process improvement strategies will accelerate improvements in safety and quality. Schmutz and colleagues have provided advancements in performance evaluation that will help health care achieve higher-quality and safer care.

[S24826862](#)

This approach integrates published evidence and the knowledge of domain experts. A robust development process is a necessary prerequisite of valid performance checklists. Establishing a widely recognized standard for developing evaluation checklists will likely support the design of appropriate measurement tools and move the field of performance assessment in health care forward.

[S24979174](#)

Medical students made statistically significant gains in their performance on an SCT over a two-year period. These findings demonstrate same-student gains in clinical reasoning over time as measured by the SCT and suggest that the SCT as a standardized instrument can help to evaluate growth in clinical reasoning skills.

[S24979164](#)

The undergraduate medical degree, leading to a license to practice, has traditionally been the defining professional milestone of the physician. Developments in health care and medical education and training, however, have changed the significance of the medical degree in the continuum of education toward clinical practice. The author discusses six questions that should lead us to rethink the current status and significance of the medical degree and, consequently, that of the physician. These questions include the quest for core knowledge and competence of the doctor, the place of the degree in the education continuum, the increasing length of training, the sharing of health care tasks with other professionals, and the nature of professional identity in a multitasking world. The author concludes by examining ways to redefine what it means to be a "medical doctor."

[S24979165](#)

Academic Medicine's 2013 Question of the Year (QOTY) asked, "What is a doctor? What is a nurse?" In this commentary, after analyzing the published responses to the 2013 QOTY, the authors offer an assessment of the evolution of the interprofessional interaction between physicians and nurses. Finally, they examine the role of health professions education in shaping the future professional roles and scopes of practice for physicians and nurses. The authors intend to carry the discussion from the present tense (What is a doctor? What is a nurse?) into the future (What will the future team of health care professionals require?) to provide a discussion of challenges to academic medicine and academic nursing in preparing the next generation of health professionals.

## ANNALS OF INTERNAL MEDICINE

[S25023250](#)

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.

[S25023249](#)

Comorbid conditions are an important determinant of harms and benefits of screening. Estimates of screening benefits and harms by comorbid condition can inform discussions between providers and patients about personalizing screening cessation decisions.

[S25023247](#)

Men who were socially well-integrated had a more than 2-fold reduced risk for suicide over 24 years of follow-up.

S25023248

Variation in the appearance of generic pills is associated with nonpersistent use of these essential drugs after MI among patients with cardiovascular disease.

## ARCHIVOS DE BRONCONEUMOLOGIA

S24630316

Las recomendaciones que se proponen pretenden ser un instrumento que facilite la toma de decisiones en pacientes con nódulo pulmonar solitario (NPS). Para una decisión óptima hay que incorporar la accesibilidad a las distintas técnicas diagnósticas y las preferencias del paciente.

La primera valoración, que incluye la tomografía computarizada torácica, separa a un grupo de pacientes con neoplasia extrapulmonar o muy alto riesgo quirúrgico que requieren manejo individualizado. Otros 2 grupos son los pacientes con NPS de hasta 8 mm y los que tienen NPS subsólido, para los que se establecen recomendaciones específicas.

Los NPS mayores de 8 mm se clasifican según su probabilidad de malignidad en baja (menor del 5%) donde se recomienda observación, alta (mayor del 65%) que se manejan con el diagnóstico de presunción de carcinoma en estadio localizado, e intermedia, donde la tomografía de emisión de positrones tiene gran rendimiento para reclasificarlos en alta o baja probabilidad. En los casos de probabilidad de malignidad intermedia o alta puede ser una opción la punción o biopsia transbronquial del nódulo.

Se recomienda la observación radiológica con tomografía computarizada de baja radiación y sin contraste en el NPS con baja probabilidad de malignidad, y la resección con videotoracoscopia en los casos no diagnosticados y con probabilidad de malignidad intermedia o alta.

S24507905

La tos en la infancia es un síntoma muy frecuente, y constituye uno de los motivos de consulta más comunes en la práctica pediátrica diaria. Las causas de tos en el niño son diferentes a las del adulto y se deben seguir las guías específicas de la edad pediátrica para su diagnóstico y tratamiento. En la mayoría de casos la causa son infecciones respiratorias banales que producen una «tos normal o esperada», pero todo niño con tos que persiste más allá de las 4 a 8 semanas se considera que tiene «tos crónica» y debe ser evaluado para descartar patologías específicas que abarcan todo el espectro de la neumología pediátrica. El tratamiento de la tos debe realizarse en función de la etiología. Con un abordaje adecuado se puede identificar la misma hasta en el 80% de los casos y el tratamiento será efectivo en el 90% de ellos. En algunos casos de «tos crónica inespecífica», tos en la que se ha descartado patología subyacente, se puede realizar un tratamiento empírico en función de las características de la tos. No hay evidencia científica que justifique el empleo de tratamientos sintomáticos que alivien la tos, como jarabes antitusivos, mucolíticos y/o antihistamínicos, ya que pueden tener efectos secundarios potencialmente graves, por lo que no se deben emplear.

## BRITISH MEDICAL JOURNAL

S25035309

Statins form the pharmacologic cornerstone of the primary and secondary prevention of atherosclerotic cardiovascular disease. In addition to beneficial cardiovascular effects, statins seem to have multiple non-cardiovascular effects. Although early concerns about statin induced hepatotoxicity and cancer have subsided owing to reassuring evidence, two of the most common concerns that clinicians have are myopathy and diabetes. Randomized controlled trials suggest that statins are associated with a modest increase in the risk of myositis but not the risk of myalgia. Severe myopathy (rhabdomyolysis) is rare and often linked to a statin regimen that is no longer recommended (simvastatin 80 mg). Randomized controlled trials and meta-analyses suggest an increase in the risk of diabetes with statins, particularly with higher intensity regimens in people with two or more components of the metabolic syndrome. Other non-cardiovascular effects covered in this review are contrast induced nephropathy, cognition, cataracts, erectile dysfunction, and venous thromboembolism. Currently, systematic reviews and clinical practice guidelines indicate that the cardiovascular benefits of statins generally outweigh non-cardiovascular harms in patients above a certain threshold of cardiovascular risk. Literature is also accumulating on the potential non-cardiovascular benefits of statins, which could lead to novel applications of this class of drug in the future.

S25002352

Hepatitis C virus (HCV) infection is a substantial health problem worldwide. Most patients infected with HCV remain chronically infected, with an increased risk of cirrhosis and hepatocellular carcinoma. Although they are associated with toxicities and low sustained viral response rates, interferon alfa and ribavirin have been the mainstay of treatment until recently. New direct acting antivirals, specifically designed to inhibit three viral proteins (the NS3/4A protease, the NS5A protein, and the NS5B RNA dependent RNA polymerase) are now becoming available. The NS3/4A inhibitor simeprevir and NS5B inhibitor sofosbuvir have recently been licensed and can reduce the length of antiviral treatment, improve response rates, and allow for interferon-free regimens for some HCV genotypes. Several other newer direct acting antivirals have shown promise in clinical studies and are likely to be licensed soon. These agents seem to facilitate the use of shortened courses of combination interferon-free therapy, which are associated with high (>95%) sustained response rates and relatively few toxicities. These regimens have also been successful in patients who were previously difficult to treat, including those with cirrhosis, HIV coinfection, and those who have undergone liver transplantation. The high cost of these agents may be the biggest challenge to their implementation worldwide.

S25011450

Individuals with a genetic variant associated with non-drinking and lower alcohol consumption had a more favourable cardiovascular profile and a reduced risk of coronary heart disease than those without the genetic variant. This suggests that reduction of alcohol consumption, even for light to moderate drinkers, is beneficial for cardiovascular health.

S25056260

This study questions the causal effect of short interpregnancy intervals on adverse birth outcomes and points to the possibility of unmeasured or inadequately specified maternal factors in previous studies.

S25038074

Neither niacin, fibrates, nor CETP inhibitors, three highly effective agents for increasing high density lipoprotein levels, reduced all cause mortality, coronary heart disease mortality, myocardial infarction, or stroke in patients treated with statins. Although observational studies might suggest a simplistic hypothesis for high density lipoprotein cholesterol, that increasing the levels pharmacologically would generally reduce cardiovascular events, in the current era of widespread use of statins in dyslipidaemia, substantial trials of these three agents do not support this concept.

S25030633

Subgroup analyses are insufficiently described in the protocols of randomised controlled trials submitted to research ethics committees, and investigators rarely specify the anticipated direction of subgroup effects. More than one third of statements in publications of randomised controlled trials about subgroup prespecification had no documentation in the corresponding protocols. Definitive judgments regarding credibility of claimed subgroup effects are not possible without access to protocols and analysis plans of randomised controlled trials.

S24986891

Peer reviewers fail to detect important deficiencies in reporting of the methods and results of randomised trials. The number of these changes requested by peer reviewers was relatively small. Although most had a positive impact, some were inappropriate and could have a negative impact on reporting in the final publication.

[S25006006](#)

Available observational data show an inverse association between leucocyte telomere length and risk of coronary heart disease independent of conventional vascular risk factors. The association with cerebrovascular disease is less certain.

[S25028249](#)

People born into families in which someone already has cerebral palsy are themselves at elevated risk, depending on their degree of relatedness. Elevated risk may extend even to third degree relatives (first cousins). The patterns of risk suggest multifactorial inheritance, in which multiple genes interact with each other and with environmental factors. These data offer additional evidence that the underlying causes of cerebral palsy extend beyond the clinical management of delivery.

[S25073782](#)

This meta-analysis provides further evidence that a higher consumption of fruit and vegetables is associated with a lower risk of all cause mortality, particularly cardiovascular mortality.

[S24994807](#)

Comprehensive and community based primary health care programmes, such as the FHP in Brazil, acting through cardiovascular disease prevention, care, and follow-up can contribute to decreased cardiovascular disease morbidity and mortality in a developing country such as Brazil.

[S24994809](#)

Choice of definition of osteoporosis and use of NOF derived FRAX intervention thresholds have major effects on the proportion of older men identified as warranting drug treatment to prevent fracture. Among men identified with osteoporosis by WHO criteria, who comprised 2% of the study population, actual observed fracture probabilities during 10 years of follow-up were highest and exceeded FRAX predicted fracture probabilities. On the basis of findings from randomized trials in women, these men are most likely to benefit from treatment. Expanding indications for treatment beyond this small group has uncertain value owing to lower observed fracture probabilities and uncertain benefits of treatment among men not selected on the basis of WHO criteria.

[S25073783](#)

A threshold for "optimal" population RBC folate concentration for the prevention of neural tube defects could be defined (for example, approximately 1000 nmol/L). Population based RBC folate concentrations, as a biomarker for risk of neural tube defects, can be used to facilitate evaluation of prevention programs as well as to identify subpopulations at elevated risk for a neural tube defect affected pregnancy due to folate insufficiency.

## BRITISH JOURNAL OF PSYCHIATRY

[S24764545](#)

Early-life conduct problems are robustly associated with later depressive disorder and may be useful targets for early intervention.

## CANADIAN MEDICAL ASSOCIATION JOURNAL

[S24821870](#)

Pregnancy is associated with a substantial risk of a serious motor vehicle crash during the second trimester. This risk merits attention for prenatal care.

## CIRCULATION

[S24895454](#)

Elderly patients had higher stroke and major bleeding rates than younger patients, but the efficacy and safety of rivaroxaban relative to warfarin did not differ with age, supporting rivaroxaban as an alternative for the elderly.

[S24982115](#)

Healthy lifestyle changes during young adulthood are associated with decreased risk and unhealthy lifestyle changes are associated with increased risk for subclinical atherosclerosis in middle age.

[S24928682](#)

In most participants, low levels of alcohol use are associated with a moderate reduction in the risk of MI; however, the strength of this association may not be uniform across different countries. An episode of heavy drinking is associated with an increased risk of acute MI in the subsequent 24 hours, particularly in older individuals.

[S24787471](#)

In the absence of proven interventions for the primary prevention of atrial fibrillation, this post hoc analysis of the PREDIMED trial suggests that extravirgin olive oil in the context of a Mediterranean dietary pattern may reduce the risk of atrial fibrillation.

## DRUGS

[S25022950](#)

Nivolumab (Opdivo®) is a fully human monoclonal antibody against programmed death receptor-1, a negative regulatory checkpoint molecule with a role in immunosuppression. The drug is administered intravenously and is approved for the treatment of unresectable malignant melanoma in Japan. The potential for intravenous nivolumab to be used in the treatment of advanced malignancies such as melanoma was initially demonstrated in phase I dose-ranging trials. Subsequently, in a noncomparative, open-label, phase II trial, almost one-quarter of Japanese patients with previously treated stage III/IV melanoma (recurrent or unresectable) achieved a partial tumour response with intravenous nivolumab 2 mg/kg every 3 weeks. The clinical benefit of the drug was durable, with patients surviving free from progression for a median of 172 days and median overall survival not yet reached. Nivolumab had an acceptable tolerability profile in this trial, with fewer than 18 % of patients experiencing grade 3 or 4 adverse events related to the drug, the most common of which was increased  $\gamma$ -glutamyl transferase. Thus, nivolumab is an emerging, promising option for the treatment of malignant melanoma.

[S24962424](#)

Drug-resistant tuberculosis is a growing threat to global public health. Recent efforts to understand the evolution of drug resistance have shown that changes in drug-target interactions are only the first step in a longer adaptive process. The emergence of transmissible drug-resistant Mycobacterium tuberculosis is the result of a multitude of additional genetic mutations, many of which interact, a phenomenon known as epistasis. The varied effects of these epistatic interactions include compensating for the reduction of the biological cost associated with the development of drug resistance, increasing the level of resistance, and possibly accommodating broader changes in the physiology of resistant bacteria. Knowledge of these processes and our ability to detect them as they happen

informs the development of diagnostic tools and better control strategies. In particular, the use of whole genome sequencing combined with surveillance efforts in the field could provide a powerful instrument to prevent future epidemics of drug-resistant tuberculosis.

[S25005775](#)

Dolutegravir (Tivicay®) is a new-generation HIV-1 integrase strand transfer inhibitor recently approved in the EU and Japan for the treatment of HIV-1 infection in adolescents and adults in combination with other antiretroviral drugs. It is suitable for once-daily administration and achieves therapeutic concentrations without the need for pharmacokinetic boosting. It has a high barrier to resistance and is generally active against viral strains resistant to first-generation integrase inhibitors. In well-designed clinical trials in treatment-naïve or treatment-experienced, integrase inhibitor-naïve patients, dolutegravir-based combinations were shown to be noninferior or superior to raltegravir-based combinations, an efavirenz-based combination and ritonavir-boosted darunavir-based combinations with respect to virological suppression (plasma HIV-1 RNA <50 copies/mL) at week 48. Dolutegravir was also effective in a high proportion of patients failing on raltegravir- or elvitegravir-based therapy as a result of integrase resistance mutations. Dolutegravir was generally well tolerated, with the vast majority of adverse events being mild or moderate in intensity; serious adverse events were uncommon. Therefore, dolutegravir is an important new addition to the expanding list of antiretroviral drugs for treating HIV-1 infection in adults and adolescents.

[S24958336](#)

Sofosbuvir (Sovaldi®) is a nucleotide hepatitis C virus (HCV) NS5B polymerase inhibitor that has pangenotypic antiviral activity and a high genetic barrier to resistance. This article reviews the clinical efficacy and tolerability of sofosbuvir in patients with chronic hepatitis C and summarizes its pharmacological properties. Interferon-free treatment with sofosbuvir plus ribavirin achieved high sustained virological response (SVR) rates in treatment-naïve and treatment-experienced patients with HCV genotype 2 or 3 infection, and also had efficacy in patients with HCV genotype 1 infection. Sofosbuvir plus ribavirin was also effective in patients co-infected with HCV and HIV, and sofosbuvir plus ribavirin administered prior to liver transplantation prevented recurrent HCV infection in the majority of patients who had HCV RNA levels below the limit of quantification at the time of transplantation. Sofosbuvir plus peginterferon- $\alpha$ -2a and ribavirin achieved high SVR rates in patients with HCV genotype 1 infection, and also appeared effective in patients with HCV genotype 4, 5 or 6 infection. Oral sofosbuvir was generally well tolerated in patients with chronic hepatitis C. The most commonly reported adverse events and laboratory abnormalities were consistent with those expected with ribavirin and peginterferon- $\alpha$ . In conclusion, sofosbuvir represents an important advance in the treatment of chronic hepatitis C.

[S24890395](#)

Airway mucus has a key role in protective innate immune responses, but excessive mucus production and secretion in proximal and in distal airways are associated with disabling symptoms (cough and sputum), lung function decline, exacerbations and mortality in patients with chronic obstructive pulmonary disease (COPD). Cellular and molecular mechanisms leading to mucin production and secretion have largely been identified using cultured epithelial cells and animal models. Cigarette smoke and microbial products are potent triggers of mucin production, which involves recognition of specific molecular patterns by cognate receptors and activation of metalloproteases at the epithelial cell surface, leading to epidermal growth factor receptor activation and mucin mRNA and protein synthesis. After mucin synthesis has occurred, mucins are tightly packed into intracytoplasmic granules. Many stimuli induce secretion of mucin granules from epithelial cells, but neutrophil serine proteases are the most potent inducers of mucin secretion. Neutrophils recruited to the airway epithelium also promote mucin production via neutrophil proteases and oxidative stress. Several drugs currently available for the treatment of COPD patients reduced mucus hypersecretion in preclinical models relevant to COPD, but their effects on mucus hypersecretion in humans have not been assessed. Testing the effects of these drugs and of novel molecules designed for reducing mucus production and/or secretion will require performing specifically designed clinical trials. These trials will be necessary to explore the hypothesis that reducing mucus hypersecretion is beneficial in COPD patients.

[S25022951](#)

Quadrivalent human papillomavirus (HPV) [types 6, 11, 16, 18] recombinant vaccine (Gardasil®; Silgard®) is composed of virus-like particles formed by self-assembly of recombinant L1 capsid protein from each of HPV types 6, 11, 16 and 18. It is indicated for use from the age of 9 years as a two- or three-dose vaccination course over 6 months for the prevention of premalignant anogenital lesions, cervical and anal cancers, and genital warts caused by the vaccine HPV types. In placebo-controlled trials, quadrivalent HPV vaccine provided high-level protection against infection or disease caused by the vaccine HPV types over 2-4 years in females aged 15-45 years who were negative for the vaccine HPV types, and provided a degree of cross-protection against certain non-vaccine HPV types. The vaccine also provided high-level protection against persistent infection, anogenital precancerous lesions and genital warts caused by the vaccine HPV types over 3 years in susceptible males aged 16-26 years. Protection has been demonstrated for up to 8 years. In subjects who were negative for the vaccine HPV types, high seroconversion rates and high levels of anti-HPV antibodies were observed in females of all age ranges from 9 to 45 years and in males aged 9-26 years. The vaccine was generally well tolerated and was usually predicted to be cost effective in girls and young women. Therefore, quadrivalent HPV vaccine offers an effective means to substantially reduce the burden of HPV-related anogenital disease in females and males, particularly cervical cancer and genital warts.

[S25034361](#)

Edoxaban is a once-daily oral anticoagulant that rapidly and selectively inhibits factor Xa in a concentration-dependent manner. This review describes the extensive clinical development program of edoxaban, including phase III studies in patients with non-valvular atrial fibrillation (NVAf) and symptomatic venous thromboembolism (VTE). The ENGAGE AF-TIMI 48 study (N = 21,105; mean CHADS2 score 2.8) compared edoxaban 60 mg once daily (high-dose regimen) and edoxaban 30 mg once daily (low-dose regimen) with dose-adjusted warfarin [international normalized ratio (INR) 2.0-3.0] and found that both regimens were non-inferior to warfarin in the prevention of stroke and systemic embolism in patients with NVAf. Both edoxaban regimens also provided significant reductions in the risk of hemorrhagic stroke, cardiovascular mortality, major bleeding and intracranial bleeding. The Hokusai-VTE study (N = 8,292) in patients with symptomatic VTE had a flexible treatment duration of 3-12 months and found that following initial heparin, edoxaban 60 mg once daily was non-inferior to dose-adjusted warfarin (INR 2.0-3.0) for the prevention of recurrent VTE, and also had a significantly lower risk of bleeding events. Both studies randomized patients at moderate-to-high risk of thromboembolic events and were further designed to simulate routine clinical practice as much as possible, with edoxaban dose reduction (halving dose) at randomisation or during the study if required, a frequently monitored and well-controlled warfarin group, a well-monitored transition period at study end and a flexible treatment duration in Hokusai-VTE. Given the phase III results obtained, once-daily edoxaban may soon be a key addition to the range of antithrombotic treatment options.

[S25030431](#)

Migraine is a neurovascular disorder that is associated with severe headache and neurologic symptoms. The pathogenesis of migraine is believed to involve trigeminovascular system activation with the primary dysfunction located in brainstem. Glutamate, the major excitatory neurotransmitter in the central nervous system, and its receptors have since long been suggested in migraine pathophysiology. Different preclinical studies have confirmed their potential role in migraine. Moreover, several glutamate receptor modulators have been studied in clinical studies, some with promising results. In this review, we will give an overview of what is known about the role of glutamate in the pathogenesis of migraine, which will be followed by an overview of available efficacy, safety and tolerability data for glutamate receptor inhibitors in clinical development for the treatment of migraine.

**DIABETES CARE**

S24742659

While metabolic risk factors associated with overweight increase future risk for MetS, T2DM, and increased IMT, overweight in isolation is also a risk factor. Therefore, overweight should be prevented and treated wherever possible.

S24760259

HD vitamin D supplementation commencing at a mean of 14 weeks' gestation does not improve glucose levels in pregnancy. However, in women with baseline levels <32 ng/mL, 5,000 IU per day was well tolerated and highly effective at preventing neonatal vitamin D deficiency.

S24760263

We conclude that shape- and barefoot plantar pressure-based orthoses were more effective in reducing submetatarsal head plantar ulcer recurrence than current standard-of-care orthoses, but they did not significantly reduce nonulcerative lesions.

S24963113

Various clinical and quality of life-related factors influence patient preferences for noninsulin diabetes medications. Treatment efficacy with regard to glycemic control and weight loss/control and the risk of treatment-related hypoglycemia and gastrointestinal effects are reported to be important drivers of patient treatment selections. Future work is needed to identify practical methods for incorporating patient preferences into treatment decision making and patient-centered care.

S24722499

High total and animal protein intake was associated with a modest elevated risk of type 2 diabetes in a large cohort of European adults. In view of the rapidly increasing prevalence of type 2 diabetes, limiting iso-energetic diets high in dietary proteins, particularly from animal sources, should be considered.

S24722497

In patients with newly diagnosed type 2 diabetes, an LCMD resulted in a greater reduction of HbA1c levels, higher rate of diabetes remission, and delayed need for diabetes medication compared with a low-fat diet.

## ENFERMEDADES INFECCIOSAS Y MICROBIOLOGIA CLINICA

S24246777

Entre los HSH la prevalencia de conductas sexuales de alto riesgo es alta, tanto con la PE como con las PO. Los factores asociados a la PANP de alto riesgo varían según el tipo de pareja sexual (p. ej., tener el VIH con una carga viral indetectable), factores que tienen que considerarse para plantear estrategias de prevención primaria y secundaria.

S23523029

Hasta fechas muy recientes eran muy pocos los genomas de *Chlamydia trachomatis* disponibles, a pesar de su importancia en salud pública. Actualmente se están secuenciando 66 genomas completos de *C. trachomatis*. Esta revolución genómica está permitiendo comprender su biología, mejorar la sensibilidad y especificidad en el diagnóstico o desarrollar herramientas epidemiológicas no solo de *C. trachomatis* sino también de especies relacionadas, como *C. pneumoniae* o *C. psittaci*. El diagnóstico basado en cultivo celular, serología o microinmunofluorescencia está siendo progresivamente sustituido por técnicas de amplificación de ácidos nucleicos, al superarse los inconvenientes de escaso rendimiento o reacciones cruzadas y mejorar la estandarización entre laboratorios. Por otra parte, el desarrollo de técnicas de tipificación (MLST y VNTR) aplicadas a *Chlamydiae* ha aumentado el conocimiento de la epidemiología local y global aportando información sobre cómo esas bacterias evolucionan, causan brotes o adquieren mecanismos de resistencia. Esta revisión se centra en los grandes avances alcanzados en el conocimiento de las diferentes especies de *Chlamydia*, en parte debido a la innovación tecnológica aplicada a la genómica como una aproximación para explicar la revolución que, tanto en el diagnóstico como en su epidemiología, se ha observado en este grupo de bacterias en los últimos años.

S24054972

La presentación clínica de la tos ferina en lactantes es similar a la infección por VRS, aunque existen algunas características que pueden ayudar a diferenciar ambos cuadros clínicos.

## EUROPEAN HEART JOURNAL

S24302270

Although the number of individuals reaching 80 who are considered to be healthy is increasing, the very elderly are likely to have long-term conditions, to report symptoms and/or be taking at least one regular medication. The impact of antihypertensive treatment has to be taken into account in this context. The treatment regimen in Hypertension in the Very Elderly Trial with a goal blood pressure of <150/80 mmHg has been shown to provide benefits in terms of a reduction in risk of total mortality, stroke, and cardiovascular events with potential benefits and no evidence of increased risk for fracture, dementia, depression, and quality-of-life outcomes. Questions remain as to the level of benefit that would be accrued in the frailer elderly and those at extreme age, for example, over 90.

S24658769

Among high-risk patients with atrial fibrillation who experienced major bleeding in ROCKET AF, the use of FFP and PCC was less among those allocated rivaroxaban compared with warfarin. However, use of PRBCs and outcomes after bleeding were similar among patients randomized to rivaroxaban or to warfarin.

S24616336

Use of ACEI/ARB was not associated with better outcomes in stable CAD outpatients without HF. The benefit of ACEI/ARB seen in randomized clinical trials was not replicated in this large contemporary cohort, which questions their value in this specific subset.

S24394381

Continuation or short-term interruption of NOAC is safe strategies for most invasive procedures. Patients at cardiovascular risk undergoing major procedures may benefit from heparin bridging, but bleeding risks need to be considered.

S23990605

In subjects with TRH, intensive lipid lowering with atorvastatin 80 mg is associated with a significant reduction in cardiovascular events.

S24561548

The benefits of apixaban vs. warfarin were consistent in patients with AF regardless of age. Owing to the higher risk at older age, the absolute benefits of apixaban were greater in the elderly.

S24353282

Patients initiating warfarin may be at an increased risk of stroke during the first 30 days of treatment, supporting the biological plausibility of a transient hypercoagulable state at the start of the treatment, although additional studies are needed to confirm these findings.

S24569028

C-reactive protein concentrations are substantially lower in Koreans than reported for whites populations. Nonetheless, C-reactive protein levels are associated with CVD and all-cause mortality in Korean men. Standard cut points for C-reactive protein may under-represent Asians at risk for CVD.

S24569032

The efficacy and safety of apixaban compared with aspirin is consistent in subgroups of patients who have previously attempted but failed VKA therapy, irrespective of the reason for discontinuation.

S24510637

Direct oral anticoagulants (DOACs) specifically target factor IIa or Xa and represent a major step forward in the treatment of acute- and long-term prevention of venous thrombo-embolism (VTE). They are at least as effective and as safe as conventional therapy (heparins and vitamin-K inhibitors) and have practical advantages, such as fixed dosing and no need for laboratory monitoring. These antithrombotic agents introduce a new paradigm for the day-to-day management of VTE. Direct oral anticoagulants should streamline the management of most patients with VTE and will facilitate care in the outpatient setting. Nevertheless, it remains uncertain how to select specific DOACs for particular profiles of patients, and the optimal management of bleeding complications is evolving.

S24810388

Long-term anticoagulation treatment with warfarin has been associated with a number of limitations in clinical practice and there is a need for more convenient long-term anticoagulation treatment. One of the non-vitamin K oral anticoagulants in development is edoxaban, a factor Xa inhibitor that is administered once daily. The pharmacological properties of edoxaban have various advantages in anticoagulant therapy. Edoxaban quickly reaches peak plasma concentrations in 1.5 h, has a half-life of 10-14 h, has relatively high bioavailability of 62% and exhibits highly selective, competitive, concentration-dependent inhibition of human factor Xa. The plasma concentrations of edoxaban are also closely correlated with suppression of thrombin generation and a range of platelet activation parameters (fragment 1+2, thrombin-antithrombin complex, and  $\beta$ -thromboglobulin), which edoxaban has been shown to rapidly inhibit. The anticoagulant activity of edoxaban is not affected by food intake or ethnicity and a number of drug-drug interaction studies have been performed. Co-administration of edoxaban with strong P-glycoprotein inhibitors, such as dronedarone, quinidine, and verapamil requires edoxaban dose-reduction by 50% to avoid the risk of over-exposure. The exposure of edoxaban may also increase in patients with a body weight  $\approx$ 60 kg and moderate renal impairment. This meant a dose-reduction strategy in patients at risk of over-exposure was utilized in Phase III clinical studies. In conclusion, the pharmacological properties of edoxaban provide rapid and specific inhibition of factor Xa, which is closely related to plasma concentrations. Given the limitations with long-term warfarin therapy, once-daily edoxaban may provide a convenient long-term alternative for patients.

S24616335

Sizeable reductions in BP, with potential for substantial CVD reduction, can be safely achieved using combinations of BP drugs in the elderly with normal high and Stage 1 hypertension.

S24898552

Renal denervation resulted in sustained lowering of blood pressure at 3 years in a selected population of subjects with severe, treatment-resistant hypertension without serious safety concerns.

S23966312

In this comprehensive analysis of the antihypertensive efficacy of ARBs by 24 h ABP, we observed a shallow dose-response curve, and uptitration marginally enhanced the antihypertensive efficacy. Blood pressure reduction with losartan at starting dose and at max dose was consistently inferior to the other ARBs.

S24513791

Based on randomized trial data, apixaban is a cost-effective alternative to warfarin and aspirin, in VKA suitable and VKA unsuitable patients with AF, respectively.

## FAMILY MEDICINE

S25058549

There is variability in how FMC are addressing PH instruction. Future research should qualitatively explore pedagogical methods and seek consensus on the competencies and best practices in PH instruction most suited to FMC.

S25058543

The CI fellowship represents a highly replicable program to connect committed and interested clinicians to research mentors with the goal of increasing scholarship and creating a growing culture of inquiry in family medicine.

S25058547

Students who completed a rural family medicine clerkship are not at an academic disadvantage. There are many possible explanations for better clinical evaluations, and a comparison of performance on the clinical skills assessment would be useful to determine whether the increased clinical experience during the rural option created a difference in clinical skills.

## GACETA SANITARIA

S24613077

Se aprecia variabilidad entre comunidades autónomas en los tipos y formas de aplicación de las actividades comunitarias realizadas por atención primaria, así como en el reconocimiento institucional y la implicación comunitaria en el desarrollo y la evaluación de la actividad.

S24666569

A pesar de observar una tendencia decreciente, las desigualdades sociales son un elemento sustantivo en la distribución de la mortalidad general en la ciudad de Cádiz.

S24485652

Se ha detectado una gran diversidad en la medición de los determinantes sociales y una falta de estudios especialmente en edades preescolares y con diseños longitudinales. Se confirman las desigualdades sociales en algunos aspectos de salud.

## JOURNAL OF THE AMERICAN BOARD OF FAMILY MEDICINE

S25002008

Family physicians face many challenges when diagnosing asthma in preschool children. These diagnostic challenges are compounded by variations in the natural history of early stage asthma, which are not fully understood, since early childhood wheezing and asthma are heterogeneous disorders with many phenotypic and variable expressions. Since no standard definition for the type, severity, or frequency of symptoms exist for this age group, clear evidence-based recommendations are lacking. Without adequate guidance, family physicians are left to make diagnostic and treatment decisions, which can lead to undertreatment of asthmatics and overtreatment of transient wheezers. New guidelines that specifically address the challenges of diagnosing asthma in this particular age group (Global Initiative for Asthma, British Thoracic Society/Scottish Intercollegiate Guidelines Network) have recently been published, and researchers are actively seeking new methods and techniques through epidemiological studies to assist primary care clinicians in the diagnostic process. This review has wide application in primary care. By recognizing the diagnostic challenges and understanding the

related best practices, family physicians will be better placed to treat, manage, and control asthma symptoms, resulting in lower morbidity rates and reduced health system costs, as well as enhancing the overall quality of life and well-being of the children affected.

[S25002009](#)

Adults with bleeding disorders may present to their family physician with minor bleeding symptoms or hematologic laboratory abnormalities discovered during evaluation for surgery or another purpose. Identifying the small proportion of adults who have an underlying bleeding disorder as the cause for such signs or symptoms may be challenging. In cases of asymptomatic hematologic laboratory abnormalities, the particular abnormality should narrow down the potentially affected hemostatic component(s), ideally streamlining subsequent investigation. In patients presenting with bleeding symptoms, a thorough history and physical examination are critical for first identifying bleeding as pathologic, then performing the appropriate diagnostic evaluation after excluding identifiable causes. Knowledge of the pathophysiologic processes contributing to impaired hemostasis in any given bleeding disorder ensures proper treatment and avoids therapies that are unnecessary or even contraindicated. Management is further determined by bleeding phenotype and, for invasive procedures, the anticipated risk for bleeding. Consultation with a hematologist may facilitate proper evaluation and treatment, particularly in adults with rare bleeding disorders or no identifiable cause for bleeding. This article reviews the diagnostic approach to hematologic laboratory abnormalities and abnormal bleeding in adults, as well as basic preventive care and hemostatic management of adults with bleeding disorders.

## JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

[S25038359](#)

After confirmed diagnosis of HIV infection, antiretroviral therapy should be initiated in all individuals who are willing and ready to start treatment. Regimens should be selected or changed based on resistance test results with consideration of dosing frequency, pill burden, adverse toxic effect profiles, comorbidities, and drug interactions.

[S25058220](#)

Two screening instruments, the GAD-7 for GAD and the Patient Health Questionnaire for panic disorder, have good performance characteristics and are feasible for use in primary care. However, further validation of these instruments is needed because neither instrument was replicated in more than 1 primary care population.

[S25038358](#)

Data support the integration of biomedical and behavioral approaches for prevention of HIV infection in clinical care settings. A concerted effort to implement combination strategies for HIV prevention is needed to realize the goal of an AIDS-free generation.

[S25027141](#)

In a multicenter cohort of black and white adults in US communities, stroke incidence and mortality rates decreased from 1987 to 2011. The decreases varied across age groups, but were similar across sex and race, showing that improvements in stroke incidence and outcome continued to 2011.

[S25005652](#)

Varenicline in combination with NRT was more effective than varenicline alone at achieving tobacco abstinence at 12 weeks (end of treatment) and at 6 months. Further studies are needed to assess long-term efficacy and safety.

[S25005656](#)

CLINICAL QUESTION:

Are antiepileptic drugs associated with reduced pain intensity in patients with neuropathic pain or fibromyalgia?

BOTTOM LINE:

In treating diabetic neuropathy and postherpetic neuralgia compared with placebo, gabapentin and pregabalin are associated with a modest increase in the number of patients experiencing meaningful pain reduction. In treating fibromyalgia, compared with placebo, pregabalin alone is associated with a small increase in the number of patients experiencing meaningful pain reduction. There is insufficient evidence for other antiepileptics.

[S25027142](#)

A history of stroke was associated with adverse outcomes following surgery, in particular if time between stroke and surgery was less than 9 months. After 9 months, the associated risk appeared stable yet still increased compared with patients with no stroke. The time dependency of risk may warrant attention in future guidelines.

## JAMA INTERNAL MEDICINE

[S24861959](#)

Both intervention formats reduced CHD risk through 12-month follow-up. The web format was less expensive.

[S24798807](#)

The UAC and the ACR yielded high sensitivity and specificity for the detection of microalbuminuria. Because the diagnostic performance of the UAC is comparable to that of the ACR, our findings indicate that the UAC of random urine samples may become the screening tool of choice for the population with DM, considering the rising incidence of DM and the constrained health care resources in many countries.

[S24763487](#)

Caloric and fat intake have increased among statin users over time, which was not true for nonusers. The increase in BMI was faster for statin users than for nonusers. Efforts aimed at dietary control among statin users may be becoming less intensive. The importance of dietary composition may need to be reemphasized for statin users.

[S24861828](#)

Low-dose oral estradiol and venlafaxine are effective treatments for VMS in women during midlife. While the efficacy of low-dose estradiol may be slightly superior to that of venlafaxine, the difference is small and of uncertain clinical relevance.

[S24798675](#)

Among postmenopausal women who discontinue alendronate therapy after 4 to 5 years, age and hip BMD at discontinuation predict clinical fractures during the subsequent 5 years. Follow-up measurements of DXA 1 year after discontinuation and of BAP or NTX 1 to 2 years after discontinuation are not associated with fracture risk and cannot be recommended.

[S24819981](#)

In older community-dwelling adults, total urinary resveratrol metabolite concentration was not associated with inflammatory markers, cardiovascular disease, or cancer or predictive of all-cause mortality. Resveratrol levels achieved with a Western diet did not have a substantial influence on health status and mortality risk of the population in this study.

[S24861560](#)

Considerable variability among studies in the methods of preference assessment, the time between assessments, and the definitions of stability preclude meta-analytic estimates of the stability of patients' preferences and the factors influencing these preferences. Although more seriously ill patients and those who engage in advance care planning most commonly have stable preferences for future treatments, further research in real-world settings is needed to confirm the utility of advance care plans for future decision making.

S24841449

Increasing physical activity may lower the risk of progression from GDM to T2DM. These findings suggest a hopeful message to women with a history of GDM, although they are at exceptionally high risk for T2DM, promoting an active lifestyle may lower the risk.

## JAMA PSYCHIATRY

S24871348

Our data show that the demographic composition of heroin users entering treatment has shifted over the last 50 years such that heroin use has changed from an inner-city, minority-centered problem to one that has a more widespread geographical distribution, involving primarily white men and women in their late 20s living outside of large urban areas.

## MEDICINA CLINICA

S23896450

Los cuidados de las personas mayores después de una enfermedad aguda o accidente han adquirido una gran relevancia en el coste sanitario, debido tanto al envejecimiento de la población como al cambio en la estructura sociofamiliar.

El objetivo principal de los cuidados postagudos (CPA) es restituir la capacidad funcional del paciente después de un episodio agudo, puesto que este determinará su evolución y contactos posteriores con el sistema sanitario. Nos hemos propuesto revisar los siguientes aspectos de los CPA: a) objetivos; b) cuantificación de las necesidades e indicadores de acceso, y c) estrategias de transferencia desde los cuidados agudos. Para ello se ha realizado una revisión sistemática de la literatura médica desde el año 1990 hasta el 2011.

Se concluye que los CPA son un instrumento eficiente para mejorar la calidad de vida de los pacientes y para la sostenibilidad del sistema sanitario público. En la selección de los candidatos hay que manejar un conjunto de indicadores tanto sanitarios como sociales. La visión transversal de todo el proceso es fundamental para evitar un incremento en los costes totales.

S24054776

La enfermedad pulmonar obstructiva crónica asocia alteraciones del estado nutricional, con prevalencia variable (2-50%) dependiendo de la zona geográfica y el diseño del estudio. Entre los instrumentos diagnósticos destacan la antropometría, la impedancia bioeléctrica, la radioabsorciometría de doble energía y la dilución de deuterio, siendo los índices de masa corporal y de masa magra las variables más utilizadas. Las consecuencias más importantes de las alteraciones nutricionales son la disfunción muscular y la limitación al ejercicio, y los factores que se han implicado en su aparición incluyen el desequilibrio entre ingesta y consumo calórico, así como entre hormonas anabólicas y catabólicas, la inflamación, el tabaco, la escasa actividad física, la hipoxemia, algunos fármacos y el envejecimiento-comorbilidades. El mecanismo molecular más importante parece ser la pérdida del equilibrio entre síntesis y destrucción proteicas. Entre las medidas terapéuticas destacan la mejora en los hábitos de vida y el soporte nutricional, aunque el uso de fármacos anabolizantes, como las secretagogas de la hormona de crecimiento, está abriendo prometedoras opciones.

S24183115

Existe una asociación entre la dislipidemia y la ETEV, siendo el riesgo de trombosis casi 4 veces mayor en individuos con esta enfermedad. Las alteraciones del perfil lipídico también están relacionadas con una mayor prevalencia de recurrencia y síndrome posttrombótico.

S23891132

El presente estudio aporta nuevas evidencias de asociación del ADE con mortalidad en una cohorte de pacientes ancianos que sobreviven a un ingreso hospitalario. El ADE fue el único parámetro de laboratorio analizado que mejoraba la capacidad pronóstica de mortalidad a un año.

S23937816

La frecuencia cardíaca refleja la actividad del sistema nervioso autónomo. Numerosos estudios han demostrado que la frecuencia cardíaca elevada en reposo se asocia con la morbimortalidad cardiovascular como factor de riesgo independiente. Se ha evidenciado una relación entre balance autonómico cardíaco e inflamación, de tal forma que la frecuencia cardíaca elevada produce una respuesta microinflamatoria e interviene en la patogénesis de la disfunción endotelial. A su vez, la disminución de la frecuencia se asocia a beneficios en insuficiencia cardíaca congestiva, infarto de miocardio, fibrilación auricular, obesidad, hiperinsulinemia, resistencia a la insulina y aterosclerosis. La alteración de otros parámetros relacionados con la frecuencia cardíaca, tales como su variabilidad y su recuperación tras realizar ejercicio, se asocia con riesgo de episodios cardiovasculares. Los fármacos que reducen la frecuencia (betabloqueantes, antagonistas del calcio e inhibidores de canales  $I_f$ ) tienen el potencial de reducir sucesos cardiovasculares. Aunque en sujetos sanos no se recomiendan intervenciones para la reducción de la frecuencia cardíaca, en determinadas enfermedades constituye un objetivo terapéutico razonable.

S23937815

Se revisan los efectos beneficiosos y los problemas relacionados con los fármacos hipoglucemiantes tradicionales y se analizan los nuevos medicamentos de esta clase relacionados con el efecto incretina: análogos del péptido similar al glucagón tipo 1 e inhibidores de las dipeptidil peptidasas tipo 4. Ambos producen, de forma dependiente de la glucosa, una reducción de la glucemia, no se relacionan con la hipoglucemia y no aumentan el peso. Otro nuevo grupo son los inhibidores del cotransportador sodio-glucosa tipo 2, que disminuyen la glucemia con bajo riesgo de hipoglucemia y con discreta pérdida de peso. Los efectos beneficiosos a largo plazo y la prevención cardiovascular no están demostrados.

Disponemos cada vez de más y mejores fármacos. Por otra parte, el tratamiento farmacológico hipoglucemiante debe ser personalizado, considerando los valores de hemoglobina glucosilada, el riesgo-beneficio, el riesgo de hipoglucemia, los cambios en el peso y el estado cardiovascular, entre otros factores.

No tenemos el hipoglucemiante ideal y no debemos olvidar que, junto al control de la hiperglucemia, el tratamiento precoz e intensivo de la dislipidemia y de la hipertensión es fundamental en la prevención cardiovascular del paciente con diabetes tipo 2.

S24559542

La prevalencia de halitosis fue del 36,7%. El uso de chicle como adyuvante en casos de halitosis disminuye los CVS, mejorando la percepción de terceros y del propio paciente.

S24361155

La exposición activa o pasiva de la madre al tabaco durante la gestación y los menores valores de hemoglobina se asocian a mayor riesgo de partos prematuros y menor peso al nacer. El abandono del tabaco evita estos efectos perjudiciales.

S23830548

La anosognosia se incrementa con el mayor deterioro. En los pacientes en fase leve las variables predictoras fueron la apatía, la desinhibición y los trastornos motores.

S24908624

Los sujetos muy ancianos, de 80 o más años de edad, constituyen el grupo etario de más rápido crecimiento demográfico en los países desarrollados. Las enfermedades cardiovasculares son la principal causa de muerte, representan una importante causa de discapacidad y generan una enorme carga económica en este grupo de edad. Sin embargo, son muy escasas las evidencias científicas disponibles que respaldan la toma de decisiones sobre prevención cardiovascular en dichos sujetos. Las escalas de riesgo actualmente



disponibles no son aplicables en los ancianos, y, además, están centradas en el riesgo de muerte cardiovascular y no aportan información sobre factores que han mostrado ser de capacidad pronóstica relevante en esta población (incapacidad funcional, demencia). Los ancianos forman un grupo muy heterogéneo de pacientes, con diferentes grados de comorbilidad y de capacidad funcional y cognitiva. Además, los cambios fisiológicos propios del envejecimiento y la frecuente presencia de polimedicación incrementan el riesgo de efectos adversos medicamentosos en los ancianos, por lo que la indicación de fármacos en esta población debe considerar siempre la relación riesgo/beneficio. Por tanto, la toma de decisiones terapéuticas en pacientes muy ancianos debe ser un proceso individualizado basado en un adecuado juicio clínico y en una valoración geriátrica integral. El presente documento de consenso tiene como objetivo proponer unas pautas de actuación prácticas de prevención cardiovascular primaria y secundaria en la población de 80 y más años de edad, realizando una serie de recomendaciones sobre la modificación del estilo de vida y el tratamiento farmacológico de los principales factores de riesgo cardiovascular.

S24029448

Durante muchos años se ha considerado que el síndrome del intestino irritable (SII) y la enfermedad celíaca (EC) eran 2 entidades completamente diferentes: la segunda relacionada con una intolerancia permanente a la ingesta de gluten, y la primera, sin ninguna relación con esta. El problema estriba en que los síntomas del SII y la EC pueden ser indistinguibles, en especial cuando predominan la diarrea, la hinchazón o el dolor abdominal. Durante la última década diversos estudios han comprobado que la separación entre la EC y el SII no es tan clara. Puede haber pacientes que habiendo sido diagnosticados de SII en realidad tienen una EC. Aún más, parece existir un grupo de enfermos que sin tener una EC presentan una sensibilidad al gluten con manifestaciones digestivas semejantes al SII. La sensibilidad al gluten se define como el conjunto de aquellos trastornos morfológicos, inmunológicos o funcionales que responden a la exclusión de gluten. Este concepto incorpora una serie de manifestaciones histológicas, inmunológicas y clínicas en ausencia de alteraciones morfológicas evidentes. Por tanto, es necesario establecer de una manera científica qué sujetos se podrán beneficiar de una dieta sin gluten, y en cuáles no está justificada.

## REVISTA ESPAÑOLA DE CARDIOLOGIA

S24952394

Hay una asociación entre los trastornos por cocaína y el infarto agudo de miocardio. Estos trastornos prolongan las estancias hospitalarias y aumentan los costes de los pacientes hospitalizados. La interrupción del uso de la droga debe ser uno de los principales objetivos terapéuticos tras el alta del paciente.

## THE LANCET

S24996590

In the USA, infectious diseases continue to exact a substantial toll on health and health-care resources. Endemic diseases such as chronic hepatitis, HIV, and other sexually transmitted infections affect millions of individuals and widen health disparities. Additional concerns include health-care-associated and foodborne infections--both of which have been targets of broad prevention efforts, with success in some areas, yet major challenges remain. Although substantial progress in reduction of the burden of vaccine-preventable diseases has been made, continued cases and outbreaks of these diseases persist, driven by various contributing factors. Worldwide, emerging and reemerging infections continue to challenge prevention and control strategies while the growing problem of antimicrobial resistance needs urgent action. An important priority for control of infectious disease is to ensure that scientific and technological advances in molecular diagnostics and bioinformatics are well integrated into public health. Broad and diverse partnerships across governments, health care, academia, and industry, and with the public, are essential to effectively reduce the burden of infectious diseases.

S24694983

Colchicine added to conventional anti-inflammatory treatment significantly reduced the rate of subsequent recurrences of pericarditis in patients with multiple recurrences. Taken together with results from other randomised controlled trials, these findings suggest that colchicine should be probably regarded as a first-line treatment for either acute or recurrent pericarditis in the absence of contraindications or specific indications.

S24703832

We have shown that simple advice is equally as effective as a more intense and comprehensive physiotherapy exercise programme. The need to identify effective and affordable strategies to prevent and treat acute through to chronic whiplash associated disorders is an important health priority. Future avenues of research might include improving understanding of the mechanisms responsible for persistent pain and disability, investigating the effectiveness and timing of drugs, and study of content and delivery of education and advice.

S24655729

High-dose simvastatin reduced the annualised rate of whole-brain atrophy compared with placebo, and was well tolerated and safe. These results support the advancement of this treatment to phase 3 testing.

S24996591

In the first three decades of life, more individuals in the USA die from injuries and violence than from any other cause. Millions more people survive and are left with physical, emotional, and financial problems. Injuries and violence are not accidents; they are preventable. Prevention has a strong scientific foundation, yet efforts are not fully implemented or integrated into clinical and community settings. In this Series paper, we review the burden of injuries and violence in the USA, note effective interventions, and discuss methods to bring interventions into practice. Alliances between the public health community and medical care organisations, health-care providers, states, and communities can reduce injuries and violence. We encourage partnerships between medical and public health communities to consistently frame injuries and violence as preventable, identify evidence-based interventions, provide scientific information to decision makers, and strengthen the capacity of an integrated health system to prevent injuries and violence.

S24702835

Preconception-initiated low-dose aspirin was not significantly associated with livebirth or pregnancy loss in women with one to two previous losses. However, higher livebirth rates were seen in women with a single documented loss at less than 20 weeks' gestation during the previous year. Low-dose aspirin is not recommended for the prevention of pregnancy loss.

S24996589

With non-communicable conditions accounting for nearly two-thirds of deaths worldwide, the emergence of chronic diseases as the predominant challenge to global health is undisputed. In the USA, chronic diseases are the main causes of poor health, disability, and death, and account for most of health-care expenditures. The chronic disease burden in the USA largely results from a short list of risk factors--including tobacco use, poor diet and physical inactivity (both strongly associated with obesity), excessive alcohol consumption, uncontrolled high blood pressure, and hyperlipidaemia--that can be effectively addressed for individuals and populations. Increases in the burden of chronic diseases are attributable to incidence and prevalence of leading chronic conditions and risk factors (which occur individually and in combination), and population demographics, including ageing and health disparities. To effectively and equitably address the chronic disease burden, public health and health-care systems need to deploy integrated approaches that bundle strategies

and interventions, address many risk factors and conditions simultaneously, create population-wide changes, help the population subgroups most affected, and rely on implementation by many sectors, including public-private partnerships and involvement from all stakeholders. To help to meet the chronic disease burden, the US Centers for Disease Control and Prevention (CDC) uses four cross-cutting strategies: (1) epidemiology and surveillance to monitor trends and inform programmes; (2) environmental approaches that promote health and support healthy behaviours; (3) health system interventions to improve the effective use of clinical and other preventive services; and (4) community resources linked to clinical services that sustain improved management of chronic conditions. Establishment of community conditions to support healthy behaviours and promote effective management of chronic conditions will deliver healthier students to schools, healthier workers to employers and businesses, and a healthier population to the health-care system. Collectively, these four strategies will prevent the occurrence of chronic diseases, foster early detection and slow disease progression in people with chronic conditions, reduce complications, support an improved quality of life, and reduce demand on the health-care system. Of crucial importance, with strengthened collaboration between the public health and health-care sectors, the health-care system better uses prevention and early detection services, and population health is improved and sustained by solidifying collaborations between communities and health-care providers. This collaborative approach will improve health equity by building communities that promote health rather than disease, have more accessible and direct care, and focus the health-care system on improving population health.

S24740087

Large declines in HIV incidence have been reported since 2001, and scientific advances in HIV prevention provide strong hope to reduce incidence further. Now is the time to replace the quest for so-called silver bullets with a public health approach to combination prevention that understands that risk is not evenly distributed and that effective interventions can vary by risk profile. Different countries have different microepidemics, with very different levels of transmission and risk groups, changing over time. Therefore, focus should be on high-transmission geographies, people at highest risk for HIV, and the package of interventions that are most likely to have the largest effect in each different microepidemic. Building on the backbone of behaviour change, condom use, and medical male circumcision, as well as expanded use of antiretroviral drugs for infected people and pre-exposure prophylaxis for uninfected people at high risk of infection, it is now possible to consider the prospect of what would be one of the most remarkable achievements in the history of public health: reduction of HIV transmission from a pandemic to low-level endemicity.

#### THE NEW ENGLAND JOURNAL OF MEDICINE

S24988556

Children with the HLA haplotype DR3-DQ2, especially homozygotes, were found to be at high risk for celiac disease autoimmunity and celiac disease early in childhood. The higher risk in Sweden than in other countries highlights the importance of studying environmental factors associated with celiac disease. (Funded by the National Institute of Diabetes and Digestive and Kidney Diseases and others.).