PERÚ Ministerio de salud | Dirección General de Medicamentos, Insumos y Drogas | DIGEMID

CenadIM
Centro Nacional de Documentación e Información de Medicamentos

Fuentes de Información, Pirámide de Haynes de las 5 "S"

Mg. Roselly Robles Hilario

Centro Nacional de Documentación e Información de Medicamentos

CENADIM

rrobles@digemid.minsa.gob.pe
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CLASIFICACIÓN DE LAS FUENTES DE INFORMACIÓN PARA LA TOMA DE DECISIONES

Tiempo requerido para su uso

"Pirámide de Haynes las 5 S"

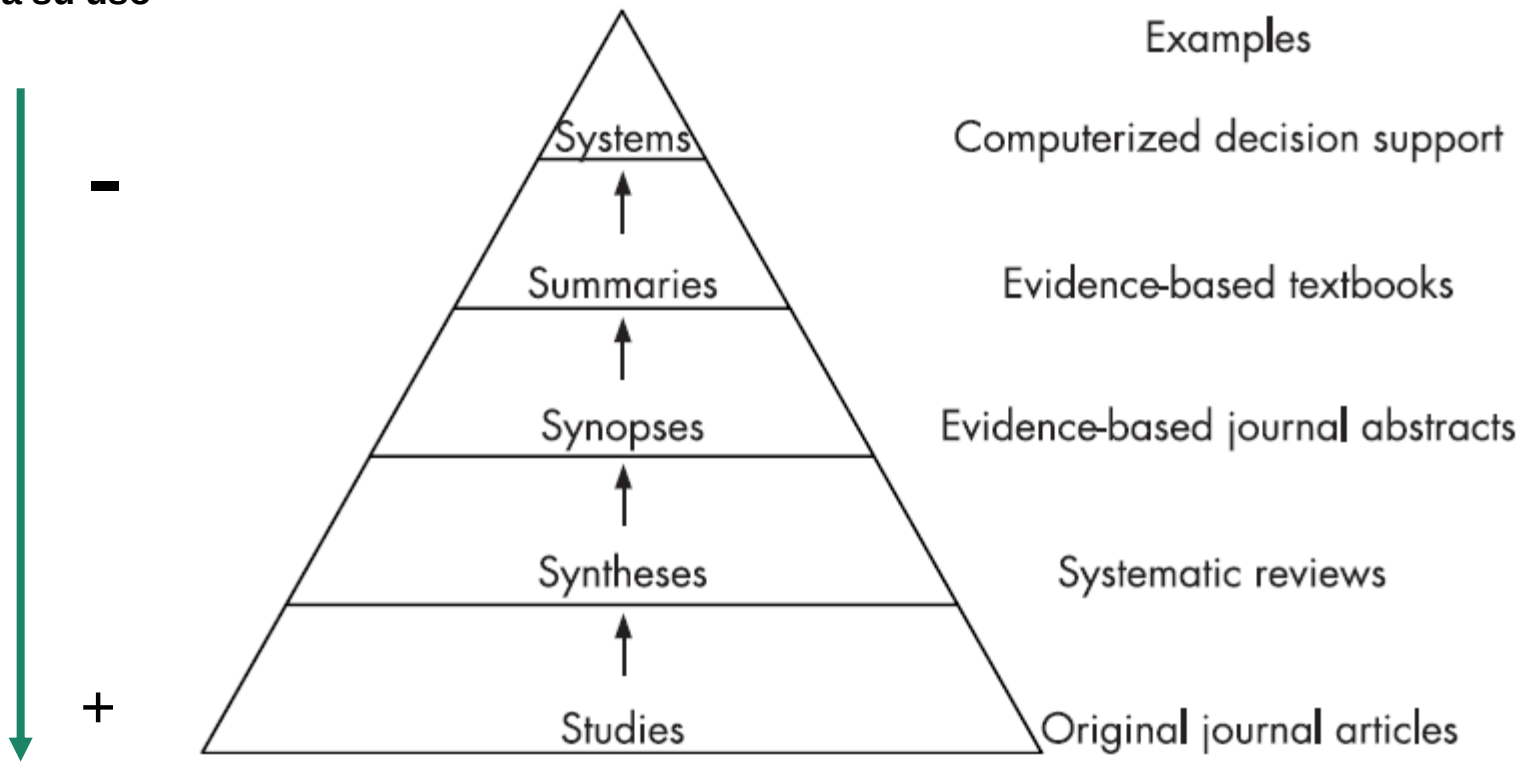


Figure 1 The "5S" levels of organisation of evidence from healthcare research.

Haynes B. *Evid Based Nurs 2007 10: 6-7*

Escenario Clínico

- Carlos es un paciente de 48 años que tiene Diabetes Mellitus Tipo 1 que se encuentra bien controlada. Sin embargo, después de 25 años de diabetes, ha desarrollado neuropatía diabética dolorosa significativa. Cuando el paciente acude a consulta menciona que siente mayor ardor y dolor en los dedos de los pies y en los pies, por lo cual pide a su médico le recete un analgésico.

- El prescriptor recuerda que en un paciente ha prescrito Gabapentina para neuralgia post-herpética y se pregunta si esto también puede ayudar a Carlos.

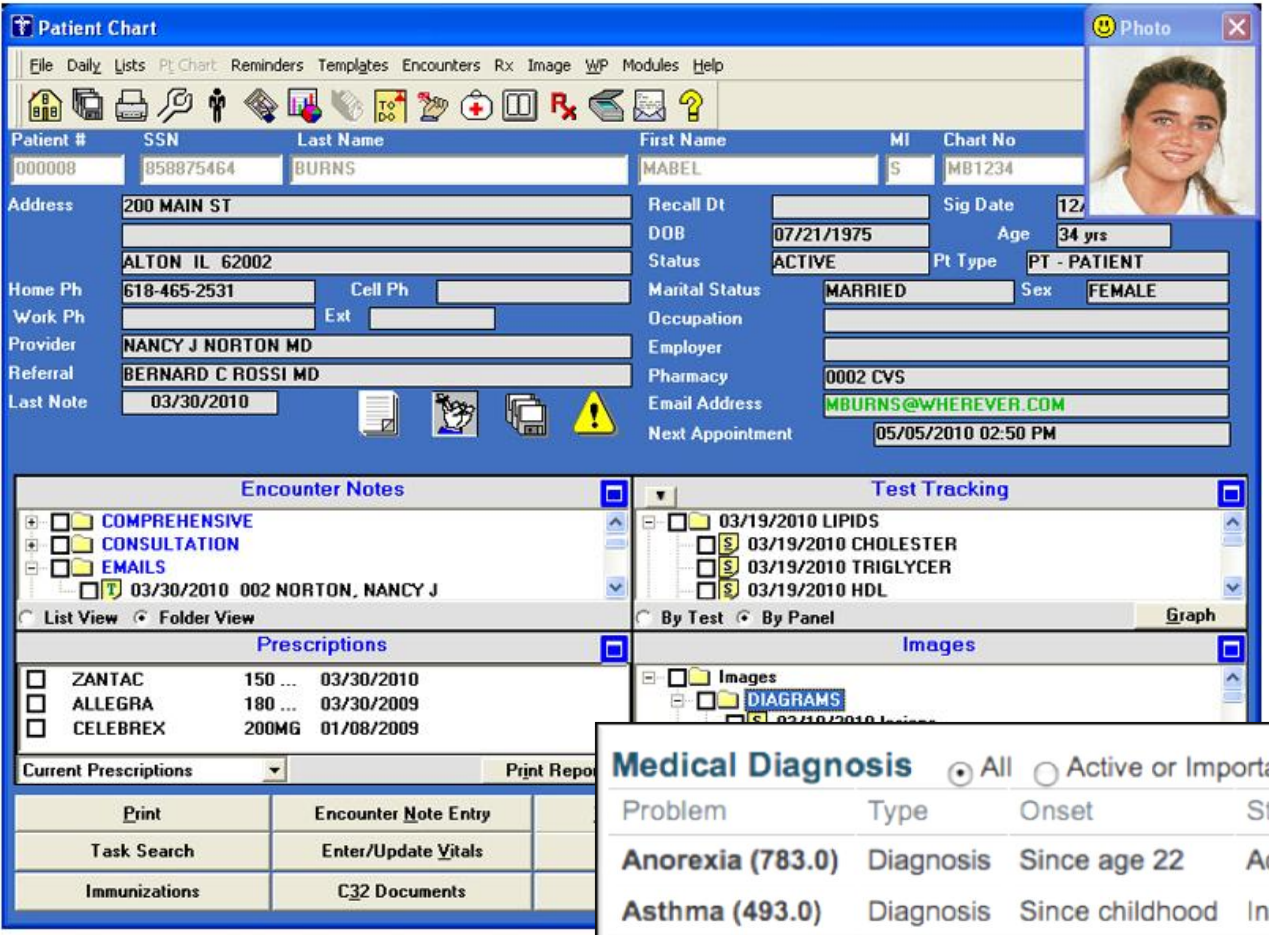
Pregunta Clínica Estructurada (PCE)

¿En los pacientes adultos con neuropatía diabética dolorosa, gabapentina es eficaz para reducir el dolor?

SISTEMA

- Forma más avanzada de información clínica, que debería integrar y reunir toda la evidencia científica relevante sobre un problema clínico concreto y enlazarla automáticamente, a través de un registro médico informatizado, con las circunstancias especificas de cada paciente.
- El sistema está integrado con la historia clínica virtual
- No están completamente desarrollados.

Robeson et al.Facilitating access to pre-processed research evidence in public health. BMC Public Health 2010, 10:95.



Definition for condition: Anorexia

An eating disorder characterized by markedly reduced appetite or total aversion to food. Anorexia is a serious psychological disorder. It is a condition that goes well beyond out-of-control dieting. The person with anorexia, most often a girl or young woman, initially begins dieting to lose weight. Over time, the weight loss becomes a sign of mastery and control. The drive to become thinner is thought to be secondary to concerns about control and fears relating to one's body. The individual continues the endless cycle of restrictive eating, often to a point close to starvation. This becomes an obsession and is similar to an addiction to a drug. Anorexia can be life-threatening.

More information about Anorexia

- What is the definition of anorexia?
- What else could it be?
- What tests will confirm the diagnosis of anorexia?
- What treatments are available for anorexia?
- What result would confirm the diagnosis of anorexia?

FIND OUT MORE

SUMARIO (compendios)

- Integra la mejor evidencia de los niveles inferiores para ofrecer la evidencia que concierne a las diferentes opciones de manejo para un problema clínico específico.
- Resúmenes colectivos de varios estudios sobre un tema.
- Comprenden los ***textos de medicina basada en evidencia*** y las ***Guías de práctica clínicas***.

Robeson et al.Facilitating access to pre-processed research evidence in public health. BMC Public Health 2010, 10:95.

Textos de Medicina Basada en Evidencia

UpToDate (Requiere suscripción)	https://www.uptodate.com/login
Clinical Evidence (Requiere suscripción)	http://clinicalevidence.bmj.com/ceweb/index.jsp
Best Practice (Requiere suscripción)	http://bestpractice.bmj.com/best-practice/welcome.html
Dynamed (Requiere suscripción)	http://www.ebscohost.com/dynamed/
PIER (Physicians' Information and Education Resources) (Requiere suscripción)	http://pier.acponline.org/index.html
Deseases - Micromedex (Requiere suscripción)	https://www.thomsonhc.com/home/dispatch

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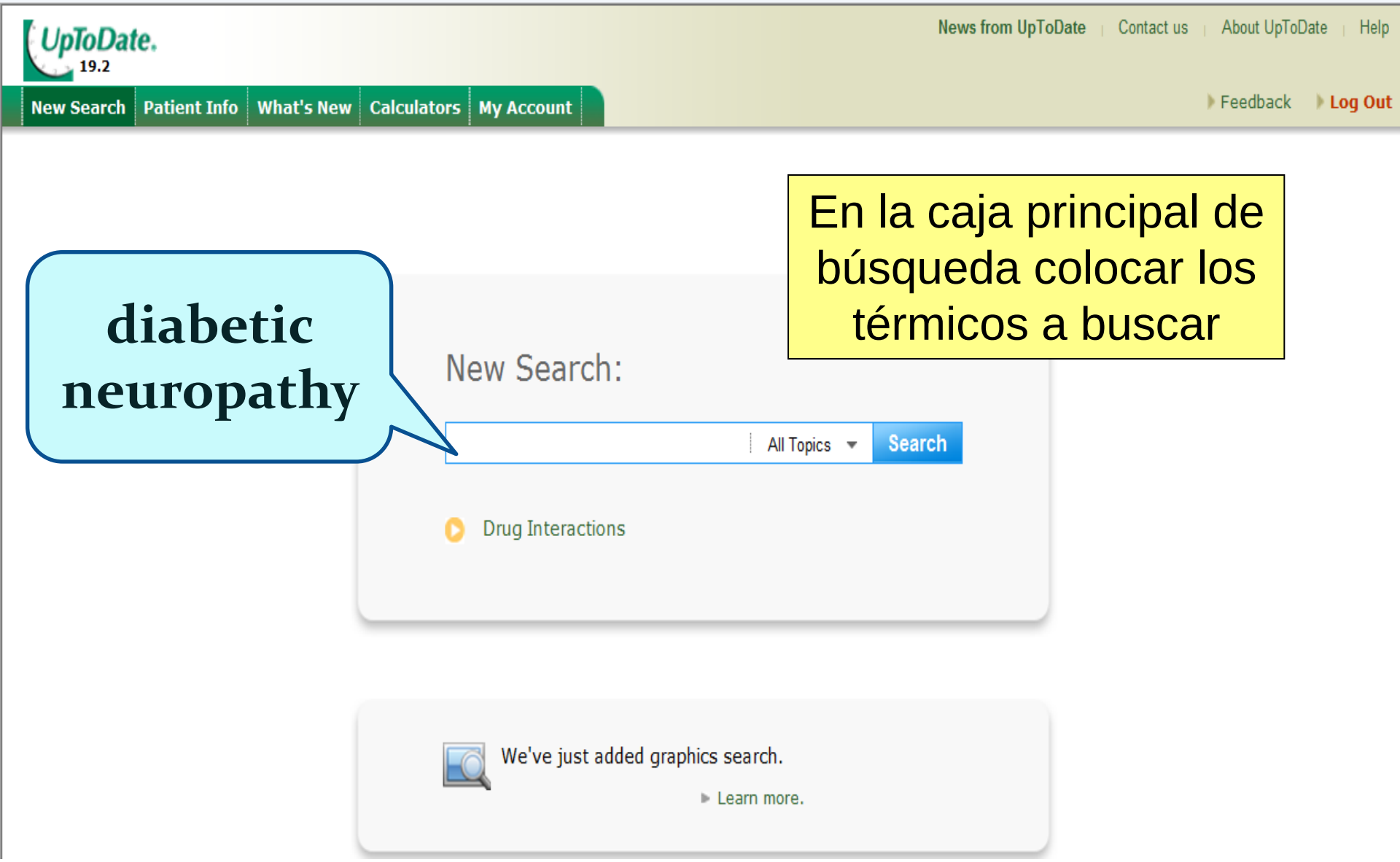
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What's New
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diabetic neuropathy
En la caja principal de búsqueda colocar los térmicos a buscar
New Search:
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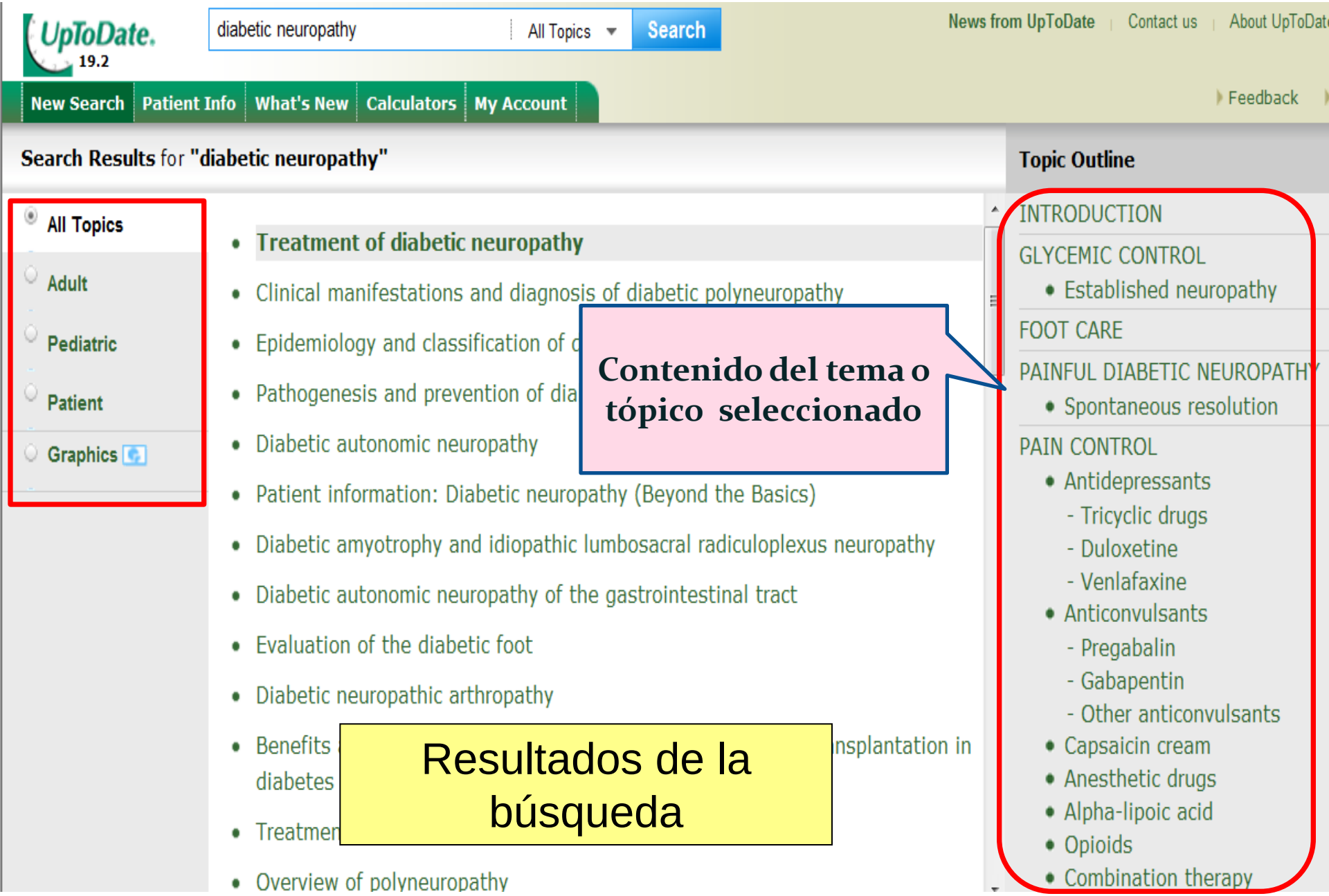
Search
Drug Interactions
We've just added graphics search.
Learn more.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19.2
diabetic neuropathy
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News from UpToDate
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New Search
Patient Info
What's New
Calculators
My Account
Feedback
Search Results for "diabetic neuropathy"
All Topics
Adult
Pediatric
Patient
Graphics
Treatment of diabetic neuropathy
Clinical manifestations and diagnosis of diabetic polyneuropathy
Epidemiology and classification of d
Pathogenesis and prevention of dia
Diabetic autonomic neuropathy
Patient information: Diabetic neuropathy (Beyond the Basics)
Diabetic amyotrophy and idiopathic lumbosacral radiculoplexus neuropathy
Diabetic autonomic neuropathy of the gastrointestinal tract
Evaluation of the diabetic foot
Diabetic neuropathic arthropathy
Benefits
nsplantation in diabetes
Treatmen
Overview of polyneuropathy
Contenido del tema o tópico seleccionado
Resultados de la búsqueda
Topic Outline
INTRODUCTION
GLYCEMIC CONTROL
Established neuropathy
FOOT CARE
PAINFUL DIABETIC NEUROPATHY
Spontaneous resolution
PAIN CONTROL
Antidepressants
- Tricyclic drugs
- Duloxetine
- Venlafaxine
Anticonvulsants
- Pregabalin
- Gabapentin
- Other anticonvulsants
Capsaicin cream
Anesthetic drugs
Alpha-lipoic acid
Opioids
Combination therapy

Treatment of diabetic neuropathy

Authors
Eva L Feldman, MD, PhD
David K McCulloch, MD

Section Editors
Jeremy M Shefner, MD, PhD
David M Nathan, MD

Deputy Editor
John F Dashe, MD, PhD

Disclosures

Last literature review version 19.2: mayo 2011 | **This topic last updated:** junio 17, 2011 (More)

INTRODUCTION — Peripheral and autonomic neuropathies are a major cause of morbidity in patients with diabetes mellitus. (See "Clinical manifestations and diagnosis of diabetic polyneuropathy" and "Diabetic autonomic neuropathy".)

The treatment of diabetic peripheral neuropathy will be reviewed here. There are three main elements in the treatment regimen:

- Glycemic control
- Foot care
- Treatment of pain

GLYCEMIC CONTROL — The most important treatment for the prevention of diabetic neuropathy is optimal glucose control. In the Diabetes Control and Complications Trial (DCCT), the occurrence of diabetic neuropathy was reduced by 60 percent over a 10-year period with rigorous blood glucose control in patients with type 1 diabetes (figure 1A-B) [1,2]. Similar findings were noted in the Stockholm Diabetes Intervention Study [3]. The effect of hyperglycemia on disease progression appears to be dose-dependent: in the Oslo Diabetes study each 1 percent rise in hemoglobin A1C (HbA1C) values was associated with a 1.3 m/sec slowing of nerve conduction at eight years [4]. (See "Pathogenesis and prevention of diabetic polyneuropathy".)

Established neuropathy — The role of glycemic control in establish… …lled studies suggest that neuropathic symptoms may improve with intensive antidiabetic therapy [5-8].

This issue was better addressed in the DCCT [2]. After follow-up for five y… …seline, treated with intensive glycemic control, had an increase in nerve conduction velocity (figure 2). Whether this effe… …is not known.

A practice statement issued by the American Diabetes Association in 2005 …ents with symptomatic diabetic polyneuropathy should be to aim for stable and optimal glycemic control [9].

FOOT CARE — We combine good glucose control with foot care. On a daily basis, patients need to inspect their feet for the presence of dry or cracking skin, fissures, plantar callus formation, and signs of early infection between the toes and around the toe nails. Regular foot examinations by the physician to detect early neuropathy are also an essential component of the treatment of diabetic patients. (See "Evaluation of the diabetic foot".)

Once a patient has diabetic neuropathy, foot care is even more important to prevent ulceration, infection, and amputation. (See "Management of diabetic foot lesions".)

PAINFUL DIABETIC NEUROPATHY — Only a small fraction of patients with diabetic polyneuropathy have painful symptoms. Patients with painful diabetic neuropathy should be treated with

Las referencias están enlazadas a la descripción del artículo original

Print

Medline ® Abstracts for References 5-8

of 'Treatment of diabetic neuropathy'

5 PubMed

TI Continuous subcutaneous insulin infusion in the management of painful diabetic neuropathy.

AU Boulton AJ, Drury J, Clarke B, Ward JD

SO Diabetes Care. 1982;5(4):386.

Nine patients with diabetic neuropathy were treated as outpatients with continuous subcutaneous insulin infusion (CSII). Painful symptoms were scored on a 10-cm horizontal graphic rating scale; motor conduction velocity (MCV) was measured in the median and peroneal nerves; and vibration perception threshold (VPT) was recorded in the great toes. All investigations were repeated after 6 wk and at the completion of 4 mo of CSII. Improved diabetic control was confirmed by significantly lower mean blood glucose levels, M-values, and glycosylated hemoglobin. Symptomatic relief was noted by all patients and was accompanied by a significant improvement in pain scores. There was also significant improvement in VPT and MCV after 6 wk of CSII, which was maintained throughout the 4-mo period. However, sensory studies in the median nerve showed no significant changes during the study. It is concluded that strict glucoregulation is indicated in all cases of symptomatic diabetic neuropathy. It remains to be seen whether strict diabetic control from diagnosis will lead to a reduction in the incidence of t

AD

PMID 7151654

Hipervínculo al PUBMED

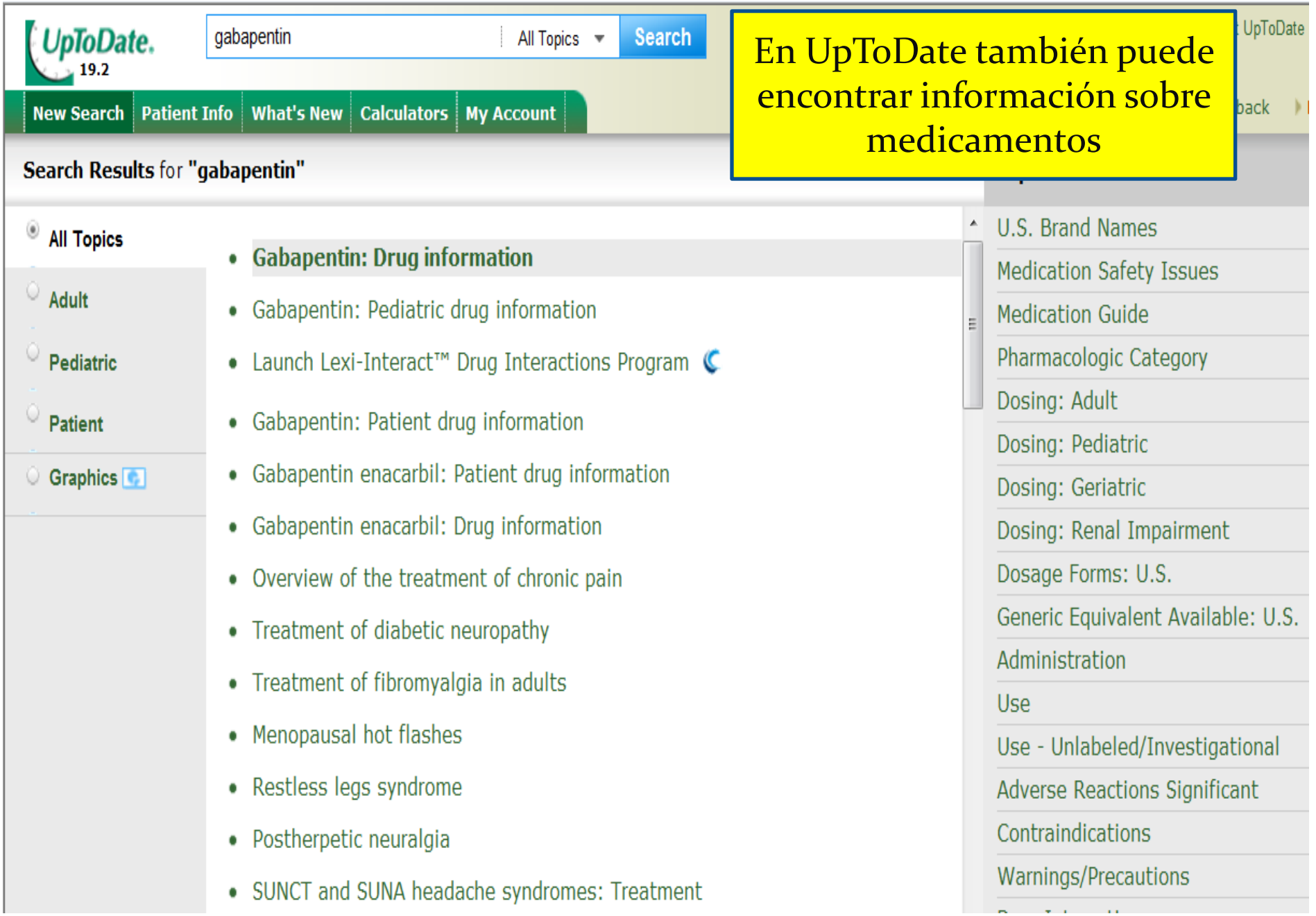
6 PubMed

TI Comparison of clinical couse and sequential electrophysiological tests in diabetics with symptomatic polyneuropathy and its implications for clinical trials.

AU Greene DA, Brown MJ, Braunstein SN, Schwartz SS, Asbury AK, Winegrad AI

SO Diabetes. 1981;30(2):139.

The use of electrophysiological (EP) tests as the primary basis for determining outcome in clinical trials of therapy for symptomatic diabetic polyneuropathy, and the frequently short duration of such trials, is based on assumptions at variance with the pathology and natural history of this disorder and with the evidence that the commonly employed EP tests predominantly reflect the status of the large myelinated nerve fibers. The course of painful, distal symmetrical, primarily sensory polyneuropathy was studied in nine chronic diabetics, aged 21--59 yr, selected for the absence of other forms of diabetic neuropathy, other causes of neuropathy, and other significant illness. All were treated with modifications of diet, insulin, and a daily multivitamin tablet, and, on a randomized basis, also received either placebo or myo-inositol tablets. Initially, and after 2, 4, and 6 mo, a standardized questionnaire was used to assess symptoms, and a standardized neurological examination and battery of EP tests were performed. A minimum of 6 mo was found necessary to assess the clinical course of this syndrome. Clinical improvement occurred in both legs and arms in four patients, as judged by improvement both in symptoms and in the extent of deficits in pinprick and temperature perception; abnormalities in sensory modalities mediated by large myelinated fibers, however, were generally unaltered after 6 mo. A nonuniform distribution of abnormal EP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Gabapentin: Pediatric drug information
Launch Lexi-Interact™ Drug Interactions Program
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Overview of the treatment of chronic pain
Treatment of diabetic neuropathy
Treatment of fibromyalgia in adults
Menopausal hot flashes
Restless legs syndrome
Postherpetic neuralgia
SUNCT and SUNA headache syndromes: Treatment
U.S. Brand Names
Medication Safety Issues
Medication Guide
Pharmacologic Category
Dosing: Adult
Dosing: Pediatric
Dosing: Geriatric
Dosing: Renal Impairment
Dosage Forms: U.S.
Generic Equivalent Available: U.S.
Administration
Use
Use - Unlabeled/Investigational
Adverse Reactions Significant
Contraindications
Warnings/Precautions
En UpToDate también puede encontrar información sobre medicamentos

Gabapentin: Drug information

(For additional information see "Gabapentin: Patient drug information" and see "Gabapentin: Pediatric drug information")

U.S. Brand Names

Neurontin®

Medication Safety Issues

Sound-alike/look-alike issues:

Neurontin® may be confused with Motrin®, Neoral®, nitrofurantoin, Noroxin®, Zarontin®

Medication Guide

An FDA-approved patient medication guide, which is available with the product information and at http://www.fda.gov/downloads/Drugs/DrugSafety/UCM229208.pdf, must be dispensed with this medication.

Pharmacologic Category

Anticonvulsant, Miscellaneous

Dosing: Adult

Anticonvulsant: Oral:

Initial: 300 mg 3 times/day, if necessary the dose may be increased up to 1800 mg/day

Maintenance: 900-1800 mg/day administered in 3 divided doses; doses of up to 2400 mg/day have been tolerated in long-term clinical studies; up to 3600 mg/day has been tolerated in short-term studies

Note: If gabapentin is discontinued or if another anticonvulsant is added to therapy, it should be done slowly over a minimum of 1 week.

Chronic pain (unlabeled use): Oral: 300-1800 mg/day given in 3 divided doses has been the most common dosage range

Diabetic neuropathy (unlabeled use): Oral: 900-3600 mg/day (Bril, 2011)

Postoperative pain (unlabeled use): 300-1200 mg 1-2 hours before surgery

Postherpetic neuralgia: Day 1: 300 mg, Day 2: 300 mg twice daily, Day 3: 300 mg 3 times/day; dose may be titrated as needed for pain relief (range: 1800-3600 mg/day, daily doses >1800 mg do not generally show greater benefit)

Restless legs syndrome (RLS) (unlabeled use): Oral: Initial: 300 mg once daily 2 hours before bedtime. Doses ≥600 mg/day have been given in 2 divided doses (late afternoon and 2 hours before bedtime). Dose may be titrated every 2 weeks until symptom relief achieved (range: 300-1800 mg/day). Suggested maintenance dosing schedule: One-third of total daily dose given at 12 pm, remaining two-thirds total daily dose given at 8 pm. (Garcia-Borreguero, 2002; Happe, 2003; Saletu, 2010; Vignatelli, 2006)

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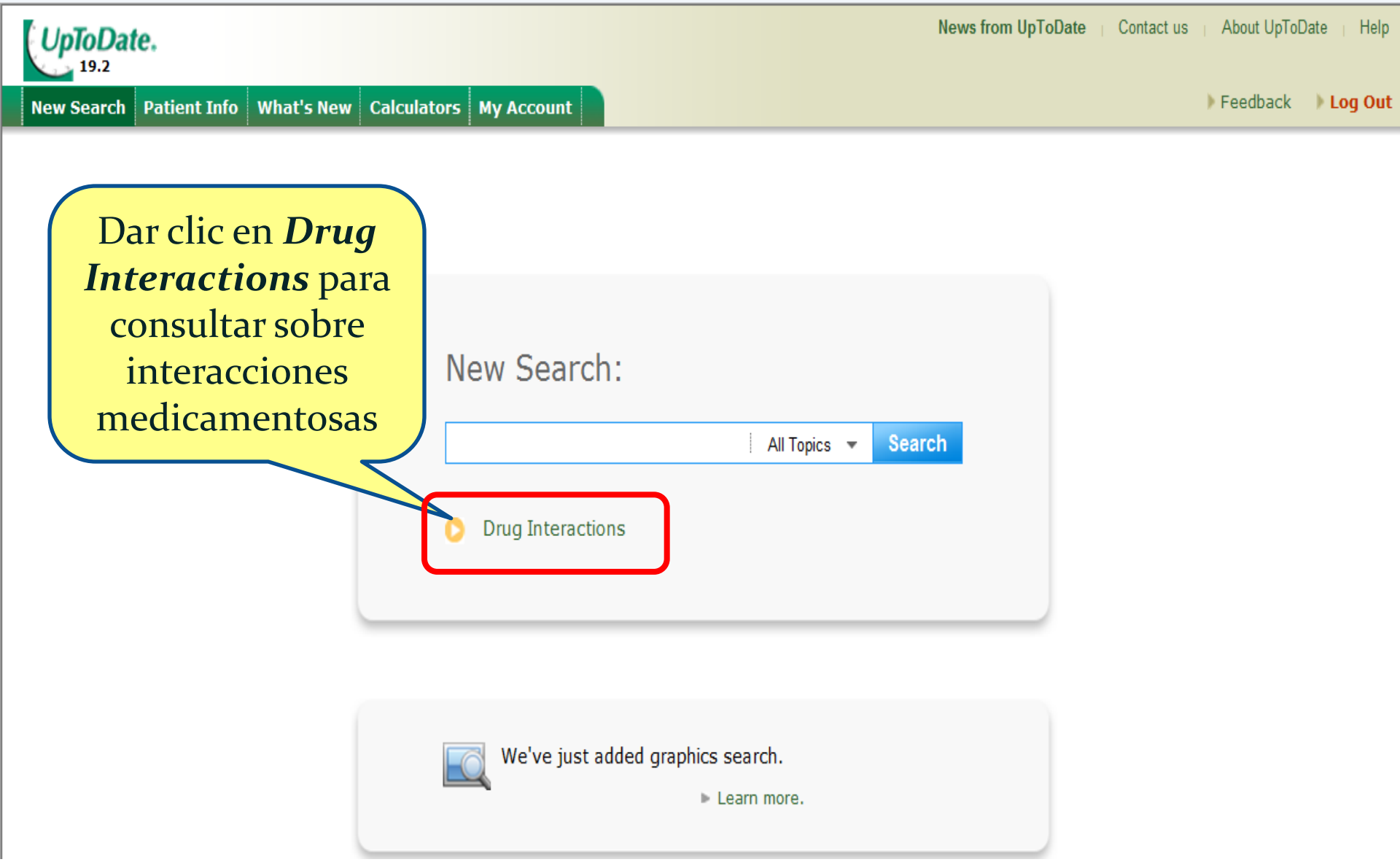
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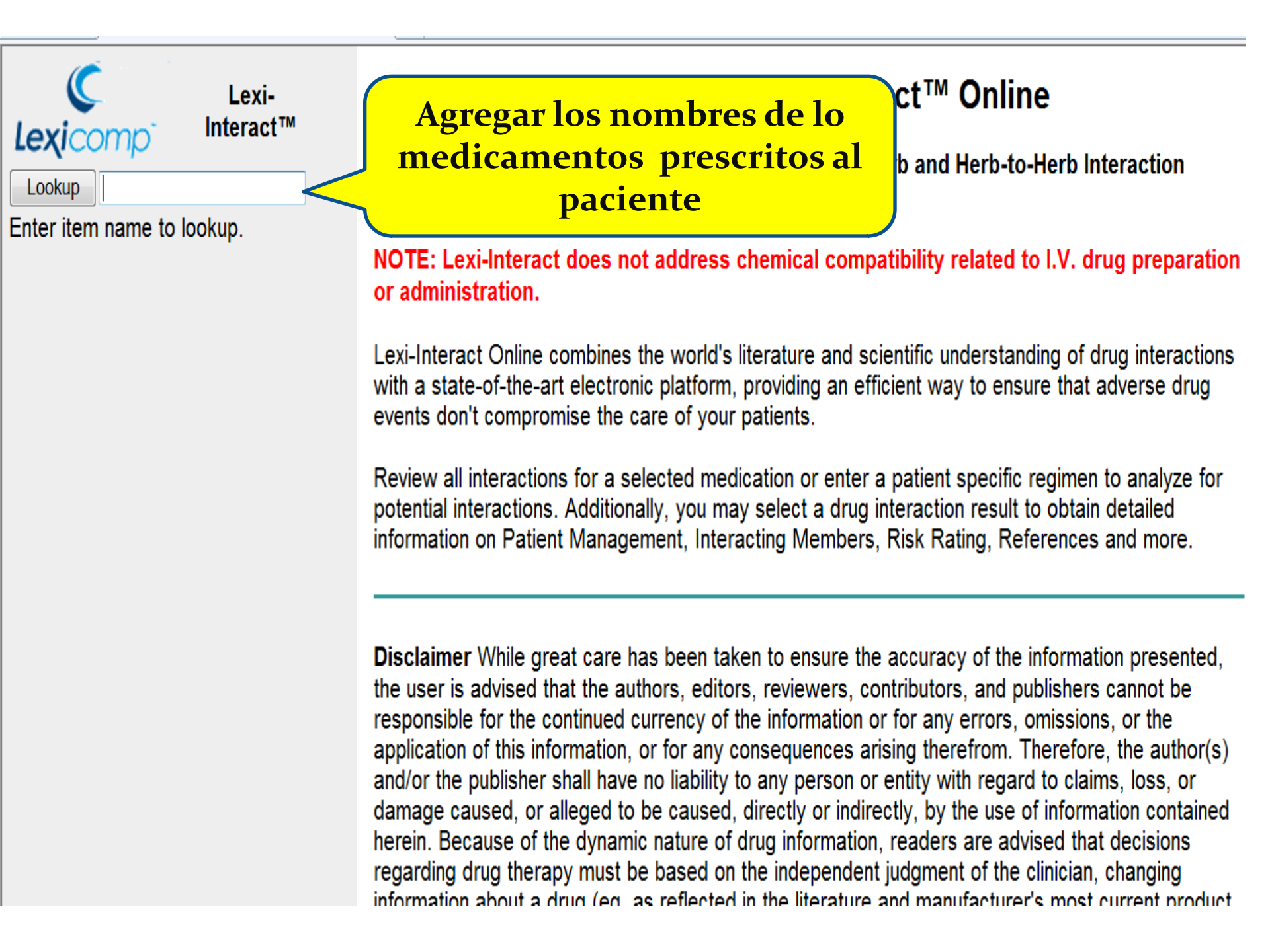
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Review all interactions for a selected medication or enter a patient specific regimen to analyze for potential interactions. Additionally, you may select a drug interaction result to obtain detailed information on Patient Management, Interacting Members, Risk Rating, References and more.
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Lexi-Interact™

Lookup

Enter item name to lookup.

Analyze | New List

- Clopidogrel
- MetFORMIN
- Propranolol
- Warfarin

- Display complete list of interactions for an individual item by clicking item name.
- Add another item(s) [Lookup] to Analyze for potential interactions between items in the list.
- Remove item from the list by clicking the check mark next to the item name.

Lexi-Comp Online™ Interaction Analysis

Customize Analysis

Only interactions at or above the selected risk rating will be displayed. A:

View interaction detail by clicking on link.

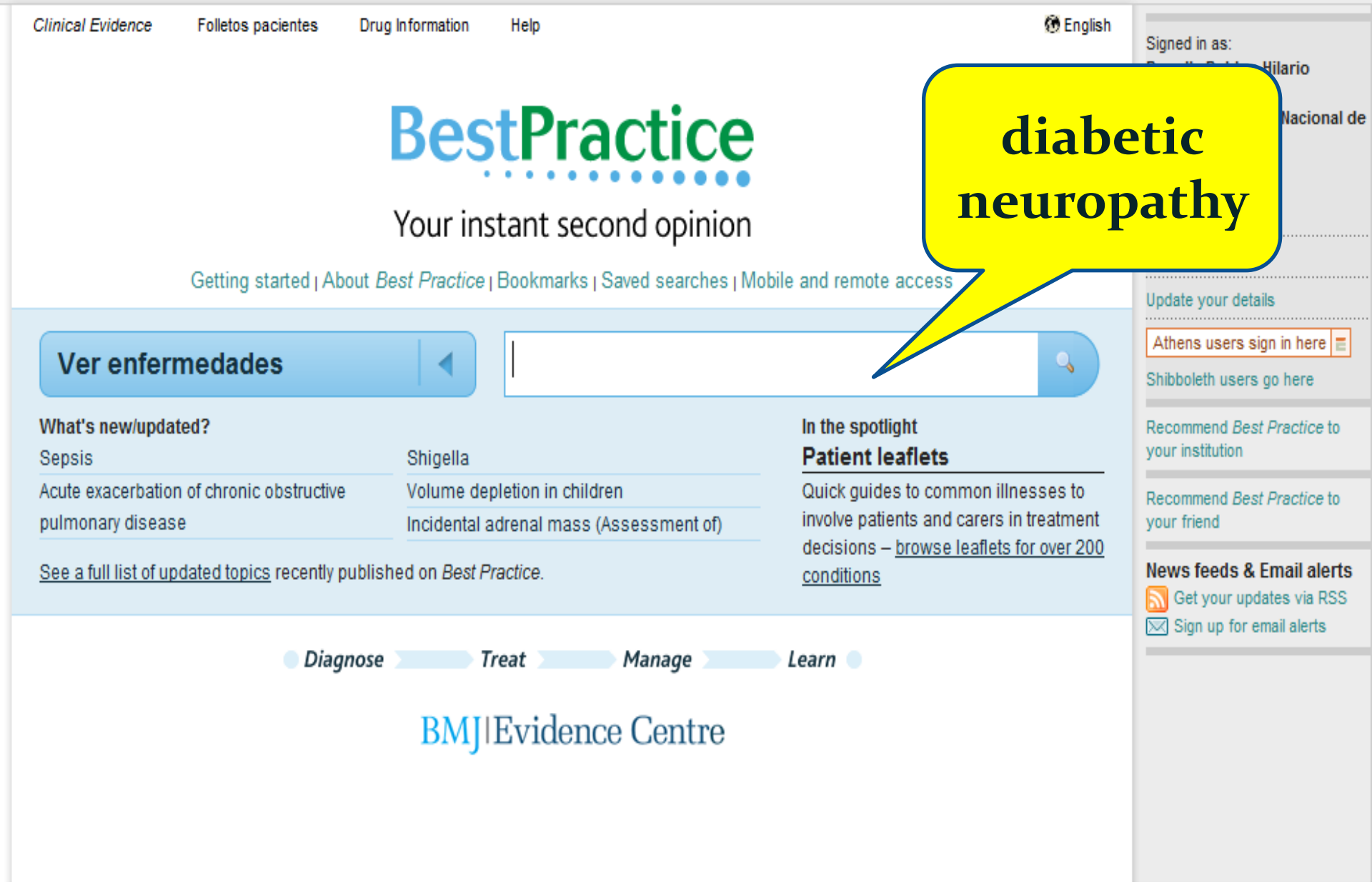
Clopidogrel
[D] Warfarin (Warfarin)

MetFORMIN
No interactions identified with others in the selection list.

Propranolol
[B] Warfarin (Warfarin)

Warfarin
[D] Clopidogrel (Clopidogrel)
[B] Propranolol (Propranolol)

Date November 13, 2011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Diabetic neuropathy

Historia clínica y examen físico

Factores clave de diagnóstico

- presence of risk factors
- asymptomatic
- pain (peripheral)
- loss of sensation (peripheral)
- dysesthesia (peripheral)
- reduced or absent ankle reflexes (peripheral)
- painless injuries (peripheral)
- resting tachycardia (autonomic)
- impaired heart rate variation (autonomic)
- urinary frequency, urgency, nocturia,

Pruebas diagnósticas

1as pruebas que se deben solicitar

- clinical diagnosis
- fasting blood sugar
- oral glucose tolerance test
- HbA1c
- serum TSH
- serum creatinine
- serum B12
- serum/urine immunoelectrophoresis

Otras pruebas a considerar

- nerve conduction studies (nerve conduction velocity, NCV)

Detalles del tratamiento

Continuado

diabetic peripheral neuropathy

- **without pain**
  - glycaemic control and foot care
- **with pain**
  - pregabalin or gabapentin and/or duloxetine + glycaemic control and foot care
  - tricyclic antidepressant (TCA) or selective serotonin-reuptake inhibitor (SSRI) + glycaemic control and foot care
  - opioid analgesics + glycaemic control

Guías de Práctica Clínica (GPC)

- “Conjunto de recomendaciones desarrolladas de manera sistemática, para ayudar a los clínicos y a los pacientes en el proceso de la toma de decisiones, sobre cuáles son las intervenciones más adecuadas para resolver un problema clínico en unas circunstancias sanitarias específicas.”

Field MJ, Lohr KN, eds. Clinical practice guidelines: Directions for a new Agency. Institute of Medicine . Washington D.C.: National Academic Press; 1990. p. 58.

Compiladores o Buscadores de GPC

National Guideline Clearinghouse	http://www.ngc.gov/
Guidelines International Network (Requiere suscripción)	http://www.g-i-n.net/
CMA INFOBASE: Clinical Practice Guidelines (CPGs) Canadian Medical Association	http://www.cma.ca/index.php/ci_id/54316/la_id/1.htm
Guiasalud.es Biblioteca de Guías de Práctica Clínica del Sistema Nacional de Salud (requiere registro previo)	http://portal.guiasalud.es/web/guest/home

http://www.guideline.gov/

U.S. Department of Health & Human Services

www.hhs.gov

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Advancing Excellence in Health Care

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1. **Evidence-based guideline: treatment of painful diabetic neuropathy. Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation.** 2011 May 17. NGC:008504
   American Academy of Neurology - Medical Specialty Society; American Academy of Physical Medicine and Rehabilitation - Medical Specialty Society; American Association of Neuromuscular and Electrodiagnostic Medicine - Medical Specialty Society. *View all guidelines by the developer(s)*

2. **Practice advisory: utility of surgical decompression for treatment of diabetic neuropathy. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology.** 2006 Jun. NGC:005159
   American Academy of Neurology - Medical Specialty Society. *View all guidelines by the developer(s)*

3. **Wisconsin essential diabetes mellitus care guidelines.** 2004 Dec (revised 2008). **[NGC Update Pending]** NGC:006765
   Wisconsin Diabetes Prevention and Control Program - State/Local Government Agency [U.S.]. *View all guidelines by the developer(s)*

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Guideline Title

Evidence-based guideline: treatment of painful diabetic neuropathy. Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation.

Bibliographic Source(s)

Bril V, England J, Franklin GM, Backonja M, Cohen J, Del Toro D, Feldman E, Iverson DJ, Perkins B, Russell JW, Zochodne D. Evidence-based guideline: treatment of painful diabetic neuropathy. Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Neurology 2011 May 17;76(20):1758-65. [40 references] PubMed

Guideline Status

This is the current release of the guideline.

Jump To | Guideline Classification | Related Content

- Scope
- Methodology
- Recommendations
- Evidence Supporting the Recommendations
- Benefits/Harms of Implementing the Guideline Recommendations
- Contraindications
- Qualifying Statements
- Implementation of the Guideline
- Institute of Medicine (IOM) National Healthcare Quality Report Categories
- Identifying Information and Availability
- Disclaimer

Dar clic en: ***identificar y disponibilidad de la información***

Scope

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Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

Availability of Companion Documents

The following are available:

- Treatment of painful diabetic neuropathy. AAN summary of evidence-based guideline for clinicians. St. Paul (MN): American Academy of Neurology. 2011. 2 p. Available in Portable Document Format (PDF) from the American Academy of Neurology (AAN) Web site.
- Treatment of painful diabetic neuropathy. Case presentation. St. Paul (MN): American Academy of Neurology. 2011. 8 p. Available in Portable Document Format (PDF) from the AAN Web site.
- Treatment of painful diabetic neuropathy. Slide presentation. St. Paul (MN): American Academy of Neurology. 2011. 50 p. Available from the AAN Web site.
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the AAN Web site.

Patient Resources

The following is available:

- Treatment of painful diabetic neuropathy. AAN summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology. 2011. 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American Academy of Neurology (AAN) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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Special Article

Evidence-based guideline: Treatment of painful diabetic neuropathy

Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation

V. Bril, MD, FRCP(C), J. England, MD, FAAN, G.M. Franklin, MD, MPH, FAAN, M. Backonja, MD, J. Cohen, MD, FAAN, D. Del Toro, MD, E. Feldman, MD, PhD, FAAN, D.J. Iverson, MD, FAAN, B. Perkins, MD, FRCP(C), MPH, J.W. Russell, MD, MS, FRPC and D. Zochodne, MD

[+] Author Affiliations

Address correspondence and reprint requests to American Academy of Neurology, 1080 Montreal Avenue, St. Paul, MN 55116 guidelines@aan.com

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- Idealmente describen la pregunta de investigación, grupos de estudio, y la medida de los efectos u otros resultados de la evidencia.

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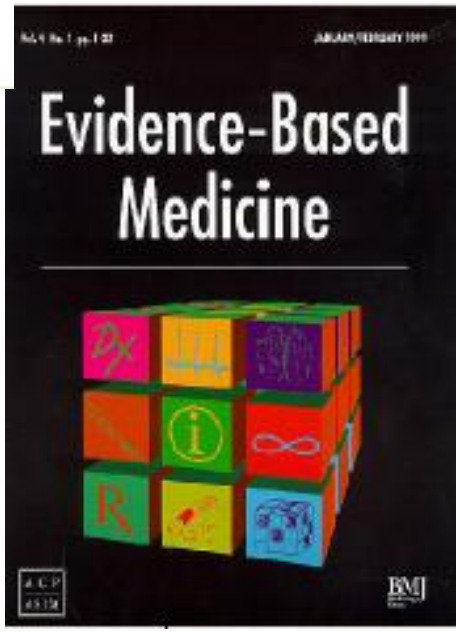

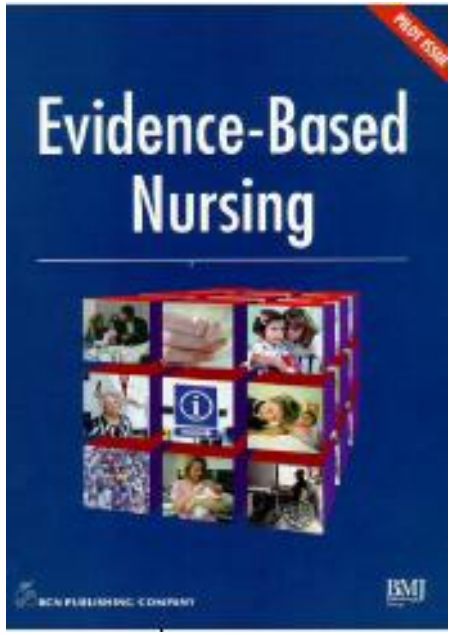

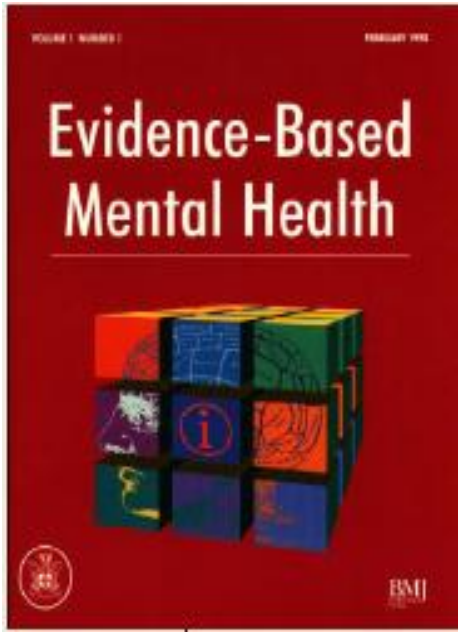

Candesartan reduced mortality and hospital admissions in chronic heart failure

Pfeffer MA, Swedberg K, Granger CB, *et al.* Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. *Lancet* 2003;**362**:759–66.
Clinical impact ratings GP/FP/Primary care ★★★★★★☆ IM/Ambulatory care ★★★★★★☆ Cardiology ★★★★★★☆

McMurray JJ, Östergren J, Swedberg K, *et al.* Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet* 2003;**362**:767–71.
Clinical impact ratings GP/FP/Primary care ★★★★★★☆ IM/Ambulatory care ★★★★★☆☆ Cardiology ★★★★★☆☆

Granger CB, McMurray JJ, Yusuf S, *et al.* Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial. *Lancet* 2003;**362**:772–6.
Clinical impact ratings GP/FP/Primary care ★★★★★★☆ IM/Ambulatory care ★★★★★☆☆ Cardiology ★★★★★★☆

Yusuf S, Pfeffer MA, Swedberg K, *et al.* Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved trial. *Lancet* 2003;**362**:777–81.
Clinical impact ratings GP/FP/Primary care ★★★★☆☆☆ IM/Ambulatory care ★★★★★☆☆ Cardiology ★★★★★★★

Q In patients with chronic heart failure (CHF), does the angiotensin-receptor blocker (ARB) candesartan reduce death and hospital admissions?

METHODS

Design: 3-component randomised, placebo controlled trial (Candesartan in Heart failure Assessment of Reduction in Mortality and morbidity [CHARM] study).

Allocation: concealed.*

Blinding: blinded (clinicians, patients, data collectors, outcome assessors, monitoring committee, manuscript writers, and data analysts).*

Follow up period: median 37.7 months.

Setting: 618 centres in 26 countries.

Patients: 7601 patients who were ⩾18 years of age and had symptomatic CHF (New York Heart Association class II–IV) for ⩾4 weeks. Major exclusion criteria included serum creatinine ⩾265 μmol/l; serum potassium ⩾5.5 mmol/l; bilateral renal artery stenosis; symptomatic hypotension; critical aortic or mitral stenosis; myocardial infarction, stroke, or open heart surgery in the previous 4 weeks; use of an ARB in the previous 2 weeks; other serious disease likely to limit 2 year survival; and potential for pregnancy. Patients were enrolled in 1 of 3 component trials: CHARM-Added involved patients with left ventricular ejection fraction (LVEF) ⩽40% who were being treated with an angiotensin converting enzyme (ACE) inhibitor for ⩾30 days (n=2548); CHARM-Alternative involved patients with LVEF ⩽40% who were intolerant of ACE inhibitors (n=2028); and CHARM-Preserved involved patients with LVEF >40% (n=3023). CHARM-Overall involved all patients.

Intervention: stratified by site and component trial and allocated to candesartan, 4 or 8 mg once daily, doubled every 2 weeks to a target dose of 32 mg once daily from 6 weeks onwards (n=3803) or placebo (n=3796).

Outcomes: all cause mortality (CHARM-Overall) and a composite outcome of cardiovascular death or hospital admission for worsening CHF in the 3 component trials. Secondary outcomes included doubling of creatinine concentrations and potassium concentration ⩾6.0 mmol/l.

Patient follow up: 7599 patients (mean age 66 y, 68% men) were included in the analysis; 7589 patients completed the study.

*See glossary.

MAIN RESULTS

Analysis was by intention to treat. Overall, all cause mortality was reduced more with candesartan than with placebo (table), mainly because of fewer cardiovascular deaths (18% *v* 20%, adjusted hazard ratio 0.87, 95% CI 0.78 to 0.96). Fewer patients who received candesartan had the composite outcome of cardiovascular death or hospital admission for CHF than did patients who received placebo in the CHARM-Added and CHARM-Alternative component trials (table). In CHARM-Preserved, the reduction in the composite outcome with candesartan reached borderline statistical significance (table). The rates of doubling creatinine concentration for the candesartan and placebo groups were 6% *v* 4% (p=0.002) (CHARM-Overall), 7% *v* 6% (p=0.5) (CHARM-Added), 5.5% *v* 1.6% (p=0.015) (CHARM-Alternative), and 6% *v* 3%, (p=0.007) (CHARM-Preserved). The rates for potassium concentration ⩾6.0 mmol/l for the candesartan and placebo groups were 2% *v* 1% (p=0.017) (CHARM-Overall), 3% *v* 1% (p=0.089) (CHARM-Added), 3% *v* 1.3% (p=0.26) (CHARM-Alternative), and 2% *v* 1% (p=0.32) (CHARM-Preserved).

CONCLUSIONS

In patients with chronic heart failure (CHF), the angiotensin receptor blocker candesartan reduced mortality (particularly cardiovascular) and hospital admissions for worsening CHF. Patients with reduced left ventricular ejection fraction with or without baseline angiotensin converting enzyme inhibitor treatment showed the most benefit.

Abstract and commentary also appear in ACP Journal Club.

For correspondence: Professor CHARM-Overall: M A Pfeffer, Brigham and Women's Hospital, Boston, MA, USA. mpfeffer@rics.bwh.harvard.edu

For correspondence: Professor CHARM-Added: J McMurray, Western Infirmary, Glasgow, UK. j.mcmurray@bio.gla.ac.uk

For correspondence: Dr CHARM-Alternative: C B Granger, Duke University Medical Center, Durham, NC, USA. grang001@mc.duke.edu

For correspondence: Professor CHARM-Preserved: S Yusuf, McMaster University, Hamilton, Ontario, Canada. yusufs@mcmaster.ca

Source of funding: AstraZeneca R&D.

Commentary

The CHARM study extends our knowledge of the role of ARBs in patients with CHF.

Least surprising but still important was the finding in the CHARM-Alternative study that candesartan resulted in a significant reduction in cardiovascular mortality and hospital admission for heart failure. The Valsartan Heart Failure Trial (ValHeFT) reached a similar conclusion,[1] and valsartan is indicated in patients with heart failure caused by systolic left ventricular dysfunction who are not taking an ACE inhibitor. However, the result of ValHeFT was determined in a retrospective analysis and included a relatively small number of patients and events. The CHARM-Alternative study, on the other hand, was prospective and adequately powered with a significant number of events.

It is likely that ARBs used at the appropriate dose, such as valsartan 160 mg twice daily or candesartan 32 mg daily, are equivalent to target doses of an ACE inhibitor, such as enalapril 10 mg twice daily. However, the therapy of choice in patients with CHF caused by systolic left ventricular dysfunction will probably remain an ACE inhibitor because of the relatively large number of patients in whom these agents have been studied and their reasonable cost.

The CHARM-Added trial is also important because it suggests that an ARB should be added to an ACE inhibitor and a β blocker in patients with mild to moderate CHF caused by systolic left ventricular dysfunction. Whereas the reduction in cardiovascular mortality in the CHARM-Added trial was moderate, the reduction in the combined endpoint of cardiovascular mortality and hospital admission for heart failure is both clinically and statistically significant. ValHeFT suggested that in a patient with CHF already treated with both an ACE inhibitor and a β blocker, adding an ARB was associated with an increased risk of death. The CHARM-Added results, however, suggest that the ValHeFT results in this particular subset were due to chance.

Somewhat less clear is the explanation for the discrepancy between ValHeFT and CHARM on cardiovascular mortality. In ValHeFT, valsartan had no effect on cardiovascular mortality and its significant benefit on the combined endpoint of cardiovascular mortality and hospital admission for heart failure was entirely the result of a reduction in hospital admissions for heart failure. In the CHARM-Added study, there was a reduction in both cardiovascular mortality and hospital admissions for heart failure. Whether this disparity reflects a difference in the effectiveness of valsartan and candesartan, their relative dosing strategy, or other factors remains to be determined. A further study of an ARB in this situation would therefore be ethical and useful.

In patients with severe heart failure, an aldosterone blocker might be the preferred agent to add to an ACE inhibitor and a β blocker rather than an ARB based on the results of the Randomized Aldactone Evaluation Study (RALES).[2] However, in RALES only a relatively small proportion of patients were receiving both an ACE inhibitor and a β blocker. Direct comparative studies of an ARB and an aldosterone blocker when added to an ACE inhibitor and a β blocker in patients with CHF caused by systolic left ventricular dysfunction are needed.

In patients with CHF and preserved systolic function (CHARM-Preserved), candesartan was shown to be of only marginal benefit. Further studies are clearly required to determine the optimal strategy to reduce cardiovascular events in this important subset of patients whose incidence is increasing because of aging and increasing incidence of hypertension and diabetes mellitus.

Bertram Pitt, MD
University of Michigan
Ann Arbor, Michigan, USA

1 Cohn JN, Tognoni G. A randomized trial of angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med* 2001;**345**:1667–75.
2 Pitt B, Zannad F, Remme WJ, *et al.* The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med* 1999;**341**:709–17.

Candesartan *v* placebo for chronic heart failure (CHF) at median 37.7 months*

Trial	Outcomes	Candesartan	Placebo	Unadjusted HR (95% CI)	Adjusted analysis† HR (CI)	RRR (CI)	NNT (CI)
Overall	All cause mortality	23%	25%	0.91 (0.83 to 1.00)	0.90 (0.82 to 0.99)	8.8% (0.9 to 16)	46 (26 to 463)
CHARM-Added	Composite	38%	42%	0.85 (0.75 to 0.96)	0.85 (0.75 to 0.96)	12% (3 to 20)	21 (12 to 79)
CHARM-Alternative	Composite	33%	40%	0.77 (0.67 to 0.89)	0.70 (0.60 to 0.81)	25% (15 to 34)	11 (8 to 17)
CHARM-Preserved	Composite	22%	24%	0.89 (0.77 to 1.03)	0.86 (0.74 to 1.00)	12% (0 to 23)	Borderline significance

*Composite endpoint = cardiovascular death or hospital admission for worsening CHF; CHARM = Candesartan in Heart failure Assessment of Reduction in Mortality and morbidity; HR = hazard ratio. Other abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article using Cox proportional hazards model.
†Adjusted for baseline covariates, including patients' characteristics, heart disease risk factors, medical history, and medical treatment.

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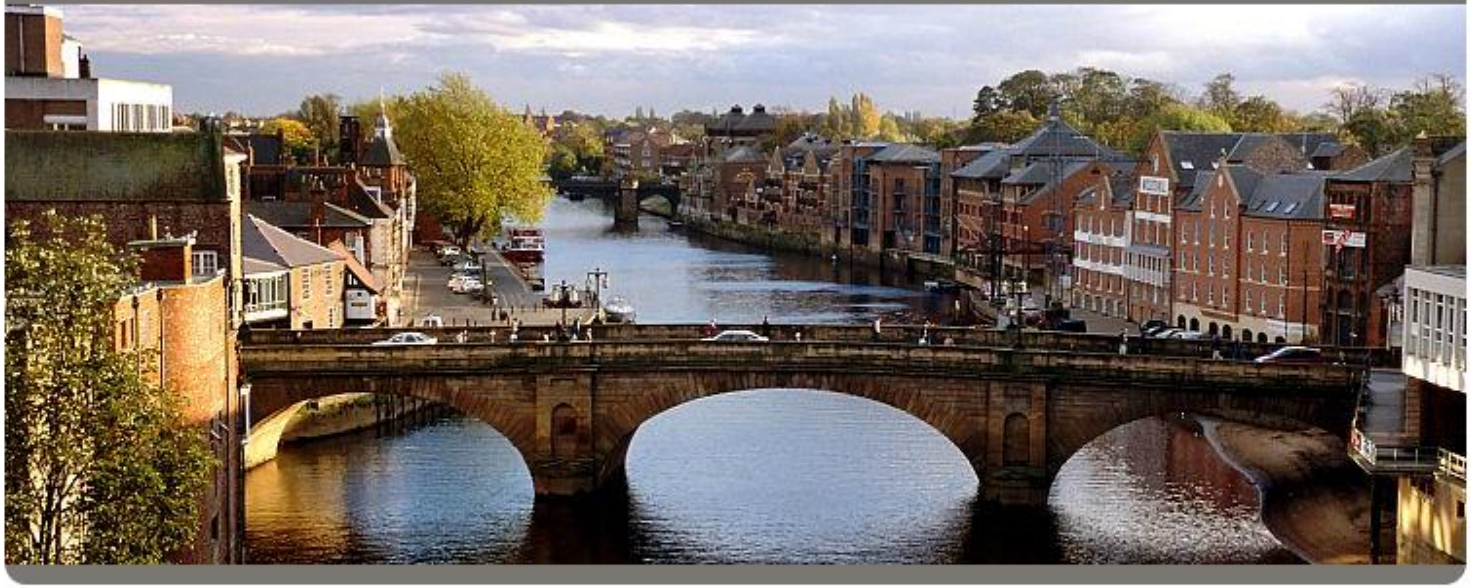

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☐	2008	DARE	Systematic review	Duloxetine for painful diabetic neuropathy and fibromyalgia pain: systematic review of randomised trials [Preview]
☐	2007	DARE	Systematic review	Antiepileptic drugs in treatment of pain caused by diabetic neuropathy [Preview]
☐	2007	DARE	Systematic review	Effects of treatments for symptoms of painful diabetic neuropathy: systematic review [Preview]
☐	2005	DARE	Systematic review	Effectiveness of vitamin B12 on diabetic neuropathy: systematic review of clinical controlled trials [Preview]
☐	2000	DARE	Systematic review	Antidepressants and anticonvulsants for diabetic neuropathy and postherpetic neuralgia: a quantitative systematic review [Preview]

Gabapentin versus tricyclic antidepressants for diabetic neuropathy and post-herpetic neuralgia: discrepancies between direct and indirect meta-analyses of randomized controlled trials

Chou R, Carson S, Chan B K

CRD summary
This review concluded that there was no difference in pain relief between gabapentin and tricyclic antidepressants in patients with diabetic neuropathy or post-herpetic neuralgia, although direct evidence was limited. The review was well conducted and these findings are likely to be reliable.

Authors' objectives
To compare gabapentin with tricyclic antidepressants for the treatment of diabetic neuropathy and post-herpetic neuralgia using direct and indirect comparisons.

Searching
MEDLINE (1966-March 2008), Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials and DARE (1st quarter 2008) were searched. Search terms were reported. Reference lists were screened and pharmaceutical companies contacted to identify additional relevant studies. No language restrictions were applied. Studies published only in abstract form were excluded.

Study selection
Randomised controlled trials (RCTs) that compared gabapentin or a tricyclic antidepressant with each other or placebo were eligible for inclusion. Included trials had to enrol at least 75% of patients with diabetic neuropathy and/or post-herpetic neuralgia. Trails were required to report on at least one of the following outcomes: pain relief (proportion of patients with >50% improvement in pain score or at least moderate pain relief or good overall response on categorical scale), withdrawal due to adverse events, overall adverse events, serious adverse events, somnolence, dizziness or vertigo, ataxia, or dry mouth. The primary review outcome was pain relief.

Gabapentin doses ranged from 900-3600 mg/day. Tricyclic antidepressants evaluated included nortriptyline (10-160mg/day), amitriptyline (12.5-150mg/day), desipramine (12.5-250mg/day), imipramine (100-225mg/day), clomipramine (50-75mg/day). Trial duration ranged from two to 12 weeks.

Two reviewers independently selected studies for inclusion. Disagreements were resolved through consensus.

Assessment of study quality
Two reviewers independently assessed study quality based on randomisation, allocation concealment, blinding of patients and outcome assessors, and use of intention-to-treat analysis. Disagreements were resolved through consensus.

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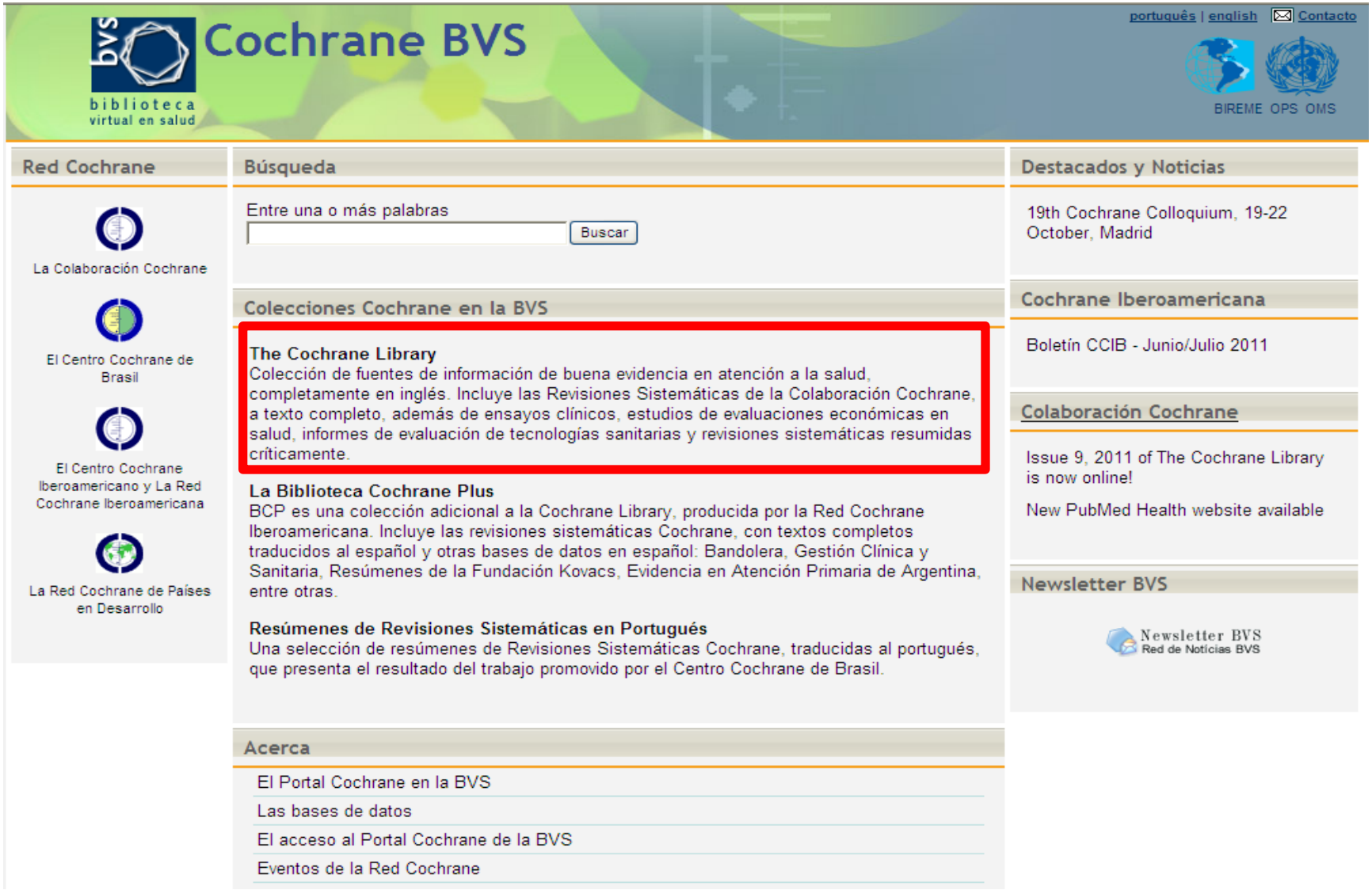

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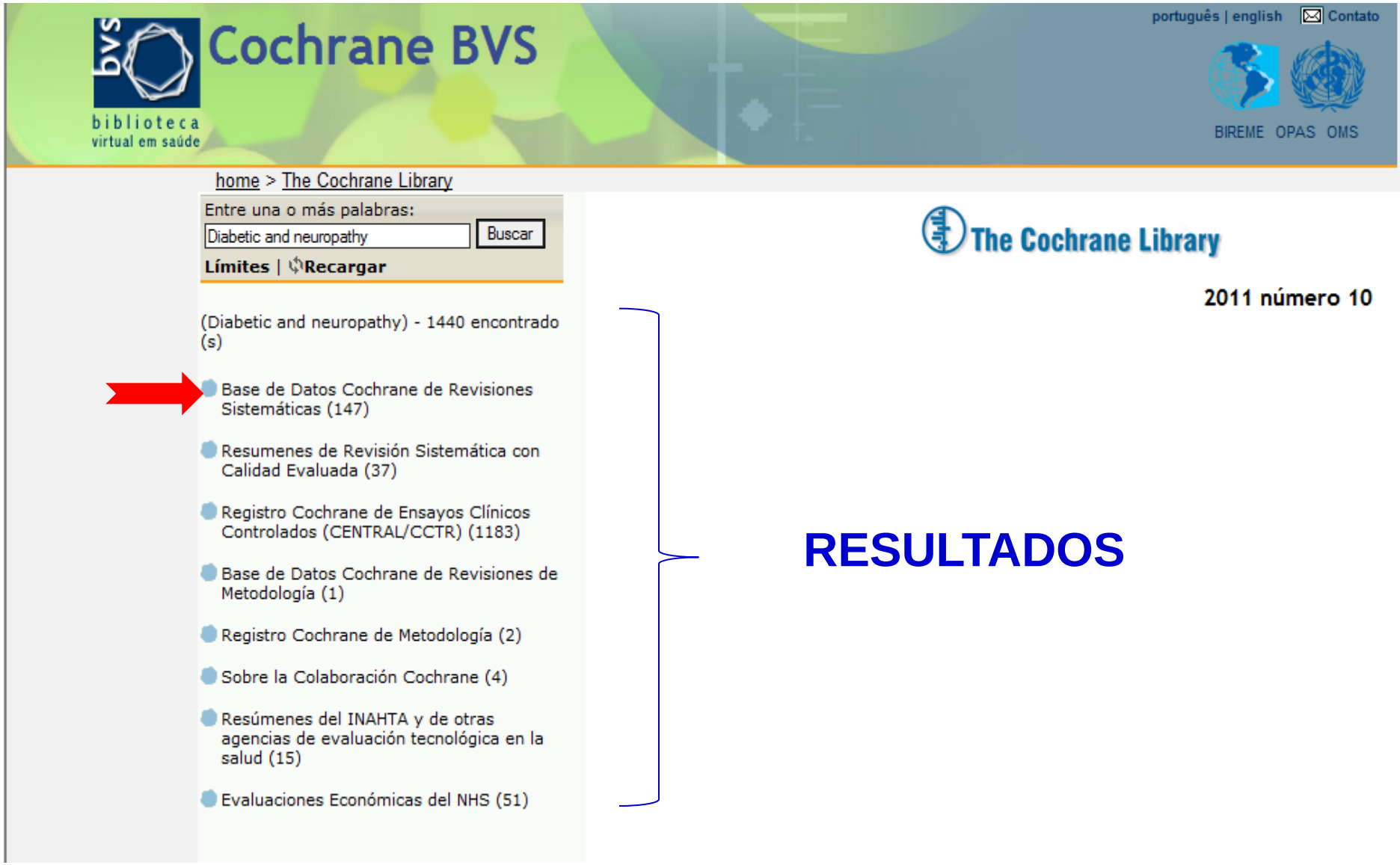
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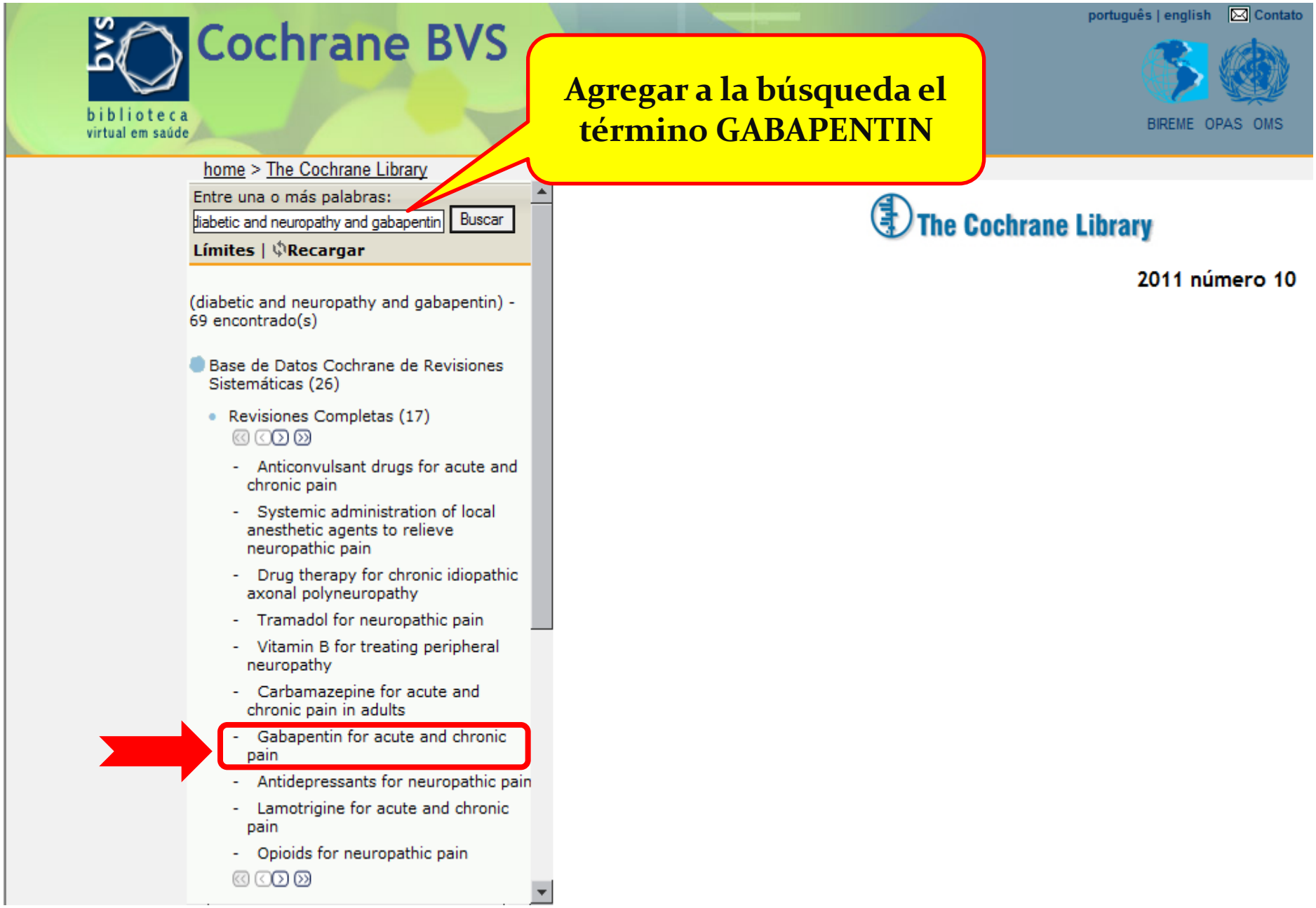
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- Tramadol for neuropathic pain
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- Carbamazepine for acute and chronic pain in adults
- Gabapentin for acute and chronic pain
- Antidepressants for neuropathic pain
- Lamotrigine for acute and chronic pain
- Opioids for neuropathic pain
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    - Lamotrigine for acute and chronic pain
    - Opioids for neuropathic pain

Opciones

Índice

versión para imprimir

documento en español (versión anterior)

GABAPENTIN FOR ACUTE AND CHRONIC PAIN

Wiffen Philip J, McQuay Henry J, Edwards Jayne, Moore R Andrew

Wiffen Philip J, McQuay Henry J, Edwards Jayne, Moore R Andrew

Cochrane Database of Systematic Reviews, Issue 10, 2011 (Status in this issue: WITHDRAWN FROM PUBLICATION FOR REASONS STATED IN THE REVIEW)

DOI: 10.1002/14651858.CD005452.pub3

This review should be cited as: Wiffen Philip J, McQuay Henry J, Edwards Jayne, Moore R Andrew. Gabapentin for acute and chronic pain. Cochrane Database of Systematic Reviews. In: *The Cochrane Library*, Issue 10, Art. No. CD005452. DOI: 10.1002/14651858.CD005452.pub3

ABSTRACT

Background

February 2009: The authors are aware of unpublished trial data for Gabapentin which could affect the results of this review. This information together with that from trials published since 2005, will be considered when this review is updated in 2009.

Objective

To evaluate the analgesic effectiveness and adverse effects of gabapentin for pain management in clinical practice.

Criteria for considering studies for this review

Randomised trials of gabapentin in acute, chronic or cancer pain were identified by MEDLINE (1966 to Nov 2004), EMBASE (1994 to Nov 2004), SIGLE (1980 to Jan 2004) and the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, Issue 4, 2004). Additional studies were identified from the reference list of the retrieved papers, and by contacting investigators. Date of most recent search: January 2004.

Selection criteria

Randomised trials reporting the analgesic effects of gabapentin in participants with subjective pain assessment as either the primary or a secondary outcome.

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ANTECEDENTES. Esta revisión actualiza partes de dos revisiones Cochrane anteriores que investigaron los efectos de la gabapentina en el dolor neuropático crónico (dolor debido al daño nervioso). Los fármacos antiepilépticos se utilizan para el tratamiento del dolor, en su mayoría para el dolor neuro

2 Nuevo (2011) Hierbas medicinales chinas para la neuropatía diabética periférica

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3 Nuevo (2009) Pregabalina para el dolor agudo y crónico en adultos

Antecedentes Los fármacos antiepilépticos se utilizan para el tratamiento del dolor desde la década del sesenta. La pregabalina es un fármaco antiepiléptico desarrollado recientemente que también se utiliza en el tratamiento del dolor neuropático. Objetivos Evaluar la eficacia analgésica y

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GABAPENTINA PARA EL DOLOR NEUROPÁTICO CRÓNICO Y LA FIBROMIALGIA EN ADULTOS

Autores
R Andrew Moore, Philip J Wiffen, Sheena Derry, Henry J McQuay

Cómo citar la revisión: Moore R, Wiffen P, Derry S, McQuay H. Gabapentina para el dolor neuropático crónico y la fibromialgia en adultos. Cochrane Database of Systematic Reviews 2011 Issue 3. Art. No.: CD007938. DOI: 10.1002/14651858.CD007938

Versión reducida de la revisión. Puede consultar la versión completa en inglés PULSANDO AQUÍ

RESUMEN

Antecedentes
Esta revisión actualiza partes de dos revisiones Cochrane anteriores que investigaron los efectos de la gabapentina en el dolor neuropático crónico (dolor debido al daño nervioso). Los fármacos antiepilépticos se utilizan para el tratamiento del dolor, en su mayoría para el dolor neuropático crónico, especialmente cuando el dolor es de tipo lacerante o urente.

Objetivos
Evaluar la efectividad analgésica y los efectos adversos de la gabapentina para el tratamiento del dolor neuropático crónico.

Estrategia de búsqueda
Se identificaron los ensayos aleatorios de la gabapentina para el dolor agudo, crónico o por cáncer en MEDLINE, EMBASE, y CENTRAL. Se obtuvieron informes de ensayos clínicos y sinopsis de estudios

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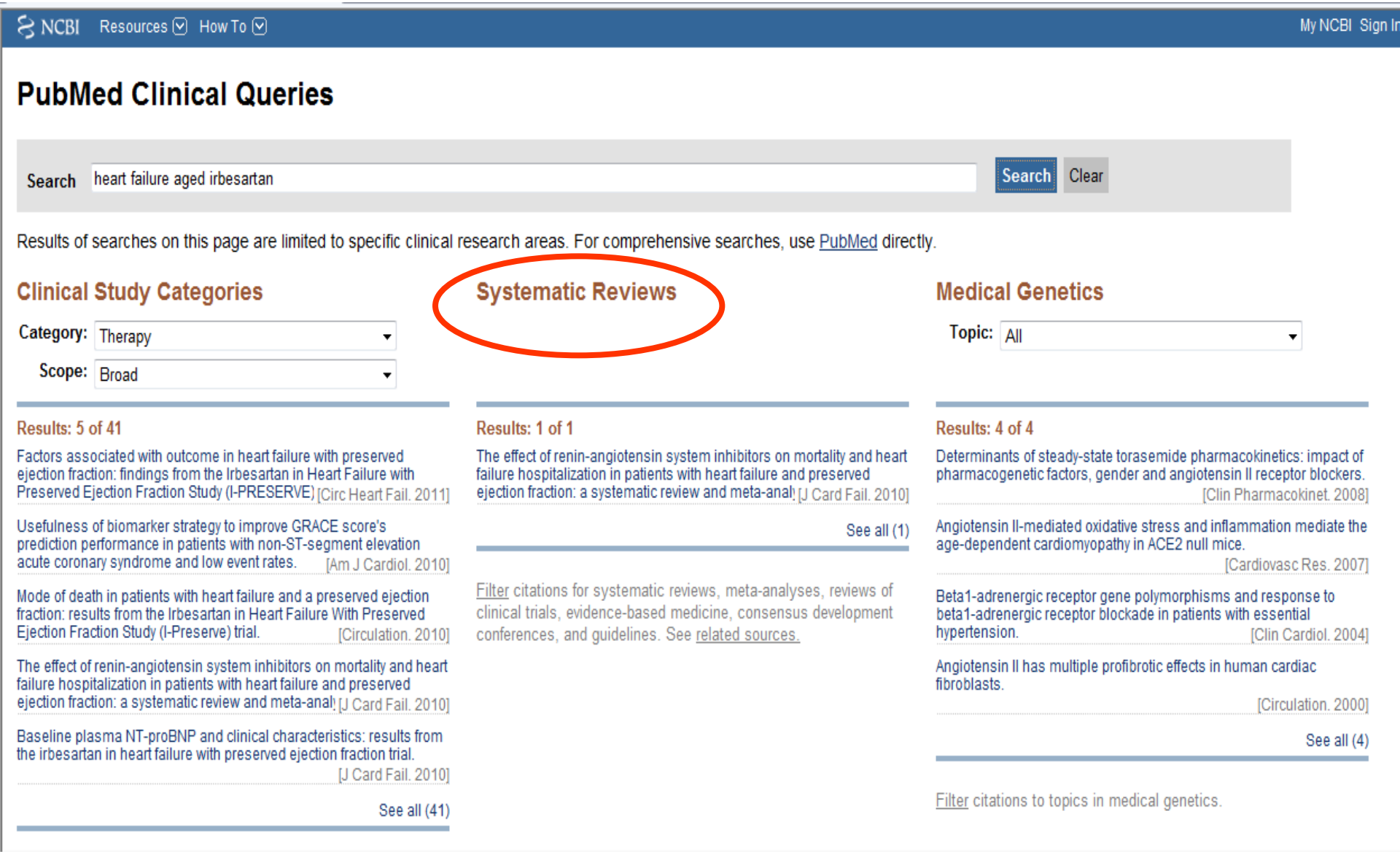

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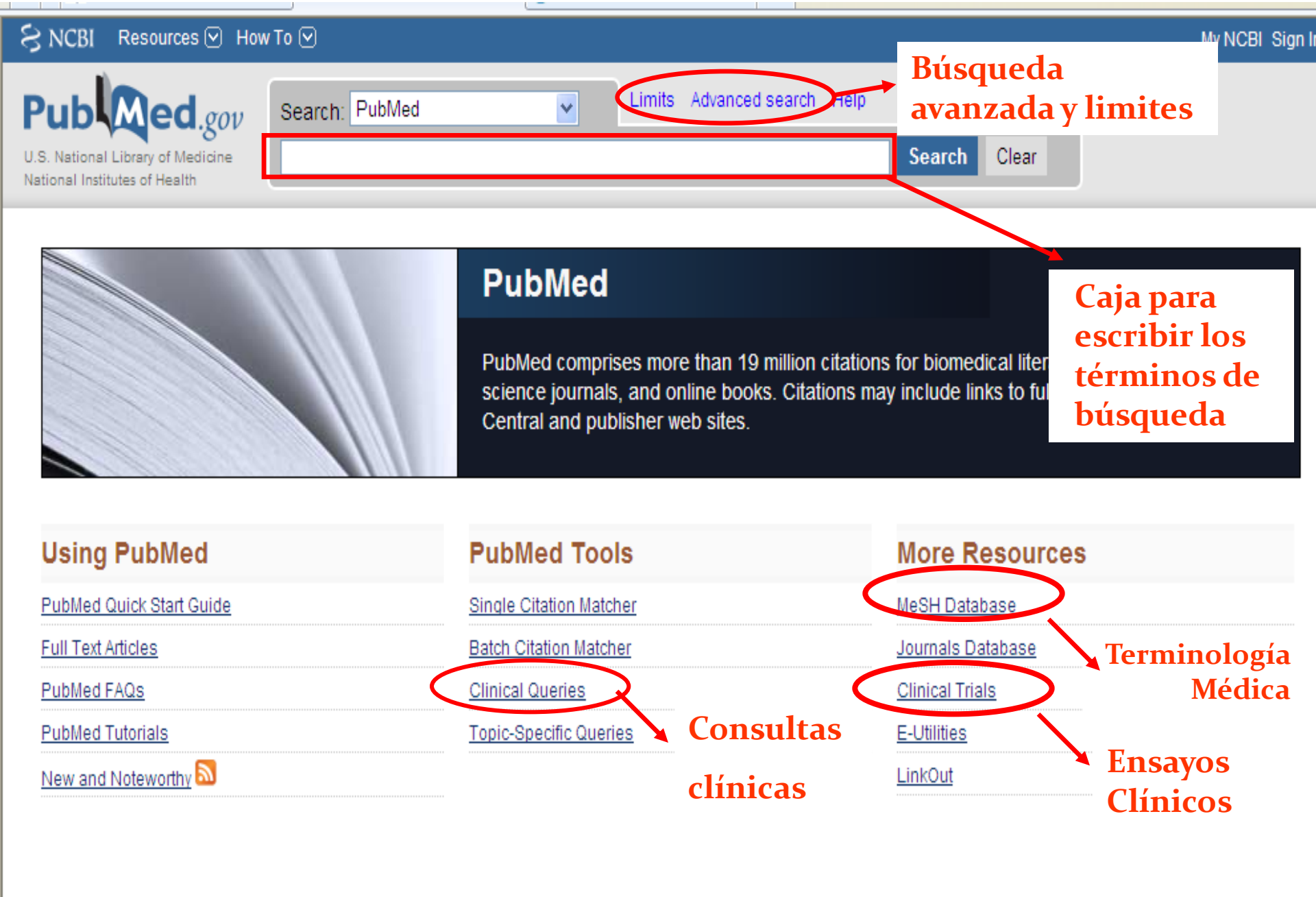

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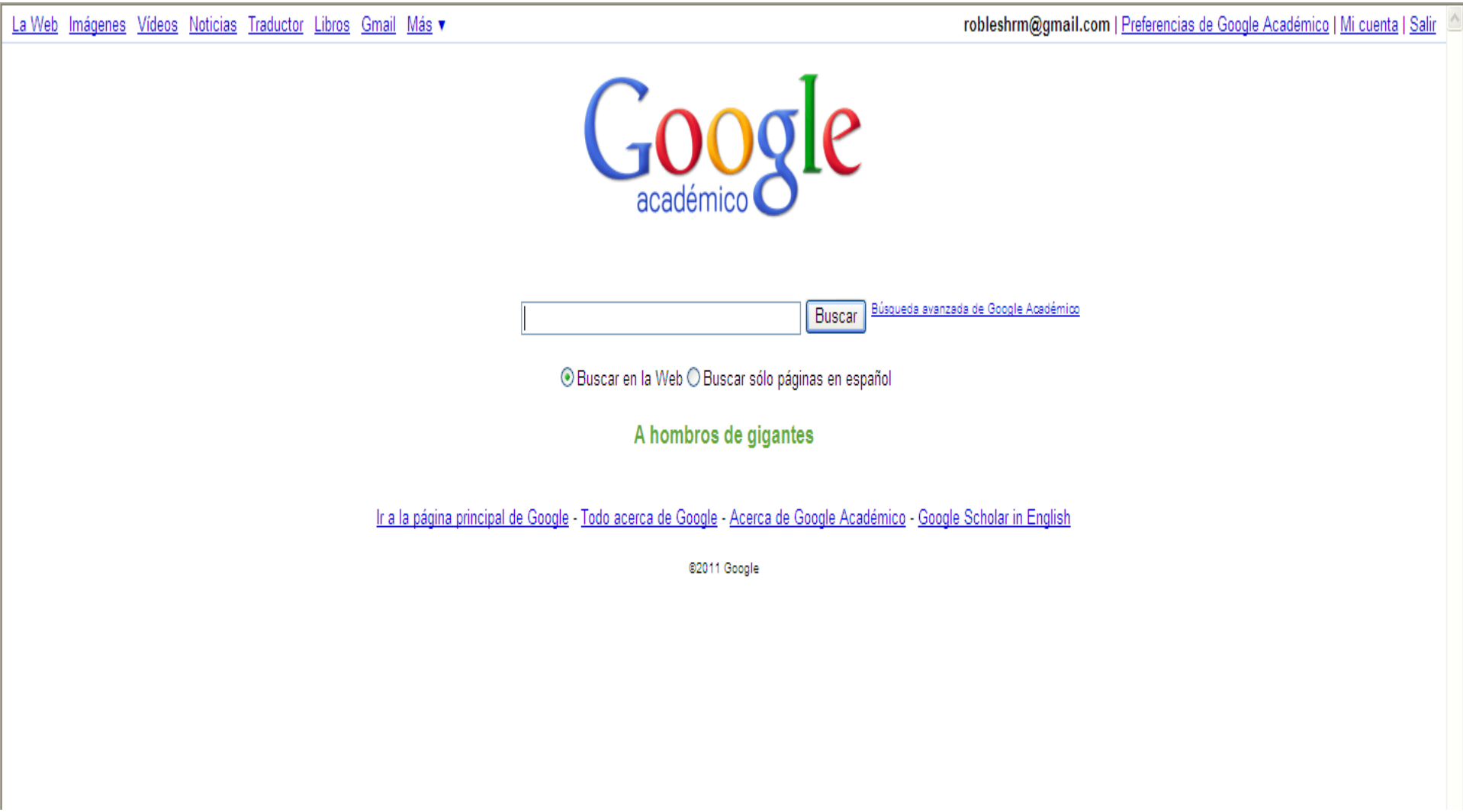


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