

Enero 2012

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RIESGOS DE ENFERMEDAD CARDIOVASCULAR A LO LARGO DE LA VIDA

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## ACADEMIC MEDICINE

[S22201631](#)

Reflective writing is being introduced in many medical schools in the United States and abroad for a variety of reasons and with a variety of goals in mind. As Wald and colleagues write, multiple methods, including the rubric introduced in their study, have been proposed for rating or grading this writing to quantify the gains obtained. The authors of this commentary detail the assumptions both about reflection and about writing implied in Wald and colleagues' work. They then describe a reciprocal model of writing as discovery, suggesting that the writing itself is what teaches the skills of reflection. Equipping medical students with a sense of story may well be the active ingredient in whatever gains are observed in teaching reflective writing.

## ANNALS OF INTERNAL MEDICINE

[S22250141](#)

High-dose vitamin D supplementation in a sample of patients with COPD did not reduce the incidence of exacerbations. In participants with severe vitamin D deficiency at baseline, supplementation may reduce exacerbations

[S22250144](#)

Long-term disability in community mobility is common among older persons. Multiple risk factors, together with subsequent precipitants, greatly increase the likelihood of long-term mobility disability

## ARCHIVES OF INTERNAL MEDICINE

[S22082706](#)

TCBT was associated with substantial, statistically significant, and sustained improvements in patient global assessment.

[S22271118](#)

Exercise reduces depressive symptoms among patients with a chronic illness. Patients with depressive symptoms indicative of mild-to-moderate depression and for whom exercise training improves function-related outcomes achieve the largest antidepressant effects.

## ATENCION PRIMARIA

[S21497416](#)

La mayoría de los pacientes tras una consulta concreta desean poder dar su opinión a la/s propuesta/s de tratamiento que surgen, sin embargo perciben que sus médicos raramente les ofrecen estas oportunidades de

participación. Determinados tipos de preguntas favorecen la detección de estas necesidades y el planteamiento de estrategias para incorporarles al proceso de TD.

S21496968

La prevalencia de desgaste profesional es similar a la de otros estudios. Las diferencias entre trabajadores sanitarios y no sanitarios podría deberse a una mayor motivación para la realización profesional, aunque puntúen de una forma más elevada en agotamiento y despersonalización. La elevación de marcadores inespecíficos de la inflamación parece confirmar los hallazgos de otros estudios.

#### CANADIAN MEDICAL ASSOCIATION JOURNAL

S22105752

The overall prevalence of diagnosed hypertension in Canada from 1998 to 2008 was high and increasing, whereas the incidence declined during the same period. These findings highlight the need to continue monitoring the effectiveness of efforts for managing hypertension and to enhance public health programs aimed at preventing hypertension.

#### CIRCULATION

S22144569

We propose that enhanced susceptibility to ischemic depolarizations akin to spreading depression predisposes migraineurs to infarction during mild ischemic events, thereby increasing the stroke risk.

S22230481

Grief over the death of a significant person was associated with an acutely increased risk of MI in the subsequent days. The impact may be greatest among individuals at high cardiovascular risk.

#### BRITISH JOURNAL OF PSYCHIATRY

S22215865

Self-help interventions appear to be an effective way of treating individuals diagnosed with social phobia and panic disorder. Further research is required to evaluate the cost-effectiveness and acceptability of these interventions.

#### DIABETES CARE

S22040840

Short-term exenatide treatment was associated with modest weight loss and decreased waist circumference in a cohort of obese nondiabetic women. A subset of individuals demonstrated robust weight loss that was detected very early in the course of treatment.

S22074723

A Western dietary pattern during adolescence may increase risk of T2DM in later life, partly through adult weight gain. Preventive measures should be aimed at developing healthy dietary habits that begin in early life and continue through adulthood.

S22100963

Subjects with type 2 diabetes not on prandial insulin who used RT-CGM intermittently for 12 weeks significantly improved glycemic control at 12 weeks and sustained the improvement without RT-CGM during the 40-week follow-up period, compared with those who used only SMBG.

S22011409

In insulin-treated subjects with type 2 diabetes, supervised exercise is safe and effective in improving glycemic control and markers of adiposity and inflammation, thus counterbalancing the adverse effects of insulin on these parameters.

S22124717

Combined lifestyle behavior is a strong predictor of all-cause and cause-specific mortality in patients with T2DM.

#### DRUGS

S22239714

Symptoms of gastro-oesophageal reflux disease (GORD or GERD) are estimated to occur in 30-50% of pregnancies, with the incidence approaching 80% in some populations. As with many other conditions in

pregnancy, medical therapy with pharmaceutical agents is a concern, as the potential teratogenicity of medications is not well known. Although prevalence numbers are high, many patients have mild and infrequent symptoms, which often respond to lifestyle and dietary modifications. The exact mechanism and pathogenesis of GERD associated with pregnancy is likely multifactorial. Treatment strategies for patients not responding to conservative therapies include a step-up approach initially starting with antacids and alginates, and progressing to histamine H<sub>2</sub> receptor antagonists followed by proton pump inhibitor (PPI) therapy if indicated by symptoms. Although PPI therapy is the most effective treatment available for GERD, the data related to the safety for use during pregnancy and postpartum breastfeeding are mostly obtained from cohort analysis. Given the significant adverse impact of GERD on quality of life and functionality, the use of this class of medications should not be overly restricted based solely on the pregnancy. Based on the studies presented, exposure to PPI therapy during pregnancy seems to predispose the fetus to minimal risk and, overall, these medications should be discussed with the primary physician if symptomatically necessary in the pregnant patient. This evidence-based review will address the management and safety of PPI therapy during pregnancy and lactation, and briefly review the pathogenesis, clinical presentation and diagnosis of GERD in this population.

#### S22191800

Aripiprazole (Abilify®) is an atypical antipsychotic indicated for the treatment of mania associated with bipolar I disorder. It is unique in its class, as it is a partial agonist of dopamine D<sub>2</sub> and D<sub>3</sub>, and serotonin 5-HT<sub>1A</sub> receptors and a modest antagonist of 5-HT<sub>2A</sub> receptors. This article reviews the pharmacological properties, clinical efficacy and tolerability of oral aripiprazole in the management of mania associated with bipolar I disorder in adults. In well designed clinical trials in patients with recent manic or mixed episodes associated with bipolar I disorder, oral aripiprazole monotherapy or adjunctive therapy to lithium or valproate improved symptoms of mania following short-term (=12 weeks) or maintenance (=100 weeks) treatment. In addition, maintenance treatment with aripiprazole (as monotherapy or adjunctive therapy) prevented the recurrence of any mood episodes or manic episodes (but not depressive episodes) in patients who had previously been stabilized and maintained on aripiprazole. Aripiprazole was generally well tolerated in these studies and was associated with a low risk of prolactin elevation, corrected QT interval prolongation and metabolic disturbances. Extrapyramidal symptoms occurred in up to 28% of aripiprazole recipients, but after longer-term treatment (=100 weeks), symptom severity did not differ significantly from that in placebo recipients. Aripiprazole treatment generally did not increase bodyweight to a clinically relevant extent; however, more patients receiving aripiprazole monotherapy than placebo had clinically significant bodyweight gain during 100 weeks' treatment. Additionally, in a comparative trial, aripiprazole monotherapy was at least as effective as haloperidol monotherapy in terms of improving symptoms of mania, but had the advantage of a lower incidence of some adverse events, such as extrapyramidal symptom-related adverse events. Further trials comparing aripiprazole with other agents, including atypical antipsychotics, would help to definitively position aripiprazole relative to these agents. Current guidelines recommend aripiprazole as a first-line option (as monotherapy or adjunctive therapy) for the short-term treatment of mania associated with bipolar I disorder, and as a first-line (as monotherapy) or second-line (as adjunctive therapy) option for preventing the recurrence of mood episodes during longer-term therapy.

#### S22235870

Opioid dependence, manifesting as addiction to heroin and pharmaceutical opioids is increasing. Internationally, there are an estimated 15.6million illicit opioid users. The global economic burden of opioid dependence is profound both in terms of HIV and hepatitis C virus transmission, direct healthcare costs, and indirectly through criminal activity, absenteeism and lost productivity. Opioid agonist medications, such as methadone and buprenorphine that stabilize neuronal systems and provide narcotic blockade are the most effective treatments. Prolonged provision of these medications, defined as maintenance treatment, typically produces improved outcomes when compared with short-duration tapers and withdrawal. The benefits of opioid agonist maintenance include decreased illicit drug use, improved retention in treatment, decreased HIV risk behaviours and decreased criminal behaviour. While regulations vary by country, these medications are becoming increasingly available internationally, especially in regions experiencing rapid transmission of HIV due to injection drug use. In this review, we describe the rationale for maintenance treatment of opioid dependence, discuss emerging uses of opioid antagonists such as naltrexone and sustained-release formulations of naltrexone and buprenorphine, and provide a description of the experimental therapies.

#### S22191799

Supraventricular tachyarrhythmia (including atrial fibrillation), hypertension and tachycardia in the perioperative setting, and acute ischaemic heart disease are generally agreed to require rapid attention and treatment. Prolonged tachyarrhythmia or hypertension can result in significant morbidity, such as cerebrovascular events, myocardial infarction and other end-organ damage. This article reviews the clinical efficacy and tolerability of intravenous infusions of esmolol for the short-term treatment of tachyarrhythmias and the short-term control of tachycardia and hypertension, and provides an overview of the pharmacological properties of the drug. Esmolol, a cardioselective  $\beta$ -blocker, has been proven effective in the control of elevated haemodynamic parameters in patients with supraventricular tachyarrhythmia, hypertension and tachycardia in the perioperative setting, and acute ischaemic heart disease, as well as being associated with a reduced risk of some clinical sequelae to increased haemodynamic parameters. Esmolol is, moreover, generally well tolerated; while it is associated with

an increased risk of hypotension, this is rapidly reversible. Definitive conclusions on the efficacy of esmolol are difficult to reach, as most trials investigating esmolol have limitations such as small patient populations, and few studies investigate the same parameters. Ideally, several further studies would be beneficial; however, as esmolol is a well established, older drug, these are less likely to occur. Despite this, esmolol, as a fast-acting, rapidly reversible, easily titratable  $\beta$ -blocker, is an established option for the short-term treatment of tachyarrhythmias and the short-term control of tachycardia and hypertension.

#### S22191793

Hypothyroidism denotes deficient production of thyroid hormone by the thyroid gland and can be primary (abnormality in thyroid gland itself) or secondary/central (as a result of hypothalamic or pituitary disease). The term 'subclinical hypothyroidism' is used to define that grade of primary hypothyroidism in which there is an elevated thyroid-stimulating hormone (TSH) concentration in the presence of normal serum free thyroxine (T4) and triiodothyronine (T3) concentrations. Subclinical hypothyroidism may progress to overt hypothyroidism in approximately 2-5% cases annually. All patients with overt hypothyroidism and subclinical hypothyroidism with TSH >10 mIU/L should be treated. There is consensus on the need to treat subclinical hypothyroidism of any magnitude in pregnant women and women who are contemplating pregnancy, to decrease the risk of pregnancy complications and impaired cognitive development of the offspring. However, controversy remains regarding treatment of non-pregnant adult patients with subclinical hypothyroidism and serum TSH values =10 mIU/L. In this subgroup, treatment should be considered in symptomatic patients, patients with infertility, and patients with goitre or positive anti-thyroid peroxidase (TPO) antibodies. Limited evidence suggests that treatment of subclinical hypothyroidism in patients with serum TSH of up to 10 mIU/L should probably be avoided in those aged >85 years. Other pituitary hormones should be evaluated in patients with central hypothyroidism, especially assessment of the hypothalamic-pituitary-adrenal axis, since hypocortisolism, if present, needs to be rectified prior to initiating thyroid hormone replacement. Levothyroxine (LT4) monotherapy remains the current standard for management of primary, as well as central, hypothyroidism. Treatment can be started with the full calculated dose for most young patients. However, treatment should be initiated at a low dose in elderly patients, patients with coronary artery disease and patients with long-standing severe hypothyroidism. In primary hypothyroidism, treatment is monitored with serum TSH, with a target of 0.5-2.0 mIU/L. In patients with central hypothyroidism, treatment is tailored according to free or total T4 levels, which should be maintained in the upper half of the normal range for age. In patients with persistently elevated TSH despite an apparently adequate replacement dose of LT4, poor compliance, malabsorption and the presence of drug interactions should be checked. Over-replacement is common in clinical practice and is associated with increased risk of atrial fibrillation and osteoporosis, and hence should be avoided.

#### S22233484

Breakthrough pain (BTP) is a transient exacerbation of pain that occurs either spontaneously, or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain. The principal pharmacological treatment of BTP is represented by the administration of opioids as needed. Oral opioids have traditionally been the only available drugs for BTP. However, the onset and duration of action of oral opioids such as morphine or oxycodone may not be suitable for treating many episodes of BTP that are of short onset and duration. Transmucosal administration of lipophilic substances has gained a growing popularity in recent years due to the rapid effect, clinically observable 10-15 minutes after drug administration, and the non-invasive form. Different technologies have been developed to provide fast pain relief with potent opioid drugs such as fentanyl, delivered by non-invasive routes (rapid onset opioids, ROOs). All the studies performed with ROOs have recommended that these drugs should be administered to opioid-tolerant patients receiving doses of oral morphine equivalents of at least 60 mg. These preparations, including oral transmucosal fentanyl citrate, fentanyl buccal tablet, sublingual fentanyl, intranasal fentanyl spray, fentanyl-pectin nasal spray and fentanyl buccal soluble film have shown better efficacy than placebo or oral opioids. Long-term studies have confirmed their efficacy and safety.

#### S22268393

Oral repaglinide (GlucNorm®; NovoNorm®; Prandin®; Surepost®) is a rapid-acting insulin secretagogue that lowers postprandial glucose (PPG) excursions by targeting early-phase insulin release, with reductions in PPG considered to be important in reducing long-term cardiovascular complications of diabetes mellitus. Repaglinide, a carbamoylbenzoic acid derivative, is chemically related to the meglitinide class of insulin secretagogues, but unrelated to the sulfonylurea insulin secretagogues. Meglitinides, including repaglinide, have a distinct binding site at the  $\beta$ -cell membrane, which differs from that of sulfonylureas, and corresponds to greater insulinotropic effects with repaglinide than with glibenclamide and/or glimepiride and a more rapid onset of action in in vitro and in vivo studies. This article reviews the clinical efficacy and tolerability of oral repaglinide in the treatment of patients with type 2 diabetes and provides an overview of its pharmacological properties. In well designed clinical trials of up to 52 weeks' duration and in the clinical practice setting, recommended dosages of repaglinide (0.5-4 mg three times daily up to 30 minutes prior to a meal) provided effective glycaemic control and were generally well tolerated in treatment-naïve or -experienced adult patients with type 2 diabetes, including elderly patients and those with renal impairment. Furthermore, as monotherapy or in combination with other oral antihyperglycaemic drugs, repaglinide was at least as effective as other oral antihyperglycaemic drugs at improving or maintaining

glycaemic control, with a tolerability profile that was generally similar to that of sulfonylurea drugs and nateglinide. Thus, repaglinide remains an effective option for the management of patients with type 2 diabetes.

#### S22221000

Saxagliptin (Onglyza™) is a dipeptidyl peptidase 4 inhibitor widely approved for the treatment of type 2 diabetes mellitus. In the EU, saxagliptin is indicated as combination therapy with metformin, a sulfonylurea, a thiazolidinedione, or insulin (with or without metformin) for the treatment of adult patients with type 2 diabetes, including those with mild to severe renal impairment. This article reviews the clinical efficacy and tolerability of add-on saxagliptin therapy in patients with type 2 diabetes, in line with its approved indications in the EU, and summarizes the drug's pharmacological properties. The clinical efficacy of saxagliptin 5 mg/day in combination with metformin, glibenclamide (glyburide), a thiazolidinedione, or insulin (with or without metformin) has been demonstrated in several randomized, double-blind, placebo-controlled, multicentre, phase III trials (18-104 weeks in duration) in patients with type 2 diabetes. In these trials, glycosylated haemoglobin (HbA<sub>1c</sub>) was changed from baseline (primary endpoint) by a greater extent with add-on saxagliptin 5 mg/day (-1.09% to +0.03%) than with comparator regimens (-0.44% to +0.69%). Two other randomized, double-blind trials showed that saxagliptin 5 mg/day as add-on therapy to metformin was noninferior to uptitrated glipizide in terms of lowering HbA<sub>1c</sub> (-0.74% vs -0.80%) at 52 weeks, or sitagliptin (-0.52% vs -0.62%) at 18 weeks. Saxagliptin 2.5 mg/day as add-on to existing anti-diabetic therapy was also effective for up to 52 weeks in a randomized, double-blind, placebo-controlled, multicentre trial in patients with type 2 diabetes and renal impairment (HbA<sub>1c</sub> was reduced by 1.08% vs 0.36%;  $p=0.007$ ). Saxagliptin as add-on therapy for up to 4 years was generally well tolerated in clinical trials. Treatment with saxagliptin did not increase the risk of hypoglycaemia or cardiovascular outcomes relative to placebo or active comparators, and was generally weight neutral. In conclusion, saxagliptin is a useful option as add-on therapy to metformin, a sulfonylurea, a thiazolidinedione, or insulin (with or without metformin) in patients with type 2 diabetes who require combination therapy.

#### S22191794

The recent impact of influenza on the working-age population of the US has led to changes in the recommendations for vaccination against seasonal influenza; however, the implications of vaccinating such a population have been debated. A review of cost-effectiveness analyses of vaccinating the working-age population of the US against seasonal influenza was conducted using articles published between January 1990 and January 2010. Studies considered for inclusion were identified using MEDLINE, EMBASE and Econlit. Reviewers worked in pairs, and each team member independently extracted relevant data using a standard abstraction form. The source and appropriateness of parameters (epidemiological data, probabilities and costs), the designs employed and the sufficiency of sensitivity analysis were considered during review. Key inputs extracted from the selected studies included influenza or influenza-like illness attack rates, outpatient visits averted, total vaccination days and lost workdays. Seven studies were identified as appropriate for this review. All studies were conducted in the US and from the societal perspective; three were randomized controlled trials and the remaining four were economic simulation models comparing vaccination and influenza antiviral drugs or no intervention; analyses focused on healthy working-age adults aged 18-49 years. Results ranged from net savings of \$US68.96 to net costs of \$US85.92 per person vaccinated (four studies) and net costs of \$US104-1005 per episode of influenza averted (one study). Only two studies reported cost-effectiveness ratios; these ranged from \$US26,565 to \$US50,512 per quality-adjusted life-year gained. Nearly all of the studies conducted sensitivity analysis; results were most sensitive to variation in wage rates, levels of worker productivity, the costs and effectiveness of vaccination, and the rate of influenza illness. Review of the included studies suggests that seasonal influenza vaccination of healthy, working-age adults is generally not cost saving, requiring an investment to generate health benefits. The decision to vaccinate such a group will depend upon the societal and payer valuation of those benefits.

#### S22217233

The anticholinergic agent tiotropium bromide (Spiriva®) is a long-acting bronchodilator that is indicated for the treatment of chronic obstructive pulmonary disease (COPD). This article reviews the clinical efficacy and tolerability of tiotropium bromide inhalation powder, administered using the HandiHaler® device, in patients with COPD, as well as reviewing its pharmacological properties and the results of pharmacoeconomic analyses. Shorter-term placebo-controlled trials in patients with COPD demonstrated significantly higher trough forced expiratory volume in 1 second (FEV<sub>1</sub>) responses with tiotropium bromide than with placebo, confirming it has a duration of action of ≈24 hours and is suitable for once-daily administration. Lung function improved to a greater extent with tiotropium bromide than with ipratropium bromide or, in most instances, salmeterol. Indacaterol was shown to be noninferior to tiotropium bromide in terms of the trough FEV<sub>1</sub> response. The large, 4-year UPLIFT® trial did not show a significant reduction in the annual rate of decline in FEV<sub>1</sub> with tiotropium bromide versus placebo in patients with COPD, although subgroup analyses demonstrated a significantly lower rate of decline with tiotropium bromide than with placebo in some patient groups (e.g. patients with moderate COPD, patients aged ≥50 years, patients not receiving maintenance therapy at baseline). Tiotropium bromide prevented exacerbations in patients with COPD, with a significantly lower exacerbation rate and a significantly longer time to first exacerbation seen with tiotropium bromide than with placebo or salmeterol. Exacerbation rates did not significantly differ between patients receiving tiotropium bromide and those receiving salmeterol/fluticasone propionate. Tiotropium bromide also had beneficial effects on health-related quality of life (HR-QOL) and other

endpoints, such as dyspnoea and rescue medication use. Combination therapy with tiotropium bromide plus formoterol with or without budesonide improved lung function to a significantly greater extent than tiotropium bromide alone in patients with COPD. In addition, exacerbation rates were lower and HR-QOL was improved with tiotropium bromide plus budesonide/formoterol versus tiotropium bromide alone. Although the addition of salmeterol/fluticasone propionate to tiotropium bromide did not reduce the COPD exacerbation rate, it did improve lung function and HR-QOL. Tiotropium bromide inhalation powder is generally well tolerated in patients with COPD, with anticholinergic adverse events (e.g. dry mouth, constipation, gastrointestinal obstruction, dysuria) among the most commonly reported adverse events. The UPLIFT® trial showed no significant difference between tiotropium bromide and placebo recipients in the risk of stroke, and the risk of serious cardiac adverse events (including congestive heart failure and myocardial infarction) was significantly lower with tiotropium bromide than with placebo. The absence of a detrimental effect on cardiovascular outcomes was supported by the results of a meta-analysis and pooled analyses. In addition, on-treatment mortality was lower with tiotropium bromide than with placebo in the UPLIFT® trial. Pooled analyses showed significantly lower cardiovascular mortality with tiotropium bromide than with placebo, with a meta-analysis demonstrating no significant difference between patients receiving tiotropium bromide and controls in cardiovascular mortality. Results of modelled pharmacoeconomic analyses conducted from a healthcare payer perspective in several developed countries suggest that tiotropium bromide is a cost-effective option in patients with COPD. In conclusion, tiotropium bromide inhalation powder is a useful option for the maintenance treatment of patients with COPD.

#### S22191797

Vardenafil orodispersible tablet (ODT) is a supralingual formulation of vardenafil that is available for the on-demand treatment of erectile dysfunction. The pharmacokinetics of vardenafil ODT are not equivalent to those of the vardenafil film-coated tablet in that the ODT formulation provides consistently greater vardenafil systemic exposure. Therefore, the two formulations are not interchangeable. The efficacy of on-demand vardenafil ODT 10 mg was established in the POTENT I and II studies, which were 6-week, randomized, double-blind, multinational trials in men with erectile dysfunction of at least 6 months duration. In both trials, vardenafil ODT improved erectile function significantly more than placebo, as indicated by International Index of Erectile Function-Erectile Function subscale scores at week 12 and overall erection success rates during treatment according to responses to questions 2 and 3 of the Sexual Encounter Profile (coprimary endpoints). In a pooled analysis of both trials, vardenafil ODT improved erectile function regardless of age, severity of erectile dysfunction at baseline or the presence or absence of underlying medical conditions. Vardenafil ODT was generally well tolerated in clinical trials, including in men aged ≥65 years, and adverse events were mostly mild or moderate in severity.

#### EUROPEAN HEART JOURNAL

#### 21804109

Pharmacogenetics is the search for heritable genetic polymorphisms that influence responses to drug therapy. The most important application of pharmacogenetics is to guide choosing agents with the greatest potential of efficacy and smallest risk of adverse drug reactions. Many studies focusing on drug-gene interactions have been published in recent years, some of which led to adaptation of FDA recommendations, indicating that we are on the verge of the clinical application of genetic information in drug therapy. This systematic review provides a comprehensive overview of the current knowledge on pharmacogenetics of all major drug classes currently used in the treatment of cardiovascular diseases.

#### FAMILY MEDICINE

#### S22241335

Students have negative views of the work life of all physicians, especially primary care physicians. Students planning careers in primary care share this negative view of their future work life, suggesting that their career choices are not based on different work life perceptions.

#### S22241336

The third year is an opportune time for medical educators to help shape and develop students' medical epistemology and stress reactions to uncertainty.

#### JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

#### S22235087

Among our cohort aged 65 years or older, incident dementia was significantly associated with increased risk of hospitalization, including hospitalization for ACSCs.

#### S22274684

In this trial of children with poorly controlled asthma without symptoms of GER who were using inhaled corticosteroids, the addition of lansoprazole, compared with placebo, improved neither symptoms nor lung function but was associated with increased adverse events.

S22235089

We identified several indices for predicting overall mortality in different patient groups; future studies need to independently test their accuracy in heterogeneous populations and their ability to improve clinical outcomes before their widespread use can be recommended.

## THE LANCET

S22225672

Debates about which policy initiatives can prevent or reduce the damage that illicit drugs cause to the public good are rarely informed by scientific evidence. Fortunately, evidence-based interventions are increasingly being identified that are capable of making drugs less available, reducing violence in drug markets, lessening misuse of legal pharmaceuticals, preventing drug use initiation in young people, and reducing drug use and its consequences in established drug users. We review relevant evidence and outline the likely effects of fuller implementation of existing interventions. The reasoning behind the final decisions for action might be of a non-scientific nature, focused more on what the public and policy-makers deem of value. Nevertheless, important opportunities exist for science to inform these deliberations and guide the selection of policies that maximise the public good.

S22225671

This paper summarises data for the prevalence, correlates, and probable adverse health consequences of problem use of amphetamines, cannabis, cocaine, and opioids. We discuss findings from systematic reviews of the prevalence of illicit drug use and dependence, remission from dependence, and mortality in illicit drug users, and evidence for acute and chronic effects of illicit drug use. We outline the regional and global distribution of use and estimated health burden from illicit drugs. These distributions are likely to be underestimates because they have not included all adverse outcomes of drug use and exclude those of cannabis--the mostly widely used illicit drug. In high-income countries, illicit drug use contributes less to the burden of disease than does tobacco but a substantial proportion of that due to alcohol. The major adverse health effects of cannabis use are dependence and probably psychotic disorders and other mental disorders. The health-related harms of cannabis use differ from those of amphetamine, cocaine, and opioid use, in that cannabis contributes little to mortality. Intelligent policy responses to drug problems need better data for the prevalence of different types of illicit drug use and the harms that their use causes globally. This need is especially urgent in high-income countries with substantial rates of illicit drug use and in low-income and middle-income countries close to illicit drug production areas.

S22100201

Most self-harming behaviour in adolescents resolves spontaneously. The early detection and treatment of common mental disorders during adolescence might constitute an important and hitherto unrecognised component of suicide prevention in young adults.

## MEDICINA CLINICA

S21420131

Este estudio muestra un alto porcentaje de diagnósticos con un bajo número de pruebas diagnósticas, destacando el rendimiento de la tabla basculante. El estudio de pacientes no seleccionados de síncope mediante un protocolo basado en las Guías Europeas y aplicado por un equipo multidisciplinario fue muy efectivo.

S21411113

La prescripción de ejercicio físico es útil especialmente para prevenir la mortalidad prematura de cualquier causa, la cardiopatía isquémica, la enfermedad cerebrovascular, la hipertensión arterial, el cáncer de colon y mama, la diabetes tipo 2, el síndrome metabólico, la obesidad, la osteoporosis, la sarcopenia, la dependencia funcional y las caídas en ancianos, el deterioro cognitivo, la ansiedad y la depresión.

Dicho beneficio se observa en ambos sexos y es mayor cuanto mayor es el volumen o la intensidad del ejercicio físico. Para obtener dichos beneficios, debe realizarse ejercicio aeróbico moderado durante un mínimo de 30 minutos, 5 días por semana, o ejercicio intenso durante un mínimo de 20 minutos, 3 días por semana. Se recomienda añadir un mínimo de 2 días no consecutivos cada semana para practicar 8-10 ejercicios que desarrollen la fuerza de la mayor parte de grupos musculares (brazos, hombros, tórax, abdomen, espalda, caderas y piernas), con 10-15 repeticiones de cada ejercicio. También es recomendable dedicar 2 sesiones de 10 minutos a la semana para realizar 8-10 ejercicios que mantengan la flexibilidad de la mayor parte de grupos de músculos y tendones. El ejercicio físico puede comportar lesiones del aparato locomotor y un riesgo cardiovascular, pero el beneficio supera al riesgo.

## NEJM

S22256806



Our data indicate that osteoporosis would develop in less than 10% of older, postmenopausal women during rescreening intervals of approximately 15 years for women with normal bone density or mild osteopenia, 5 years for women with moderate osteopenia, and 1 year for women with advanced osteopenia.

[S22276822](#)

Differences in risk-factor burden translate into marked differences in the lifetime risk of cardiovascular disease, and these differences are consistent across race and birth cohorts.

[BMJ](#)

[S22214758](#)

Publication, availability, and selection biases are a potential concern for meta-analyses of individual participant data, but many reviewers neglect to examine or discuss them. These issues warn against uncritically viewing any meta-analysis that uses individual participant data as the most reliable. Reviewers should seek individual participant data from all studies identified by a systematic review; include, where possible, aggregate data from any studies lacking individual participant data to consider their potential impact; and investigate funnel plot asymmetry in line with recent guidelines.

[S22236411](#)

The present review provides evidence that treatment with GLP-1R agonists leads to weight loss in overweight or obese patients with or without type 2 diabetes mellitus.

[S22217630](#)

The algorithm has good discrimination and calibration and, after independent validation in an external cohort, could potentially be used to identify those at highest risk of ovarian cancer to facilitate early referral and investigation. Further research is needed to assess how best to implement the algorithm, its cost effectiveness, and whether, on implementation, it has any impact on health outcomes.

[S22218098](#)

Very elderly patients with hypertension may gain immediate benefit from treatment. Sustained differences in reductions of total mortality and cardiovascular mortality reinforce the benefits and support the need for early and long term treatment.

[S22113564](#)

Overdiagnosis from the detection of non-progressive disease by screening mammography was limited in 1991-2006 in Isère. Because carcinoma in situ accounted for less than 15% of all incident breast cancer cases, its contribution to overdiagnosis was relatively limited and imprecise.

[S22155336](#)

This analysis supports the claim that the introduction of breast cancer screening might have caused net harm for up to 10 years after the start of screening.

[S22232535](#)

This study with a high response rate of 89% at 35 days in men undergoing biopsy in the context of a randomised controlled trial has shown that although prostate biopsy is well tolerated by most men, it is associated with significant symptoms in a minority and affects attitudes to repeat biopsy and primary care resource use. These findings will inform men who seek PSA testing for detection of prostate cancer and assist their physicians during counselling about the potential risks and effect of biopsy. Variability in the adverse event profile between centres suggests that patients' outcomes could be improved and healthcare use reduced with more effective administration of local anaesthetic and antibiotics

[S22214757](#)

Based on the results for 2005, at least 3000 records describing randomised controlled trials but not indexed using RCT [pt] may have been entered into Medline between 2006 and 2011. Researchers and healthcare decision makers relying on using RCT [pt] may be missing important evidence in their searches, particularly for design and methods, baseline characteristics, long term follow-up, and secondary data analyses.

[S22223828](#)

Cognitive decline is already evident in middle age (age 45-49).