Sesión de actualización bibliográfica

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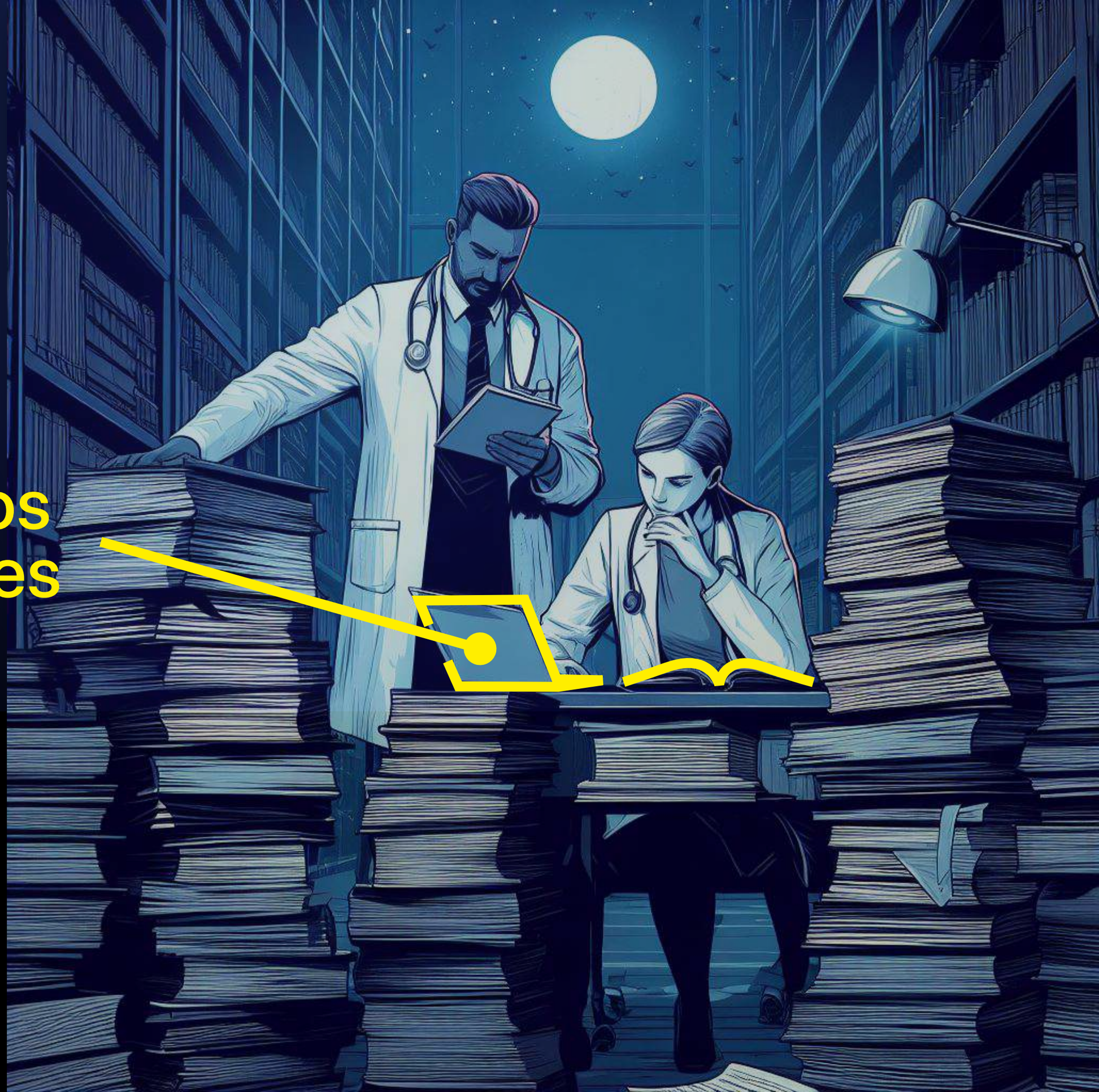
Servicio de Medicina Interna
Consorcio Hospital General Universitario de Valencia

Dr. David Rodrigo Domínguez | R5 Medicina Interna
Dra. Lara Beltran Segura | R2 Medicina Interna

2 artículos principales



Micro-**resúmenes**

ARTÍCULO PRINCIPAL 1

Kim DH, Lee SB, Park CM, Levin R, Metzger E, Bateman BT, et al. Comparative Safety Analysis of Oral Antipsychotics for In-Hospital Adverse Clinical Events in Older Adults After Major Surgery. Annals of Internal Medicine [Internet]. 5 de septiembre de 2023 [citado 2 de octubre de 2023]; Disponible en: https://www.acpjournals.org/doi/10.7326/M22-3021

Annals of Internal Medicine

ORIGINAL RESEARCH

Comparative Safety Analysis of Oral Antipsychotics for In-Hospital Adverse Clinical Events in Older Adults After Major Surgery

A Nationwide Cohort Study

Dae Hyun Kim, MD, ScD; Su Been Lee, BA; Chan Mi Park, MD, MPH; Raisa Levin, MS; Eran Metzger, MD; Brian T. Bateman, MD, ScM; E. Wesley Ely, MD, MPH; Pratik P. Pandharipande, MD, MSCI; Margaret A. Pisani, MD, MPH; Richard N. Jones, ScD; Edward R. Marcantonio, MD, ScM*; and Sharon K. Inouye, MD, MPH*

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Limitation: Residual confounding by delirium severity; lack of untreated group; restriction to oral low-to-moderate dose treatment.

Conclusion: These results suggest that atypical antipsychotics and haloperidol have similar rates of in-hospital adverse clinical events in older patients with postoperative delirium who receive an oral low-to-moderate dose antipsychotic drug.

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Previous studies have compared a limited number of antipsychotics and few evaluated adverse clinical events associated with antipsychotics in the postoperative setting (6). Older surgical patients are particularly susceptible to the adverse effects of antipsychotics due to surgical stress, pain, sleep disorders, and concurrent use of central nervous system–active drugs in the postoperative period. Because enrolling a large number of older patients with postoperative delirium in an RCT can be challenging (25), a carefully designed, real-world, comparative safety study may help to inform the choice of antipsychotics. Informed by previous research on harms associated with antipsychotics in dementia, we hypothesized that [illegible] would be associ[illegible]

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Contexto

El **síndrome confusional agudo** (SCA) es la complicación más frecuente durante el postquirúrgico en los pacientes geriátricos.

↑ estancia hospitalaria
institucionalización
declive funcional
mortalidad
gasto sanitario

La **primera línea** de tratamiento incluye medidas no farmacológicas → percibidas como **inefectivas o poco factibles** por los clínicos.

↓ uso del haloperidol frente a los nuevos antipsicóticos.

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  - Primarias: Mortalidad
  - Secundarias:
    - Arritmias
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- Otras variables: Edad, sexo, raza, tipo de seguro, procedencia del paciente, tipo de cirugía, estancia en UCI, ventilación mecánica, transfusiones, maniobras RCP, diálisis, tipo de hospital, área geográfica.

ARTÍCULO PRINCIPAL

Métodos

- Estudio de **cohortes retrospectivo**: base de datos nacional Premier Healthcare Enero 2009 – Marzo 2018.

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Métodos

- Estudio de **cohortes retrospectivo**: base de datos nacional Premier Healthcare Enero 2009 – Marzo 2018.

- **Criterios**:

✓ Prescripción de antipsicóticos de novo
✓ Cirugía mayor durante los primeros 7 días

✗ Tratamiento previo con antipsicóticos
✗ Indicación médica diferente a SCA
✗ Otros AP: Ziprasidona, aripiprazol.
✗ Uso simultáneo de >2 AP
✗ Inicio >7 días post cirugía.

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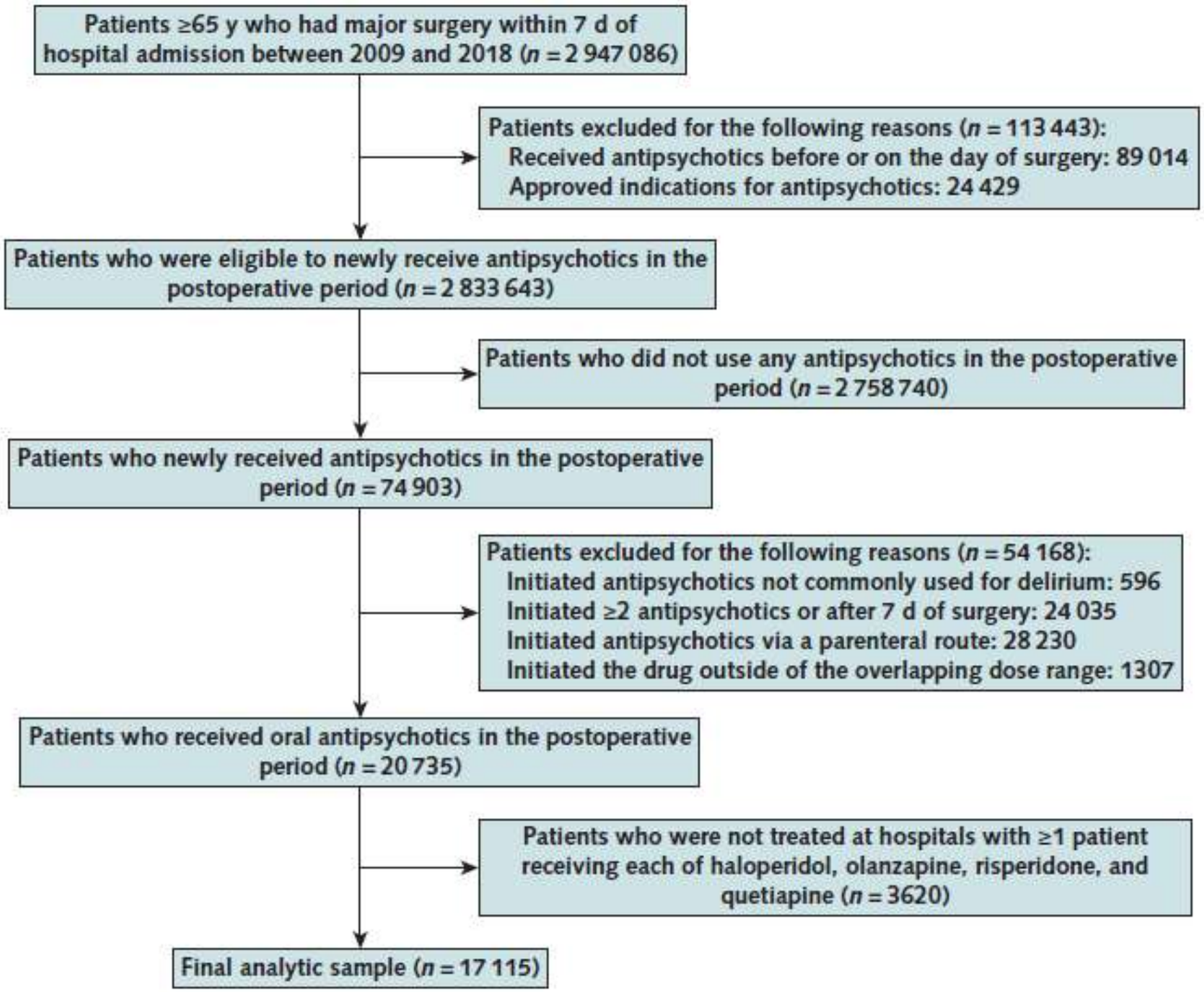

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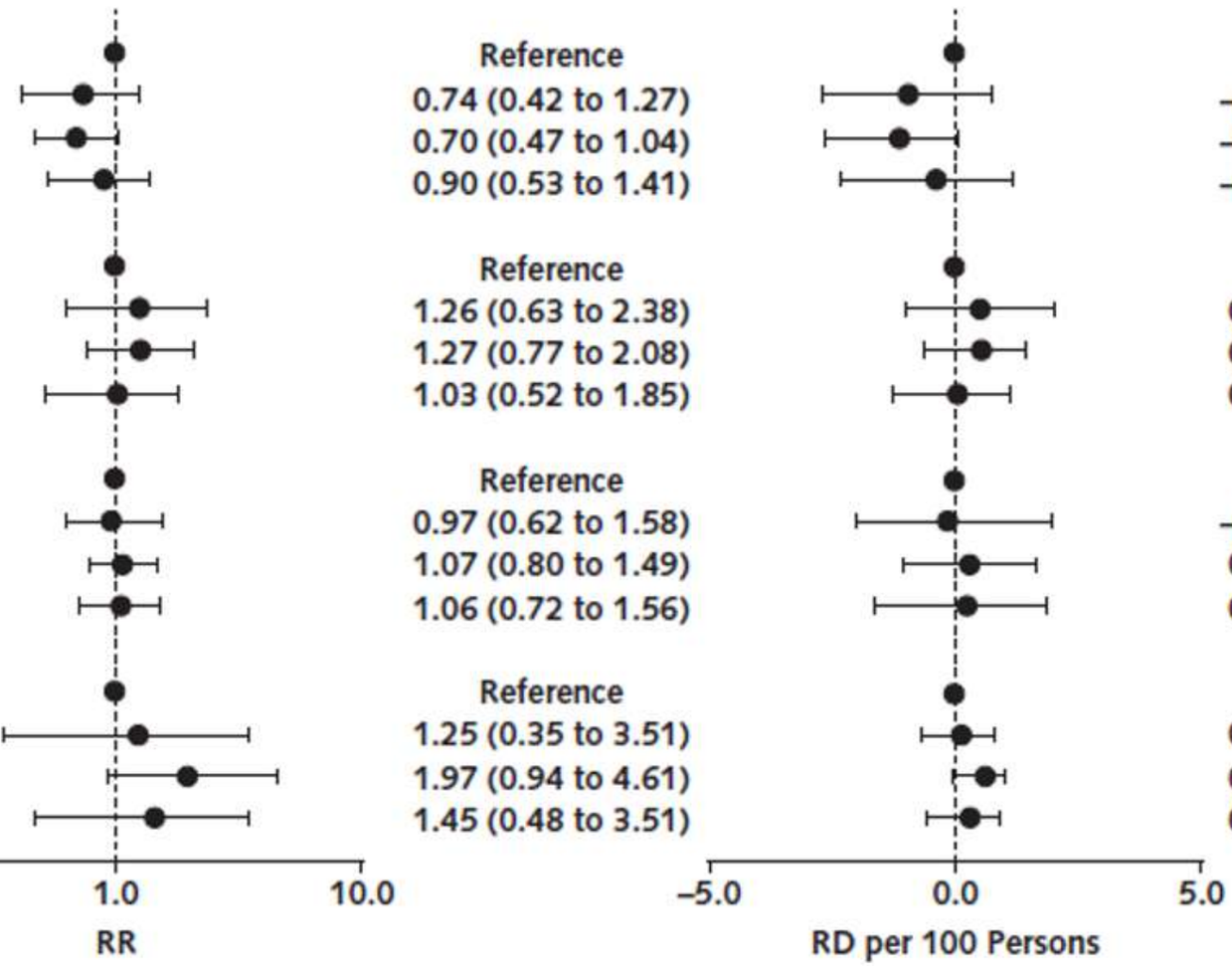
- **Seguimiento** ↾
  - 1º día tratamiento,
  - aparición de evento,
  - alta hospitalaria, o
  - 14 días (independientemente de la duración, por intención de tratar).

Resultados

Figure 2. Postoperative oral antipsychotic drug use and in-hospital adverse events.

	Weighted, *n*	Events, *n* (%)	RR (95% CI)	RD (95% CI)
Primary outcome: in-hospital death				
Haloperidol	295	10.9 (3.7)	Reference	Reference
Olanzapine	319	8.8 (2.8)	0.74 (0.42 to 1.27)	–0.96 (–2.65 to 0.78)
Quetiapine	317	8.2 (2.6)	0.70 (0.47 to 1.04)	–1.11 (–2.60 to 0.10)
Risperidone	310	10.3 (3.3)	0.90 (0.53 to 1.41)	–0.38 (–2.32 to 1.21)
Secondary outcome: cardiac arrhythmia event				
Haloperidol	295	5.9 (2.0)	Reference	Reference
Olanzapine	319	8.1 (2.5)	1.26 (0.63 to 2.38)	0.52 (–0.99 to 2.08)
Quetiapine	317	8.1 (2.6)	1.27 (0.77 to 2.08)	0.54 (–0.63 to 1.42)
Risperidone	310	6.4 (2.1)	1.03 (0.52 to 1.85)	0.05 (–1.30 to 1.19)
Secondary outcome: pneumonia				
Haloperidol	295	12.8 (4.3)	Reference	Reference
Olanzapine	319	13.4 (4.2)	0.97 (0.62 to 1.58)	–0.15 (–1.99 to 2.00)
Quetiapine	317	14.7 (4.6)	1.07 (0.80 to 1.49)	0.31 (–1.07 to 1.68)
Risperidone	310	14.2 (4.6)	1.06 (0.72 to 1.56)	0.25 (–1.60 to 1.91)
Secondary outcome: stroke or TIA				
Haloperidol	295	1.8 (0.6)	Reference	Reference
Olanzapine	319	2.5 (0.8)	1.25 (0.35 to 3.51)	0.15 (–0.67 to 0.82)
Quetiapine	317	3.9 (1.2)	1.97 (0.94 to 4.61)	0.61 (–0.08 to 1.08)
Risperidone	310	2.8 (0.9)	1.45 (0.48 to 3.51)	0.28 (–0.57 to 0.97)



The propensity score overlap-weighted analysis was performed to evaluate the association of antipsychotics with in-hospital adverse clinical events according to the intention-to-treat analysis (follow-up truncated at 14 days from the drug initiation). RD = risk difference; RR = risk ratio; TIA = transient ischemic attack.

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Postoperative delirium is the most common complication after major surgery in older adults (1). Delirium is associated with prolonged hospitalization, institutional discharge, function decline, and mortality, as well as excess health care costs (2, 3). Nonpharmacologic interventions are recommended as the first-line strategy for preventing and managing delirium (4). Despite this recommendation, antipsychotics are often used off-label to manage behavioral symptoms of delirium because nonpharmacologic interventions alone are often considered as infeasible or ineffective by clinicians (5). Although randomized controlled trials (RCTs) found no clear efficacy of antipsychotics in treating delirium (6-10), the comparative safety of haloperidol and atypical antipsychotics in patients with delirium remains uncertain.

Previous studies have compared a limited number of antipsychotics and few evaluated adverse clinical events associated with antipsychotics in the postoperative setting (6). Older surgical patients are particularly susceptible to the adverse effects of antipsychotics due to surgical stress, pain, sleep disorders, and concurrent use of central nervous system-active drugs in the postoperative period. Because enrolling a large number of old-

Resultados

No se observaron diferencias estadísticamente significativas en la mortalidad ni eventos adversos entre haloperidol y el resto de AP (risperidona, olanzapina, quetiapina).

- arritmia cardíaca: 2.0-2.6%.
- neumonía: 4,2-4,6%
- ACV/AIT: 0,6-1,2%

ARTÍCULO PRINCIPAL

Kim DH, Lee SB, Park CM, Levin R, Metzger E, Bateman BT, et al. Comparative Safety Analysis of Oral Antipsychotics for In-Hospital Adverse Clinical Events in Older Adults After Major Surgery. Annals of Internal Medicine [Internet]. 5 de septiembre de 2023 [citado 2 de octubre de 2023]; Disponible en: https://www.acpjournals.org/doi/10.7326/M22-3021

Annals of Internal Medicine

ORIGINAL RESEARCH

Comparative Safety Analysis of Oral Antipsychotics for In-Hospital Adverse Clinical Events in Older Adults After Major Surgery

A Nationwide Cohort Study

Dae Hyun Kim, MD, ScD; Su Been Lee, BA; Chan Mi Park, MD, MPH; Raisa Levin, MS; Eran Metzger, MD; Brian T. Bateman, MD, ScM; E. Wesley Ely, MD, MPH; Pratik P. Pandharipande, MD, MSCI; Margaret A. Pisani, MD, MPH; Richard N. Jones, ScD; Edward R. Marcantonio, MD, ScM*; and Sharon K. Inouye, MD, MPH*

Background: Antipsychotics are commonly used to manage postoperative delirium. Recent studies reported that haloperidol use has declined, and atypical antipsychotic use has increased over time.

Objective: To compare the risk for in-hospital adverse events associated with oral haloperidol, olanzapine, quetiapine, and risperidone in older patients after major surgery.

Design: Retrospective cohort study.

Setting: U.S. hospitals in the Premier Healthcare Database.

Patients: 17 115 patients aged 65 years and older without psychiatric disorders who were prescribed an oral antipsychotic drug after major surgery from 2009 to 2018.

Interventions: Haloperidol (≤4 mg on the day of initiation), olanzapine (≤10 mg), quetiapine (≤150 mg), and risperidone (≤4 mg).

Measurements: The risk ratios (RRs) for in-hospital death, cardiac arrhythmia events, pneumonia, and stroke or transient ischemic attack (TIA) were estimated after propensity score overlap weighting.

Results: The weighted population had a mean age of 79.6 years, was 60.5% female, and had in-hospital death of 3.1%. Among the 4 antipsychotics, quetiapine was the most prescribed (53.0% of total exposure). There was no statistically significant difference in the risk for in-hospital death among patients treated with haloperidol (3.7%, reference group), olanzapine (2.8%; RR, 0.74 [95% CI, 0.42 to 1.27]), quetiapine (2.6%; RR, 0.70 [CI, 0.47 to 1.04]), and risperidone (3.3%; RR, 0.90 [CI, 0.53 to 1.41]). The risk for nonfatal clinical events ranged from 2.0% to 2.6% for a cardiac arrhythmia event, 4.2% to 4.6% for pneumonia, and 0.6% to 1.2% for stroke or TIA, with no statistically significant differences by treatment group.

Limitation: Residual confounding by delirium severity; lack of untreated group; restriction to oral low-to-moderate dose treatment.

Conclusion: These results suggest that atypical antipsychotics and haloperidol have similar rates of in-hospital adverse clinical events in older patients with postoperative delirium who receive an oral low-to-moderate dose antipsychotic drug.

Primary Funding Source: National Institute on Aging.

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Resultados

- **Características de la población**: Haloperidol el AP menos usado, pero más usado en pluripatológicos, mayor edad y en polifarmacia.
- 💊 Proporción de pacientes con necesidad de **medicación equivalente a > 50mg de cloprormacina** para control de síntomas: mayor con **olanzapina**, menor con risperidona.

PREGUNTA SORPRESA

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ARTÍCULO PRINCIPAL 2

López-Bueno R, Ahmadi M, Stamatakis E, Yang L, Del Pozo Cruz B. Prospective Associations of Different Combinations of Aerobic and Muscle-Strengthening Activity With All-Cause, Cardiovascular, and Cancer Mortality. JAMA Intern Med. 1 de septiembre de 2023;183(9):982.

Research

JAMA Internal Medicine | Original Investigation

Prospective Associations of Different Combinations of Aerobic and Muscle-Strengthening Activity With All-Cause, Cardiovascular, and Cancer Mortality

Rubén López-Bueno, PhD; Matthew Ahmadi, PhD; Emmanuel Stamatakis, PhD; Lin Yang, PhD; Borja del Pozo Cruz, PhD

IMPORTANCE Studies examining the associations of different combinations of intensity-specific aerobic and muscle strengthening activity (MSA) with all-cause and cause-specific mortality are scarce; the few available estimates are disparate.

OBJECTIVE To examine the prospective associations of different combinations of moderate aerobic physical activity (MPA), vigorous aerobic physical activity (VPA), and MSA with all-cause, cardiovascular (CVD), and cancer mortality.

DESIGN, SETTING, AND PARTICIPANTS This nationwide prospective cohort study used data from the US National Health Interview Survey. A total of 500 705 eligible US adults were included in the study and followed up during a median of 10.0 years (5.6 million person-years) from 1997 to 2018. Data were analyzed from September 1 to September 30, 2022.

EXPOSURES Self-reported cumulative bouts (75 weekly minutes) of MPA and VPA with recommended MSA guidelines (yes or no) to obtain 48 mutually exclusive exposure categories.

MAIN OUTCOMES AND MEASURES All-cause, CVD, and cancer mortality. Participants were linked to the National Death Index through December 31, 2019.

RESULTS Overall, 500 705 participants (mean [SD] age, 46.4 [17.3] years; 210 803 [58%] female; 277 504 [77%] White) were included in the study. Compared with the reference group (doing no MPA or VPA and less than recommended MSA), the category associated with the lowest hazard ratio (HR) for all-cause mortality was more than 0 to 75 minutes of MPA combined with more than 150 minutes of VPA and 2 or more MSA sessions per week (HR, 0.50; 95% CI, 0.42-0.59). The optimal combinations for CVD and cancer mortality risk reduction were more than 150 to 225 minutes of MPA, more than 0 to 75 minutes of VPA, and 2 or more MSA sessions per week (HR, 0.30; 95% CI, 0.15-0.57), and more than 300 minutes of MPA, more than 0 to 75 minutes of VPA, and 2 or more MSA sessions per week (HR, 0.44; 95% CI, 0.23-0.82), respectively. Adjusted mortality rates represented an approximately 50% lower mortality rate for all-cause and cancer mortality and an approximately 3-fold lower mortality rate for CVD mortality.

CONCLUSIONS AND RELEVANCE This cohort study demonstrated that balanced levels of MPA, VPA, and MSA combined may be associated with optimal reductions of mortality risk. Higher-than-recommended levels of MPA and VPA may further lower the risk of cancer and all-cause mortality, respectively.

Supplemental content

Author Affiliations: Author

PREGUNTA SORPRESA

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EXPOSURES Self-reported cumulative bouts (≥5 weekly minutes) of MPA and VPA with recommended MSA guidelines (yes or no) to obtain 48 mutually exclusive exposure categories.

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El ejercicio físico ha demostrado reducir el riesgo de **mortalidad** por **todas** las causas, **cardiovascular** y por **cáncer.**

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FALSO

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Supplemental content

Contexto

La evidencia científica respalda el beneficio del **ejercicio físico** moderado a vigoroso en la **↓mortalidad** por causa cardiovascular, cáncer, y por todas las causas.

La OMS recomienda al menos:

- 150-300 min semanales de actividad física **moderada** (AFM), de
- 75-150 min semanales de actividad física **vigorosa**, o una combinación equivalente de ambas, con
- actividad de fuerza muscular al menos **2 días/semana**

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Objetivos

- Determinar **efecto de combinaciones** entre actividad física aerobia de intensidad moderada (AFM), de intensidad vigorosa (AFV), y ejercicio de fuerza muscular (EFM) sobre la **mortalidad** por todas las causas, y específicas por causa cardiovascular (CV) y por cáncer.

- **Variables**:
  - **1as** — mortalidad por todas las causas, causa CV y cáncer.
  - **2as** — edad, sexo, raza, estado civil, nivel de formación académica, hábito tabáquico, hábito alcohólico, factores de riesgo cardiovascular, IMC, altura, limitación functional, año de realización de cuestionario, minutos semanales de AFIM y AFIV.

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Métodos

- Estudio observacional de **cohortes prospectivo anidado (1997-2018)**
  - Población del NHIS (Encuesta nacional de sanidad)
    - Población no institucionalizada >18 a.
    - Realizada de forma anual por CDC y Centro nacional de estadística de sanidad para la prevención
  - Realización de entrevistas por entrevistadores con formación específica
  - Muestreo aleatorio estratificado por múltiples etapas.
- **Criterios**: Población 646.201
  - ✕ Cáncer conocido
  - ✕ Enfermedad CV conocida
  - ✕ Enfisema
  - ✕ ACV
  - ✕ Pacientes sin datos de variables primarias o secundarias.
  - ✕ Incapacidad para EFA, o para EFM
  - ✕ Exclusión de datos de mortalidad durante 2 primeros años → Sesgo de causalidad.

ARTÍCULO PRINCIPAL

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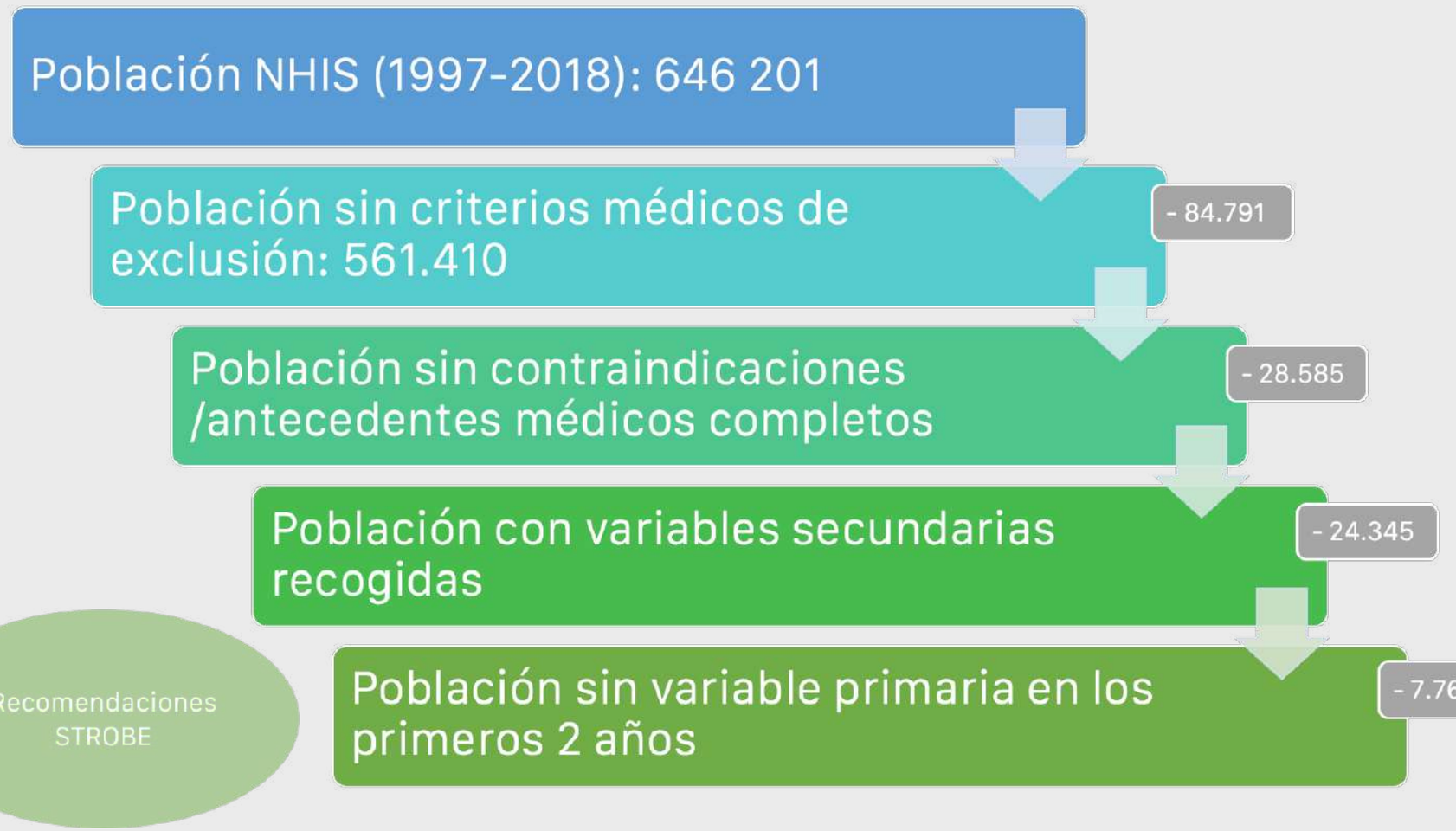

Recomendaciones STROBE

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Métodos

- **Cuestionario** elaborado por laboratorio de investigación del CDC — Basado en preguntas de cuestionarios previos validadas.

1) **Frecuencia** de AF**M**: ¿Cuánto tiempo realizas ejercicio que cause sólo sudoración leve, y/o aumento de la respiración leve o moderado de al menos 10 minutos?
2) **Duración** de AF**M**: ¿Durante cuánto tiempo realizas dicha actividad cada vez?
3) **Frecuencia** de AF**V**: ¿Con cuanta frecuencia realizas actividad física intensa de al menos 10 minutos de duración, que cause sudoración profusa, aumento intenso de la respiración y de la frecuencia cardíaca?
4) **Duración** de AF**V**: ¿Durante cuánto tiempo realizas dicha actividad cada vez?
5) **Frecuencia** de E**FM**: ¿Con cuánta frecuencia realizas ejercicios específicamente diseñados para fortalecimiento muscular (p. ej levantamiento de pesas, calistenia)? (2 cat. >2/semana, o <2/semana).

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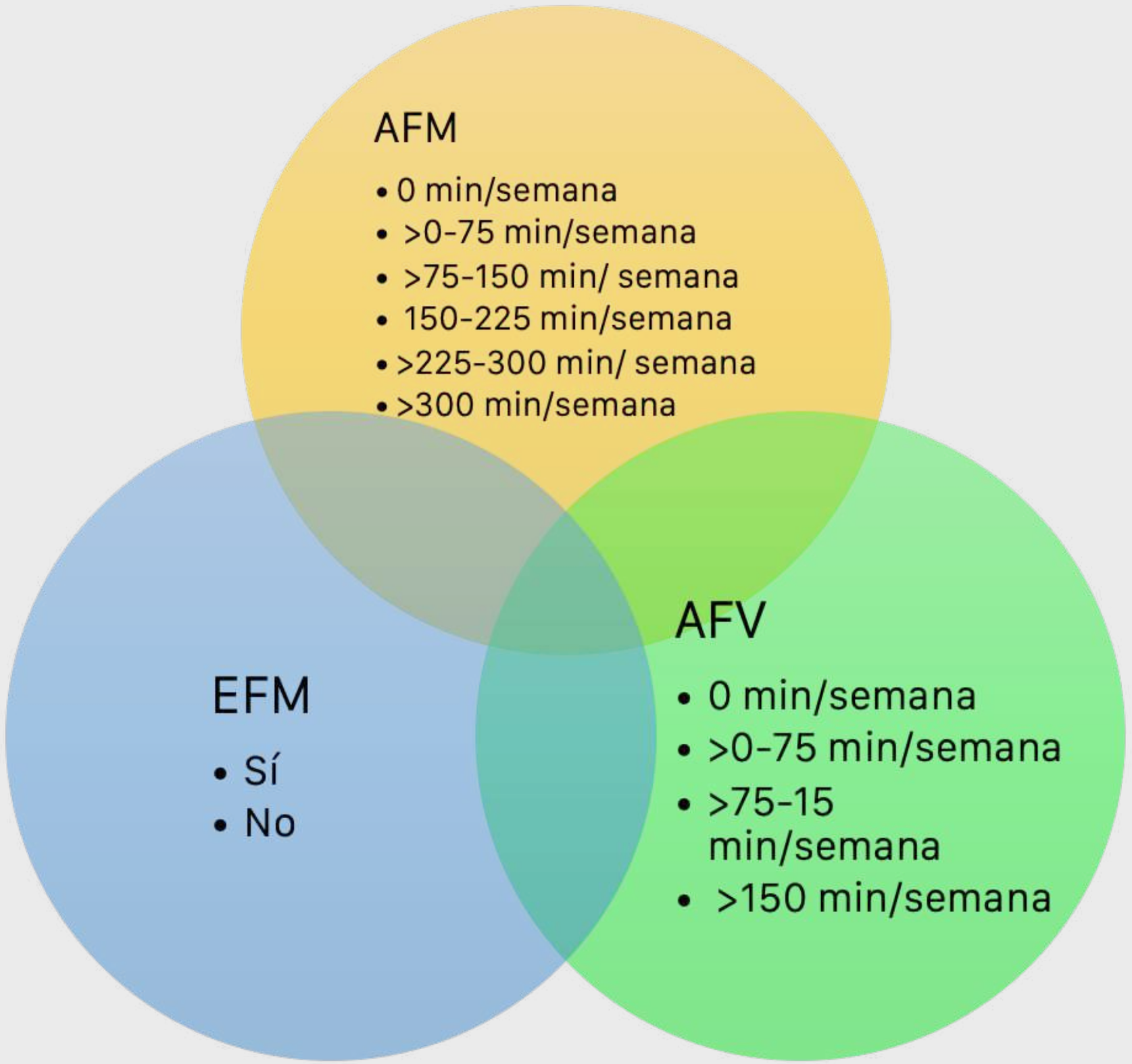

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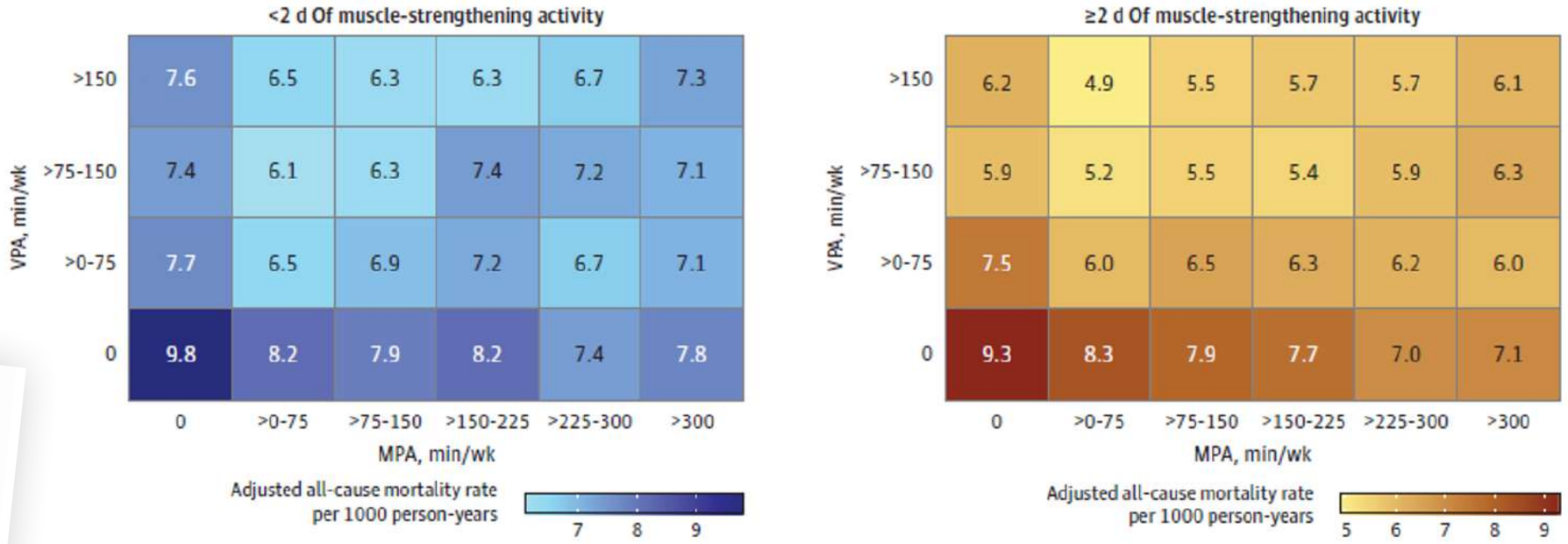
Resultados ajustados

⊡ **mortalidad** por todas las causas

Figure. Adjusted Mortality Rates for All-Cause, Cardiovascular, and Cancer Mortality Among US Adults by Physical Activity Combination



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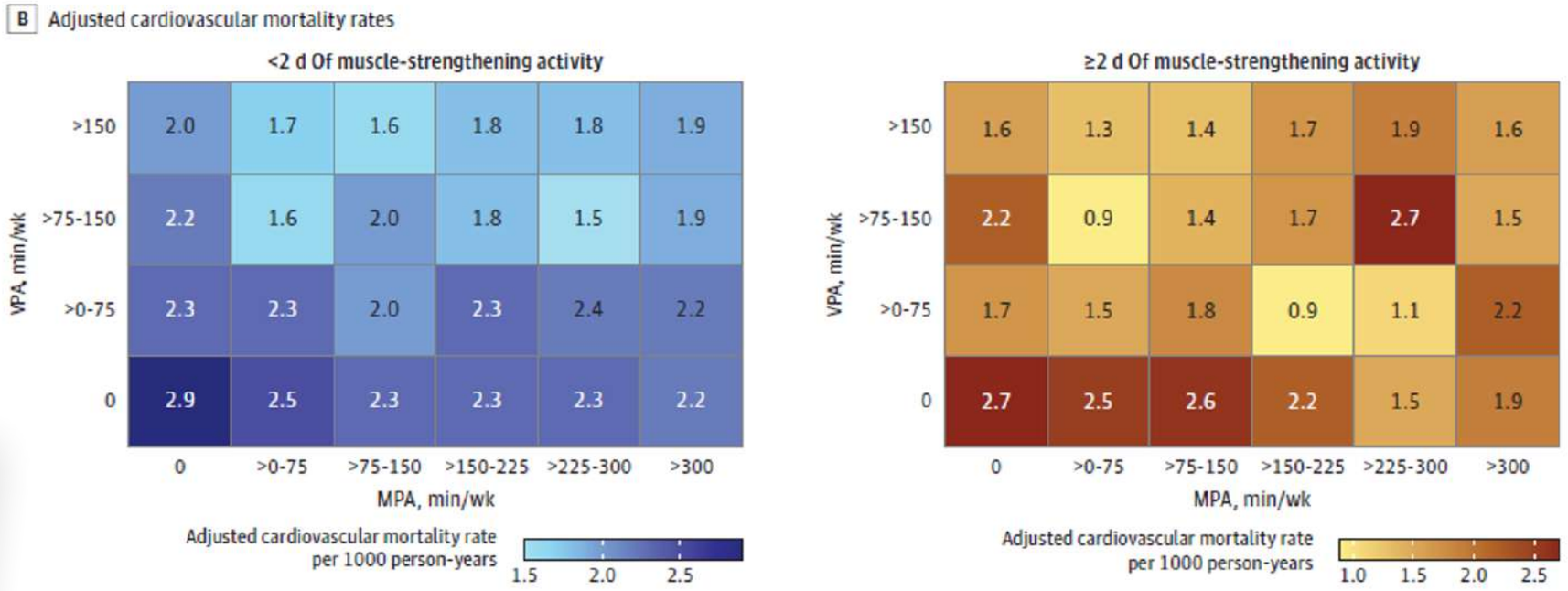
⊡ **mortalidad** cardiovascular



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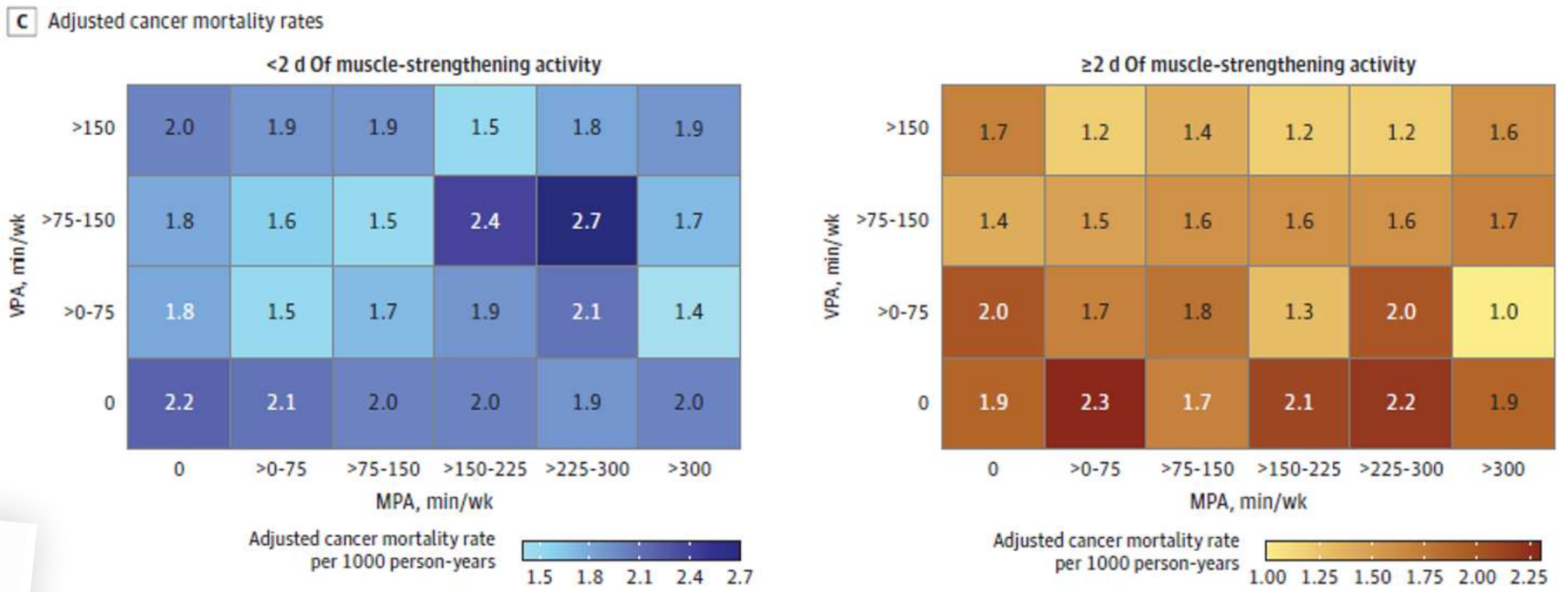

ortality rates were adjusted for age, sex, race, marital status, educational ttainment, smoking status, alcohol consumption, chronic condition, body mass ndex, functional limitation, survey year, and moderate physical activity (MPA) o vigorous physical activity (VPA). Rates were computed using the estimated weighted mortality rates of the study cohort (8.4, 2.5, and 2.0 deaths per 1000 adults aged ≥18 years per year for all-cause, cardiovascular, and cancer mortality, respectively). Models accounted for the National Health Interview Survey complex design and weights.

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Resultados

- Cualquier combinación de EFM, AFM y AFV que disminuya cualquier mortalidad **requiere la combinación** de los tres tipos de ejercicio físico

¿Beneficios independientes de AFM y AFV para mortalidad por cáncer y por todas las causas, respectivamente?

- **AFV** para ↓ de **mortalidad por todas las causas**.
  >150 min AFV + EFM + 0-75min AFM

- **AFM** para ↓ de **mortalidad por cáncer y CV**
  >300min de AFM + 0-75min AFV + EFM
  150-225 AFM + 0-75min AFV + EFM

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CONCLUSIONS AND RELEVANCE This cohort study demonstrated that balanced levels of MPA, VPA, and MSA combined may be associated with optimal reductions of mortality risk. Higher-than-recommended levels of MPA and VPA may further lower the risk of cancer and all-cause mortality, respectively.

Limitaciones

- Evaluación de AFM, AFV y EFM en base a medida **autoinformada:**
  - Sesgo de memoria
  - Sesgo de clasificación — tendencia a la falta de asociación dosis-respuesta con la mortalidad
- Potenciales factores confusores en base a variables no medidas
- Imposibilidad de medición repetida de la exposición: necesidad de asumir no-variabilidad de la misma a lo largo del seguimiento.

PREGUNTA SORPRESA

López-Bueno R, Ahmadi M, Stamatakis E, Yang L, Del Pozo Cruz B. Prospective Associations of Different Combinations of Aerobic and Muscle-Strengthening Activity With All-Cause, Cardiovascular, and Cancer Mortality. JAMA Intern Med. 1 de septiembre de 2023;183(9):982.

Research

JAMA Internal Medicine | Original Investigation

Prospective Associations of Different Combinations of Aerobic and Muscle-Strengthening Activity With All-Cause, Cardiovascular, and Cancer Mortality

Rubén López-Bueno, PhD; Matthew Ahmadi, PhD; Emmanuel Stamatakis, PhD; Lin Yang, PhD; Borja del Pozo Cruz, PhD

Supplemental content

IMPORTANCE Studies examining the associations of different combinations of intensity-specific aerobic and muscle strengthening activity (MSA) with all-cause and cause-specific mortality are scarce; the few available estimates are disparate.

OBJECTIVE To examine the prospective associations of different combinations of moderate aerobic physical activity (MPA), vigorous aerobic physical activity (VPA), and MSA with all-cause, cardiovascular (CVD), and cancer mortality.

DESIGN, SETTING, AND PARTICIPANTS This nationwide prospective cohort study used data from the US National Health Interview Survey. A total of 500 705 eligible US adults were included in the study and followed up during a median of 10.0 years (5.6 million person-years) from 1997 to 2018. Data were analyzed from September 1 to September 30, 2022.

EXPOSURES Self-reported cumulative bouts (≥5 weekly minutes) of MPA and VPA with recommended MSA guidelines (yes or no) to obtain 48 mutually exclusive exposure categories.

MAIN OUTCOMES AND MEASURES All-cause, CVD, and cancer mortality. Participants were linked to the National Death Index through December 31, 2019.

RESULTS Overall, 500 705 participants (mean [SD] age, 46.4 [17.3] years; 210 803 [58%] female; 277 504 [77%] White) were included in the study. Compared with the reference group (doing no MPA or VPA and less than recommended MSA), the category associated with the lowest hazard ratio (HR) for all-cause mortality was more than 0 to 75 minutes of MPA combined with more than 150 minutes of VPA and 2 or more MSA sessions per week (HR, 0.50; 95% CI, 0.42-0.59). The optimal combinations for CVD and cancer mortality risk reduction were more than 150 to 225 minutes of MPA, more than 0 to 75 minutes of VPA, and 2 or more MSA sessions per week (HR, 0.30; 95% CI, 0.15-0.57), and more than 300 minutes of MPA, more than 0 to 75 minutes of VPA, and 2 or more MSA sessions per week (HR, 0.44; 95% CI, 0.23-0.82), respectively. Adjusted mortality rates represented an approximately 50% lower mortality rate for all-cause and cancer mortality and an approximately 3-fold lower mortality rate for CVD mortality.

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El ejercicio físico ha demostrado reducir el riesgo de **mortalidad** por **todas** las causas, **cardiovascular** y por **cáncer.**

VERDADERO

FALSO

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VERDADERO

Micro-**resúmenes**

MICRORRESUMEN

5 nuevas **guías** clínicas **ESC**

1. Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, et al. 2023 ESC Guidelines for the management of cardiomyopathies. European Heart Journal. 1 de octubre de 2023;44(37):3503-626.

2. Delgado V, Ajmone Marsan N, De Waha S, Bonaros N, Brida M, Burri H, et al. 2023 ESC Guidelines for the management of endocarditis. European Heart Journal. 25 de agosto de 2023;ehad193.

3. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. European Heart Journal. 25 de agosto de 2023;ehad192.

4. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal. 1 de octubre de 2023;44(37):3627-39.

5. Rossello X, Dan GA, Dweck MR, Galbraith M, Hinterbuchner L, Jankowska EA, et al. 2023 ESC Guidelines for the management of acute coronary syndromes.

- Cardiomiopatías,
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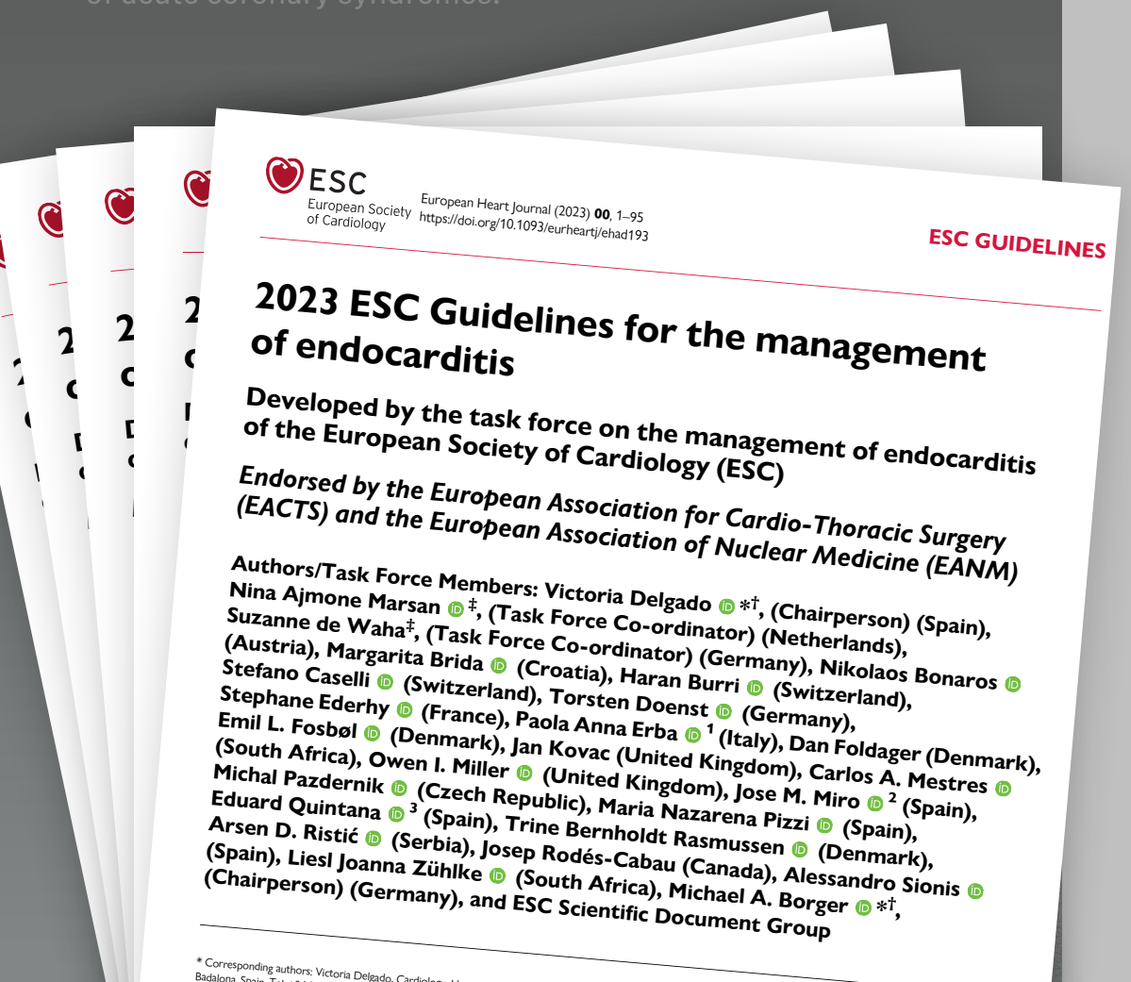
- SCA,



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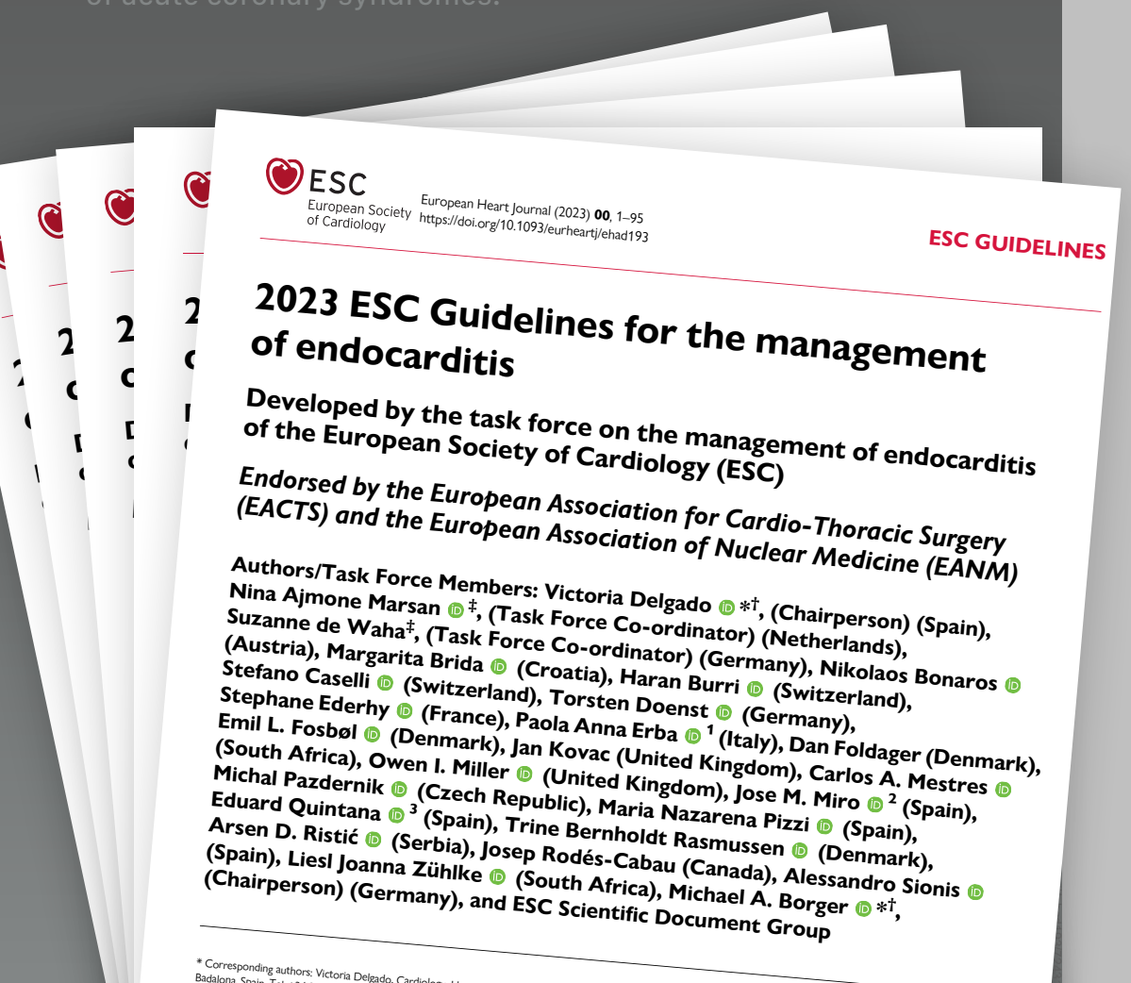

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- Guías ESC 2023 de **endocarditis**: profilaxis antibiótica, incorporación de nuevas pruebas de imagen (TC cardíaco, PET, WBC SPECT), equipo multidisciplinar, indicación qx...

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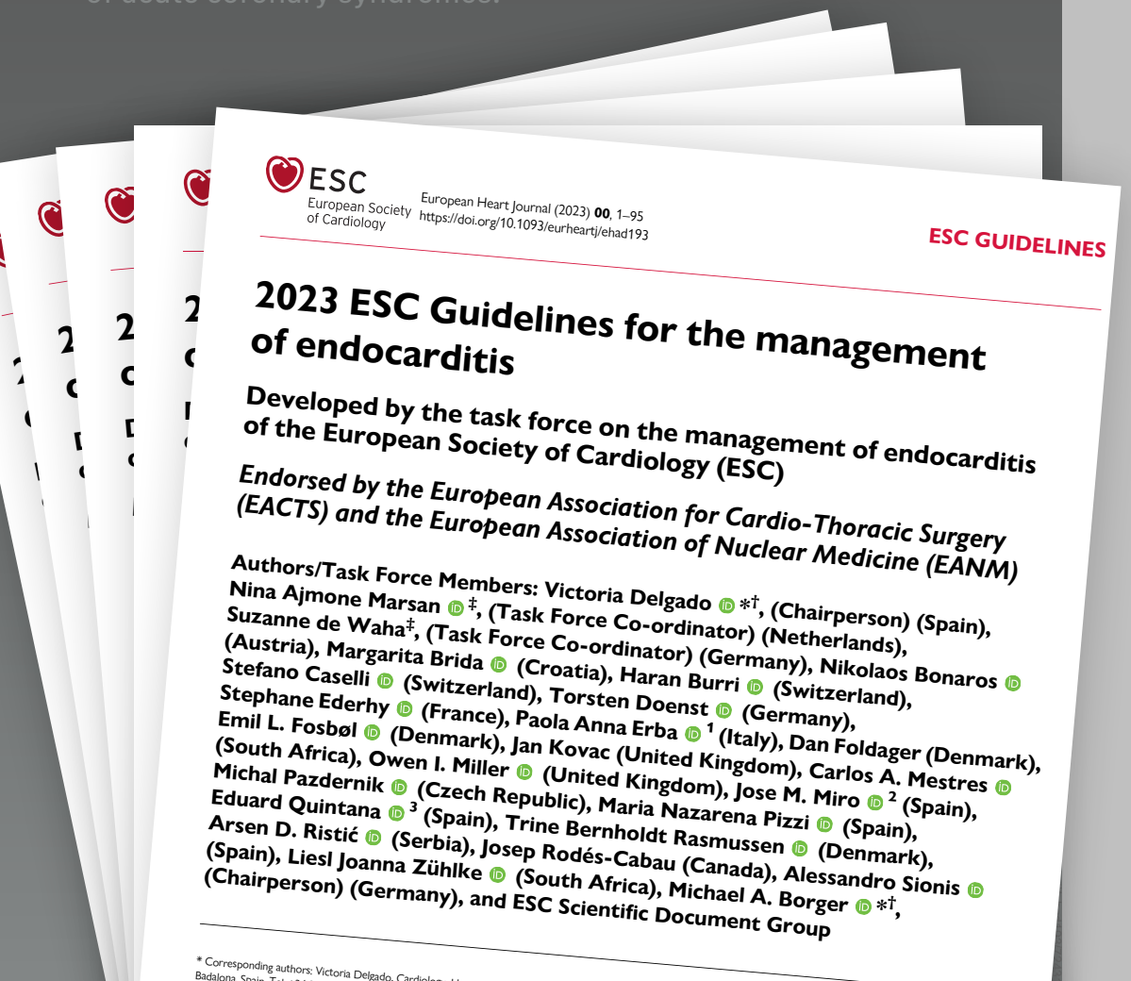

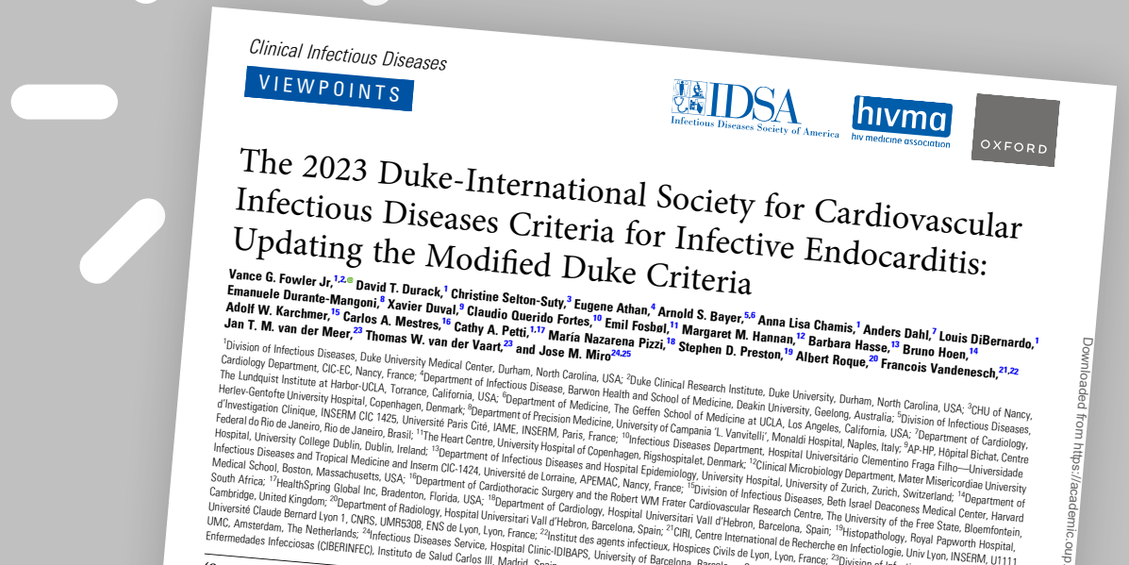

PREGUNTA SORPRESA

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Clinical Infectious Diseases
VIEWPOINTS
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria

Vance G. Fowler Jr,[1,2,©] David T. Durack,[1] Christine Selton-Suty,[3] Eugene Athan,[4] Arnold S. Bayer,[5,6] Anna Lisa Chamis,[1] Anders Dahl,[7] Louis DiBernardo,[1] Emanuele Durante-Mangoni,[8] Xavier Duval,[9] Claudio Querido Fortes,[10] Emil Fosbøl,[11] Margaret M. Hannan,[12] Barbara Hasse,[13] Bruno Hoen,[14] Adolf W. Karchmer,[15] Carlos A. Mestres,[16] Cathy A. Petti,[1,17] María Nazarena Pizzi,[18] Stephen D. Preston,[19] Albert Roque,[20] Francois Vandenesch,[21,22] Jan T. M. van der Meer,[23] Thomas W. van der Vaart,[23] and Jose M. Miro[24,25]

[1]Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina, USA; [2]Duke Clinical Research Institute, Duke University, Durham, North Carolina, USA; [3]CHU of Nancy, Cardiology Department, CIC-EC, Nancy, France; [4]Department of Infectious Disease, Barwon Health and School of Medicine, Deakin University, Geelong, Australia; [5]Division of Infectious Diseases, The Lundquist Institute at Harbor-UCLA, Torrance, California, USA; [6]Department of Medicine, The Geffen School of Medicine at UCLA, Los Angeles, California, USA; [7]Department of Cardiology, Herlev-Gentofte University Hospital, Copenhagen, Denmark; [8]Department of Precision Medicine, University of Campania "L. Vanvitelli", Monaldi Hospital, Naples, Italy; [9]AP-HP, Hôpital Bichat, Centre d'Investigation Clinique, INSERM CIC 1425, Université Paris Cité, IAME, INSERM, Paris, France; [10]Infectious Diseases Department, Hospital Universitário Clementino Fraga Filho—Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil; [11]The Heart Centre, University Hospital of Copenhagen, Rigshospitalet, Denmark; [12]Clinical Microbiology Department, Mater Misericordiae University Hospital, University College Dublin, Dublin, Ireland; [13]Department of Infectious Diseases and Hospital Epidemiology, University Hospital, University of Zurich, Zurich, Switzerland; [14]Department of Infectious Diseases and Tropical Medicine and Inserm CIC-1424, Université de Lorraine, APEMAC, Nancy, France; [15]Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA; [16]Department of Cardiothoracic Surgery and the Robert WM Frater Cardiovascular Research Centre, The University of the Free State, Bloemfontein, South Africa; [17]HealthSpring Global Inc, Bradenton, Florida, USA; [18]Department of Cardiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [19]Histopathology, Royal Papworth Hospital, Cambridge, United Kingdom; [20]Department of Radiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [21]CIRI, Centre International de Recherche en Infectiologie, Univ Lyon, INSERM, U1111, Université Claude Bernard Lyon 1, CNRS, UMR5308, ENS de Lyon, Lyon, France; [22]Institut des agents infectieux, Hospices Civils de Lyon, Lyon, France; [23]Division of Infectious Diseases, Amsterdam UMC, Amsterdam, The Netherlands; [24]Infectious Diseases Service, Hospital Clinic-IDIBAPS, University of Barcelona, Barcelona, Spain; and [25]Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain

(See the Editorial Commentary by Paras on pages 527–8.)

The microbiology, epidemiology, diagnostics, and treatment of infective endocarditis (IE) have changed significantly since the Duke Criteria were published in 1994 and modified in 2000. The International Society for Cardiovascular Infectious Diseases (ISCVID) convened a multidisciplinary Working Group to update the diagnostic criteria for IE. The resulting 2023 Duke-ISCVID IE Criteria propose significant changes, including new microbiology diagnostics (enzyme immunoassay for *Bartonella* species, polymerase chain reaction, amplicon/metagenomic sequencing, in situ hybridization), imaging (positron emission computed tomography with 18F-fluorodeoxyglucose, cardiac computed tomography), and inclusion of intraoperative inspection as a new Major Clinical Criterion. The list of "typical" microorganisms causing IE was expanded and includes pathogens to be considered as typical only in the presence of intracardiac prostheses. The requirements for timing and separate venipunctures for blood cultures were removed. Last, additional predisposing conditions (transcatheter valve implants, endovascular cardiac implantable electronic devices, prior IE) were clarified. These diagnostic criteria should be updated periodically by making the Duke-ISCVID Criteria available online as a "Living Document."

Keywords. endocarditis; Duke Criteria; PET/CT; echocardiography; ISCVID.

The Duke Criteria for diagnosis of infective endocarditis (IE) were originally published in 1994 [1] and modified in 2000 [2]. Their primary purpose was to serve as a research tool to standardize the definition of a clinically protean condition. Their presence paved the way for a steady stream of multinational investigations [3–7] that transformed our understanding of the disease. However, the microbiology, diagnostics, epidemiology, and treatment of IE have changed significantly since the debut of these criteria. For example, endovascular cardiac implantable electronic devices (CIEDs), including permanent pacemakers and cardioverter-defibrillators, are now present in at least 10% of contemporary IE case series [6], and constitute a significant risk factor

Los 'criterios de Duke modificados' de endocarditis (del año 2000) incluyen el **cardio-TC**.

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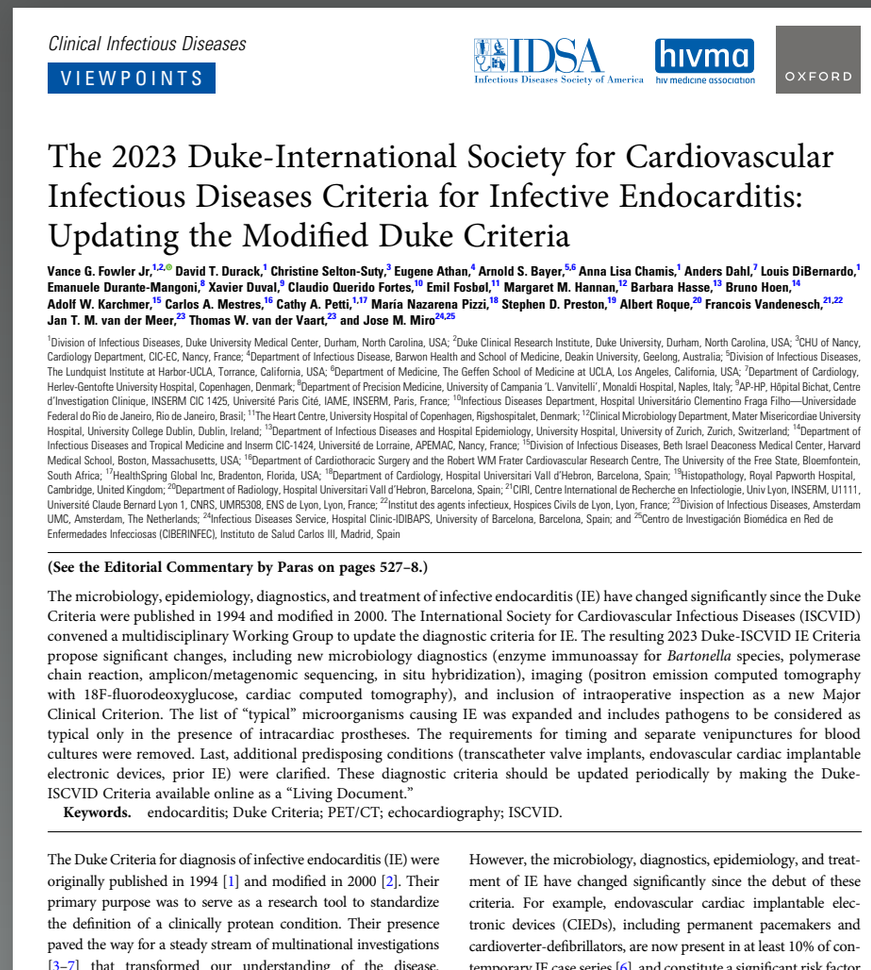

Clinical Infectious Diseases

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Nuevos criterios de **Duke**

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Clinical Infectious Diseases
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The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria

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(See the Editorial Commentary by Paras on pages 527–8.)

The microbiology, epidemiology, diagnostics, and treatment of infective endocarditis (IE) have changed significantly since the Duke Criteria were published in 1994 and modified in 2000. The International Society for Cardiovascular Infectious Diseases (ISCVID) convened a multidisciplinary Working Group to update the diagnostic criteria for IE. The resulting 2023 Duke-ISCVID IE Criteria propose significant changes, including new microbiology diagnostics (enzyme immunoassay for *Bartonella* species, polymerase chain reaction, amplicon/metagenomic sequencing, in situ hybridization), imaging (positron emission computed tomography with 18F-fluorodeoxyglucose, cardiac computed tomography), and inclusion of intraoperative inspection as a new Major Clinical Criterion. The list of "typical" microorganisms causing IE was expanded and includes pathogens to be considered as typical only in the presence of intracardiac prostheses. The requirements for timing and separate venipunctures for blood cultures were removed. Last, additional predisposing conditions (transcatheter valve implants, endovascular cardiac implantable electronic devices, prior IE) were clarified. These diagnostic criteria should be updated periodically by making the Duke-ISCVID Criteria available online as a "Living Document."

Keywords. endocarditis; Duke Criteria; PET/CT; echocardiography; ISCVID.

The Duke Criteria for diagnosis of infective endocarditis (IE) were originally published in 1994 [1] and modified in 2000 [2]. Their primary purpose was to serve as a research tool to standardize the definition of a clinically protean condition. Their presence paved the way for a steady stream of multinational investigations [3–7] that transformed our understanding of the disease. However, the microbiology, diagnostics, epidemiology, and treatment of IE have changed significantly since the debut of these criteria. For example, endovascular cardiac implantable electronic devices (CIEDs), including permanent pacemakers and cardioverter-defibrillators, are now present in at least 10% of contemporary IE case series [6], and constitute a significant risk factor

Criterios **mayores**

A. Microbiologic Major Criteria

(1) Positive blood cultures

i. Microorganisms that commonly cause IE[a] isolated from 2 or more separate blood culture sets (Typical)[b]

or

ii. **Microorganisms that occasionally or rarely cause IE isolated from 3 or more separate blood culture sets (Nontypical)[b]**

(2) Positive laboratory tests

i. Positive polymerase chain reaction (PCR) or other nucleic acid-based technique[c] for *Coxiella burnetii*, *Bartonella* species, or *Tropheryma whipplei* from blood

or

ii. *Coxiella burnetii* antiphase I immunoglobulin G (IgG) antibody titer >1:800 [24][d], or isolated from a single blood culture

or

iii. Indirect immunofluorescence assays (IFA) for detection of IgM and IgG antibodies to *Bartonella henselae* or *Bartonella quintana* with immunoglobulin G (IgG) titer ≥1:800 [24, 25][d]

B. Imaging Major Criteria

(1) Echocardiography and **cardiac computed tomography (CT)** imaging

i. Echocardiography and/or **cardiac CT** showing vegetation,[e] valvular/leaflet perforation,[f] valvular/leaflet aneurysm,[g] abscess,[h] pseudoaneurysm,[i] or intracardiac fistula[j]

or

ii. Significant new valvular regurgitation on echocardiography as compared with previous imaging. Worsening or changing of preexisting regurgitation is not sufficient.

or

iii. New partial dehiscence of prosthetic valve as compared with previous imaging [52]

(2) Positron emission computed tomography with 18F-fluorodeoxyglucose ([18F]FDG PET/CT imaging)

Abnormal metabolic activity[k] involving a native or prosthetic valve, ascending aortic graft (with concomitant evidence of valve involvement), intracardiac device leads or other prosthetic material[l,m]

C. Surgical Major Criteria

Evidence of IE documented by direct inspection during heart surgery neither Major Imaging Criteria nor subsequent histologic or microbiologic confirmation[n]

[a]*Staphylococcus aureus*; *Staphylococcus lugdunensis*; *Enterococcus faecalis*; all streptococcal species (except for *Streptococcus pneumoniae* and *Streptococcus pyogenes*), *Granulicatella* and *Abiotrophia* spp., *Gemella* spp., HACEK group microorganisms (*Haemophilus* species, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*). In the setting of intracardiac prosthetic material, the following additional bacteria should be included as "typical" pathogens: coagulase negative staphylococci, *Corynebacterium striatum* and *Corynebacterium* jeikeium, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Cutibacterium acnes*, nontuberculous mycobacteria (especially *M. chimaerae*), and *Candida* spp.

[b]"Blood culture set" is defined as a simultaneously drawn pair of 1 aerobic and 1 anaerobic bottle. "Positive" blood culture set is defined as microbial growth from at least 1 of the bottles. Blood cultures from separate venipuncture sites are strongly recommended whenever possible for evaluating suspected IE.

[c]Amplicon (16S or 18S) or metagenomic (shotgun) sequencing.

[d]Or equivalent titre results on other methodologies.

[e]Oscillating intracardiac mass on valve or other cardiac tissue, **endovascular CIED** or other implanted material in the absence of an alternative anatomic explanation.

[f]Interruption of valvular endocardial tissue continuity.

[g]Elongation with saccular outpouching of valvular tissue.

[h]Perivalvular (or perigraft) soft tissue lesion with variable degree of evolution to an organized collection.

[i]Perivalvular cavity communicating with the cardiovascular lumen.

[j]Communication between 2 neighboring cardiac chambers through a perforation.

[k]For prosthetic valve endocarditis (PVE), intense, focal/multifocal, or heterogeneous FDG uptake patterns; for native valve endocarditis and cardiac device leads, any abnormal uptake pattern [53–55].

[l]Performed at least 3 months after prosthetic valve surgical implantation [40].

[m]Some prosthetic valves may have intrinsic non-pathological FDG uptake [42, 56]. An isolated FDG-PET positive generator pocket in the absence of intracardiac infection does not qualify as a Major Criterion. PET/CT can be useful in detecting extracardiac foci of infection [51, 57].

[n]Addition of this major criterion should not be interpreted as giving license to not send appropriate samples for histopathology and microbiological studies.

MICRORRESUMEN

Nuevos criterios de **Duke**

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Clinical Infectious Diseases
VIEWPOINTS

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Criterios **menores**

A. Predisposition
- **Previous history of IE**
- Prosthetic valve[o]
- Previous valve repair[o]
- Congenital heart disease[p]
- More than mild regurgitation or stenosis of any etiology
- **Endovascular intracardiac implantable electronic device (CIED)**
- Hypertrophic obstructive cardiomyopathy
- Injection drug use

B. Fever *Documented temperature greater than 38.0 °C (100.4 °F)*

C. Vascular Phenomena *Clinical or radiological evidence of arterial emboli, septic pulmonary infarcts,* ***cerebral or splenic abscess,*** *mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions, purulent purpura*

D. Immunologic Phenomena Positive rheumatoid factor, Osler nodes, Roth spots, or immune complex-mediated glomerulonephritis[q]

E. Microbiologic Evidence, Falling Short of a Major Criterion
1) Positive blood cultures for a microorganism consistent with IE but not meeting the requirements for Major Criterion[r]

or

2) Positive culture, PCR, or other nucleic acid based test (amplicon or shotgun sequencing, *in situ* hybridization) for an organism consistent with IE[r] from a sterile body site other than cardiac tissue, cardiac prosthesis, or arterial embolus; or a single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence [51]

F. Imaging Criteria

Abnormal metabolic activity as detected by [18F]FDG PET/CT within 3 mo of implantation of prosthetic valve, ascending aortic graft* (with concomitant evidence of valve involvement)*, intracardiac device leads or other prosthetic material

G. Physical Examination Criteria[s]
New valvular regurgitation identified on auscultation if echocardiography is not available. Worsening or changing of preexisting murmur not sufficient

[o]Placed either by open-heart surgical or transcatheter approach.

[p]Includes cyanotic CHD (tetralogy of Fallot, univentricular heart, complete transposition, truncus arteriosus, hypoplastic left heart); endocardial cushion defects; ventricular septal defect; left-sided lesions (bicuspid aortic valve; aortic stenosis and insufficiency, mitral valve prolapse, mitral stenosis and insufficiency); right-sided lesions (Ebstein anomaly, anomalies of the pulmonary valve, congenital tricuspid valve disease); patent ductus arteriosus; and other congenital anomalies, with or without repair [58–60].

[q]Defined as either:
(1) Unexplained presence of either acute kidney injury (AKI, defined later) or acute on chronic kidney injury (defined later) plus 2 of the following: hematuria, proteinuria, cellular casts on inspection of urinary sediment, or serologic perturbations (hypocomplementemia, cryoglobulinemia, and/or presence of circulating immune complexes);
Or
(2) renal biopsy consistent with immune complex-mediated renal disease.
AKI: new unexplained reduction of estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2.
Acute or chronic kidney injury: reduction by at least 1 ordinal level of function: eg, from "moderately decreased" to "severely decreased"; or from "severely decreased" to "kidney failure."
Interpretive ranges for eGFR: normal ≥60 mL/min/1.73 m^2; moderately decreased 30–59 mL/min/1.73 m^2; severely decreased 15–29 mL/min/1.73 m^2; kidney failure <15 ml/min/1.73 m^2.

[r]Excludes single positive blood cultures or sequencing based assays for microorganisms that commonly contaminate blood cultures or rarely cause IE.

[s]Applicable only when echocardiography is unavailable. Based on expert opinion.

MICRORRESUMEN

Guías ESC 2011–2022: cada vez más recomendaciones pero escasa evidencia.

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- **Sólo el 16%** de recomendaciones están respaldadas por la evidencia de mayor calidad (A).
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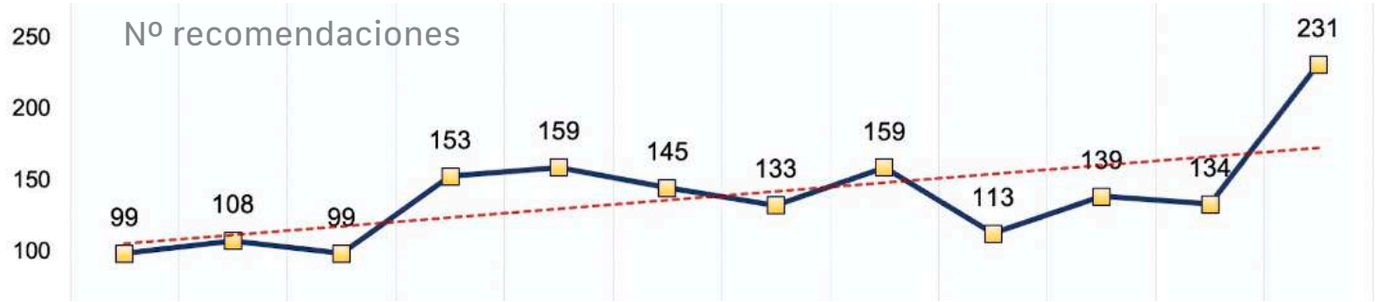

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Review Article

Comparative analysis of level of evidence and class of recommendation for 50 clinical practice guidelines released by the European Society of Cardiology from 2011 to 2022

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ARTICLE INFO

Keywords:
Arrhythmia
Atrial fibrillation
Diabetes
Guidelines
Heart failure
Pacing
Prevention

ABSTRACT

Background: The European Society of Cardiology (ESC) clinical practice guidelines are essential tools for decision-making.
Aim: To analyze the level of evidence (LOE) and the class of recommendations in the ESC guidelines released in the last 12 years.
Methods: We evaluated 50 ESC guidelines released from 2011 to 2022, related to 27 topics and categorized them into seven macro-groups. We analyzed every recommendation in terms of LOE and class of recommendation, calculating their relative proportions and changes over time in consecutive editions of the same guideline.
Results: A total of 6972 recommendations were found, with an increase in number per year over time. Among the 50 ESC guidelines, the proportional distribution of classes of recommendations was 49% for Class I, 29% for Class IIa, 15% for Class IIb, and 8% for Class III. Overall, 16% of the recommendations were classified as LOE A, 31% LOE B and 53% LOE C. The field of preventive cardiology had the largest proportion of LOE A, while the lowest was in the field of valvular, myocardial, pericardial and pulmonary diseases. The overall proportion of LOE A recommendations in the most recent guidelines compared to their prior versions increased from 17% to 20%.
Conclusions: The recommendations included in the ESC guidelines widely differ in terms of quality of evidence, with only 16% supported by the highest quality of evidence. Although a slight global increase in LOE A recommendations was observed in recent years, further scientific research efforts are needed to increase the quality of evidence.

1. Introduction

The term "Evidence-based Medicine" (EBM) first appeared in medical literature in 1991 when Gordon Guyatt, a faculty member at McMaster Medical School in Hamilton, Ontario, published an Editorial entitled "Evidence-based Medicine" [1]. Sackett et al. [2], appropriately defined EBM as the "*conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients*". This new approach for taking decisions in clinical practice derived from the need to go beyond the traditional way of making clinical choices which relied mainly upon the basis of clinical experience. At present, randomized controlled trials (RCTs) are considered the gold standard for assessing the efficacy of medical interventions and treatments [1,3,4]. According to the EBM approach, the combination of multiple RCTs in systematic reviews and meta-analyses allows to achieve the highest level of evidence that medical literature can produce [5]. The need to synthesize scientific evidence promoted the development of clinical practice guidelines in different medical fields and adherence to consensus guidelines became a standard reference for assessing the quality of care. Indeed, several studies in the cardiology setting showed how adherence to guidelines is associated with better outcomes [6–10].

The European Society of Cardiology (ESC), regularly publishes Clinical Practice Guidelines on different topics related to cardiovascular care, using a consistent grading system based on classes of

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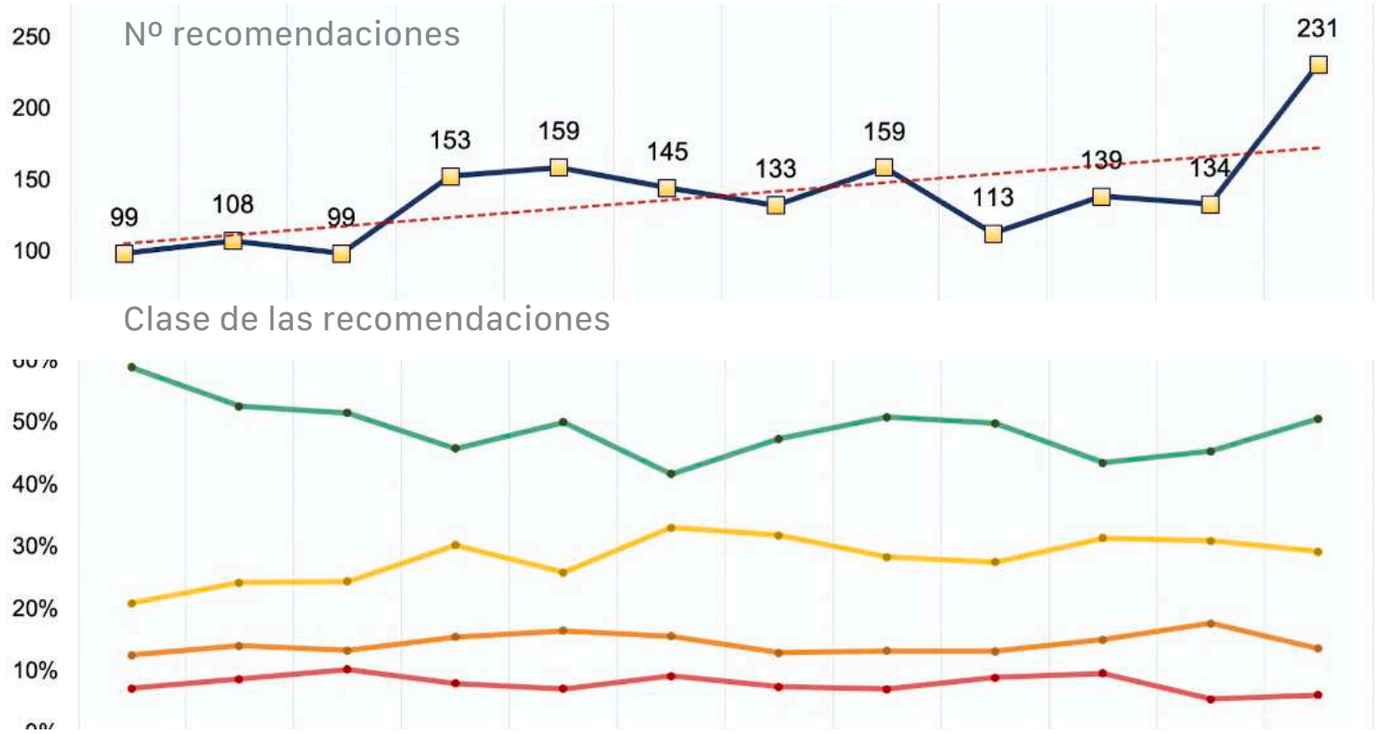

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The European Society of Cardiology (ESC), regularly publishes Clinical Practice Guidelines on different topics related to cardiovascular

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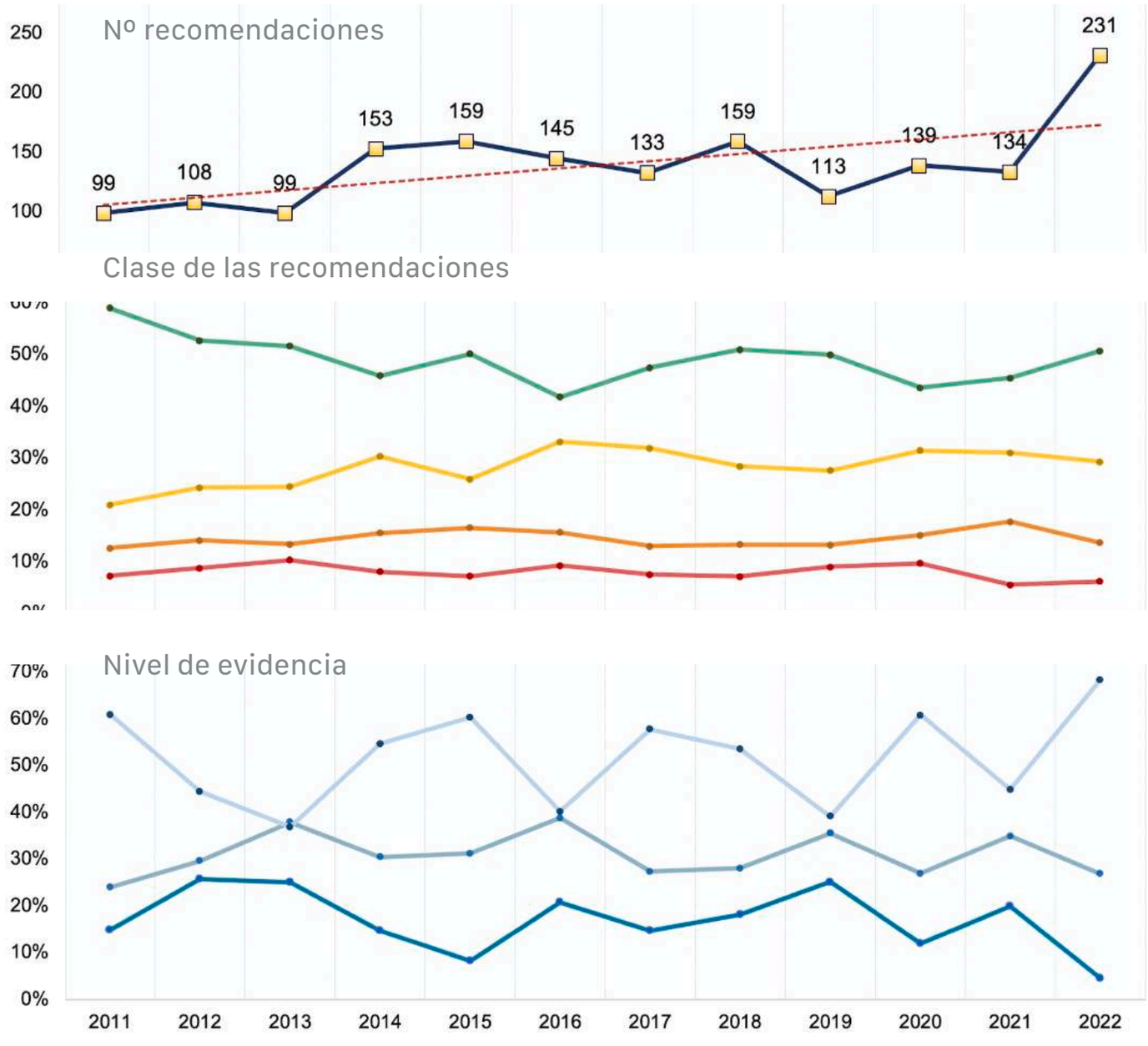
- Las de IC tuvieron el mayor descenso en la proporción de recomendaciones de clase III (↓62%)



MICRORRESUMEN

↓Mg^{2+} grave y refractaria tratada con iSGLT2 en casos sin DM2

Shah CV, Hammad N, Bhasin-Chhabra B, Rashidi A. SGLT2 Inhibitors in Management of Severe Hypomagnesemia in Patients Without Diabetes: A Report of 4 Cases. Kidney Medicine. septiembre de 2023;5(9):100697.

- Los 4 👤 presentaban ↓Mg2+ asociada a inhibidores de la calcineurina o a QT (platinos).
- Parece un **efecto de clase** de iSGLT2.
- Especulan que los **mecanismos** potenciales podrían incluir el aumento de la secreción de glucagón y arginina-vasopresina — ↑ reabsorción de Mg 2+ en TCD

Case Report

Kidney Medicine

SGLT2 Inhibitors in Management of Severe Hypomagnesemia in Patients Without Diabetes: A Report of 4 Cases

Chintan V. Shah, Nour Hammad, Bhavna Bhasin-Chhabra, and Arash Rashidi

Sodium/glucose cotransporter 2 (SGLT2) inhibitors have demonstrated a class effect in improving serum magnesium levels in patients with diabetes. Additionally, recent reports have shown their promising beneficial effects in the treatment of refractory hypomagnesemia in patients with diabetes. However, their role in treating hypomagnesemia in patients without diabetes remains unexplored. Here, we report 4 cases of severe and refractory hypomagnesemia that showed dramatic improvement after initiating SGLT2 inhibitors in patients without diabetes. Case 1 had calcineurin inhibitor-associated severe hypomagnesemia. Cases 2, 3, and 4 had refractory hypomagnesemia associated with platinum-based chemotherapy with or without gastrointestinal losses. Case 1 was able to withdraw from high-dose oral magnesium supplementation. Cases 2 and 3 achieved independence from intravenous magnesium supplementation, whereas case 4 had decreased intravenous magnesium requirements. All the cases demonstrated sustainably improved serum magnesium levels. Withdrawal of SGLT2 inhibitors in case 4 resulted in worsening serum magnesium levels and intravenous magnesium requirements. The extraglycemic benefit of this group of medications not only suggests the need for further studies to better understand the effect of SGLT2 inhibitors on magnesium homeostasis but also supports expanded use in a larger patient population.

Complete author and article information provided before references.

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Kidney Med. 5(9):100697. Published online July 1, 2023.

doi: 10.1016/j.xkme.2023.100697

INTRODUCTION

Sodium/glucose cotransporter 2 (SGLT2) inhibitors, which initially emerged as a treatment option for patients with type 2 diabetes, have also been shown to improve clinical outcomes in patients with a variety of heart and kidney diseases with or without diabetes.[1] The beneficial effect of SGLT2 inhibitors on magnesium balance in patients with diabetes with or without hypomagnesemia has been noted as a class effect in recent meta-analysis data from randomized clinical trials.[2–4] Moreover, some reports have demonstrated their role in the treatment of refractory hypomagnesemia in patients with diabetes with or without overt urinary magnesium wasting.[5,6] However, their role in the treatment of hypomagnesemia in patients without diabetes remains unexplored. Here, to the best of our knowledge, we report the first series of 4 patients without diabetes with severe hypomagnesemia successfully treated with SGLT2 inhibitors.

showed a 24-hour magnesium urine level of 90 mg with a fractional excretion of magnesium (FEMg) of 9.73%. Later, empagliflozin 10 mg daily was initiated and increased to 25 mg daily after 2 months. Her oral magnesium supplements were completely withdrawn 2 months after empagliflozin was initiated, and serum magnesium levels remain stable without any further episodes of hypomagnesemia at 5 months of follow-up. Repeat FEMg was reduced to 4.88% after the administration of empagliflozin (Table 1).

Case 2

A woman in her 70s presented with a history of locally advanced serous ovarian cancer status post debulking procedure, including radical abdominal hysterectomy with bilateral salpingo-oophorectomy and diverting loop ileostomy. She received chemotherapy with docetaxel and carboplatin. Following chemotherapy, the patient developed multiple electrolyte abnormalities, including hypokalemia

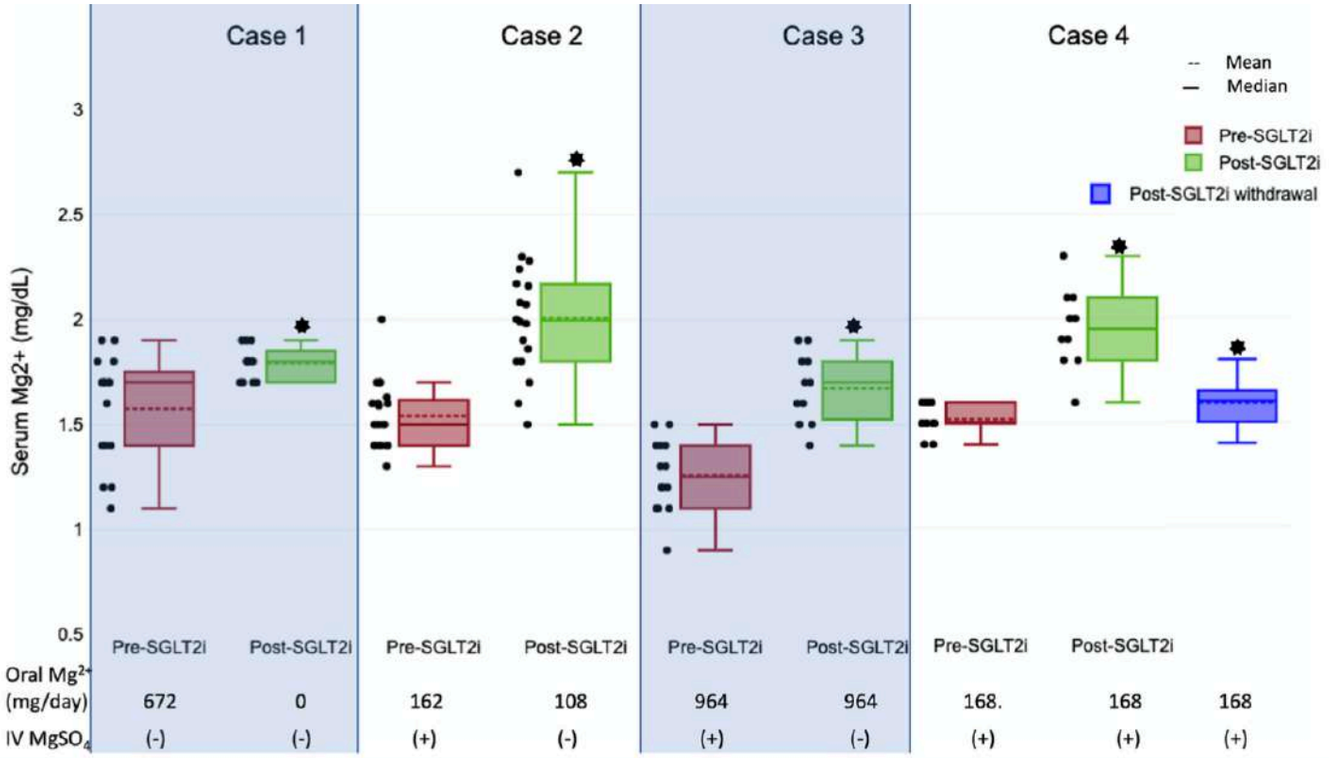

Figure 1. Sodium/glucose cotransporter 2 (SGLT2) inhibition was associated with increased serum magnesium levels in case 1 (1.60 ± 0.24, n=15 vs 1.79 ± 0.079, n=12; $P = 0.02$), case 2 (1.54 ± 0.16, n=20 vs 2.0 ± 0.28, n=18; $P < 0.001$), case 3 (1.25 ± 0.17, n=14 vs 1.67 ± 0.16, n=11; $P < 0.001$) and case 4 (1.52 ± 0.07, n=10 vs 1.95 ± 0.19, n=10; $P < 0.001$). SGLT2 inhibition was associated with a decrease in oral magnesium supplementation in case 1 (672 mg vs 0 mg) and case 2 (162 mg vs 108 mg), allowed withdrawal from intravenous magnesium sulfate (IV $MgSO_4$) dependence in case 2 and case 3, and decreased the need for IV MgSO4 supplementation in case 4. Withdrawal of SGLT2 inhibition in case 4 was associated with a decrease in serum magnesium levels (1.95 ± 0.19, n=10 vs 1.59 ± 0.10, n=12; $P < 0.001$) and an increase in requirements for IV $MgSO_4$ (12 gm vs 20 gm IV $MgSO_4$ at 1 month pre- vs post-SGLT2i withdrawal, respectively). Abbreviations: IV $MgSO_4$, intravenous magnesium sulfate; SGLT2i, sodium-glucose cotransporter 2 inhibitor; oral Mg, oral elemental magnesium.

MICRORRESUMEN

Existe dosis-respuesta entre la **carga anticolinérgica** y el riesgo de **eventos CV agudos** (hasta ×2)

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Association between recently raised anticholinergic burden and risk of acute cardiovascular events: nationwide case-case-time-control study

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Cite this as: *BMJ* 2023;382:e076045
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Accepted: 26 August 2023

ABSTRACT

OBJECTIVE
To evaluate the association between recently raised anticholinergic burden and risk of acute cardiovascular events in older adults.

DESIGN
Case-case-time-control study (ie, incorporating a case crossover design and a control crossover design consisting of future cases).

SETTING
Taiwan's National Health Insurance Research Database.

PARTICIPANTS
317 446 adults aged ≥65 who were admitted to hospital because of an incident acute cardiovascular event between 2011 and 2018. Acute cardiovascular events included myocardial infarction, strokes, arrhythmias, conduction disorders, and cardiovascular death.

MAIN OUTCOME MEASURES
The anticholinergic burden was measured for each participant by adding up the anticholinergic scores for individual drugs using the Anticholinergic Cognitive Burden Scale. Scores were classified into three levels (0 points, 1-2 points, and ≥3 points). For each participant, anticholinergic burden levels during hazard periods (day −1 to −30 before the cardiovascular event) were compared with randomly selected 30 day reference periods (ie, periods between days −61 and −180). Conditional logistic regression determined odds ratios with 95% confidence intervals to evaluate the association between acute cardiovascular events and recently raised anticholinergic burden.

RESULTS
The crossover analyses included 248 579 current cases. Participants' average age on the index date was 78.4 years (standard deviation 0.01), and 53.4% were men. The most frequently prescribed drugs with anticholinergic activity were antihistamines (68.9%), gastrointestinal antispasmodics (40.9%), and diuretics (33.8%). Among patients with varying levels of anticholinergic burden in different periods, more patients carried higher levels of anticholinergic burden during hazard periods than during reference periods. For example, 17 603 current cases had 1-2 points of anticholinergic burden in the hazard period with 0 points in the reference period, while 8507 current cases had 0 points in the hazard period and 1-2 points in the reference period. In the comparison of 1-2 points versus 0 points of anticholinergic burden, the odds ratio was 1.86 (95% confidence interval 1.83 to 1.90) in the case crossover analysis and 1.35 (1.33 to 1.38) in the control crossover analysis, which yielded a case-case-time-control odds ratio of 1.38 (1.34 to 1.42). Similar results were found in the comparison of ≥3 versus 0 points (2.03, 1.98 to 2.09) and ≥3 versus 1-2 points (1.48, 1.44 to 1.52). The findings remained consistent throughout a series of sensitivity analyses (eg, cut-off points for anticholinergic burden categories were redefined and different scales were used to measure anticholinergic burden).

CONCLUSIONS
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Entre **20** y el **50%**

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RESEARCH

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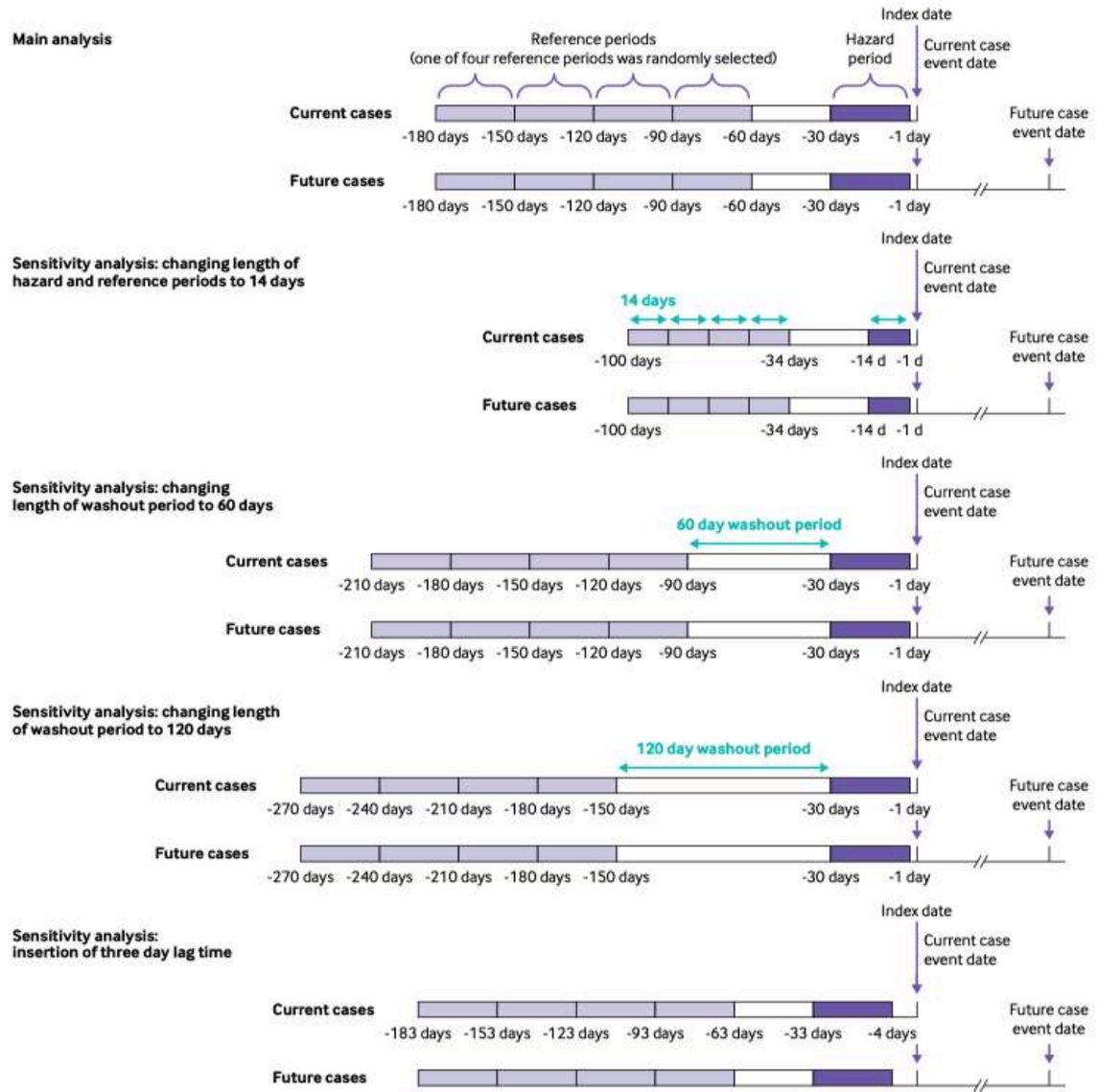

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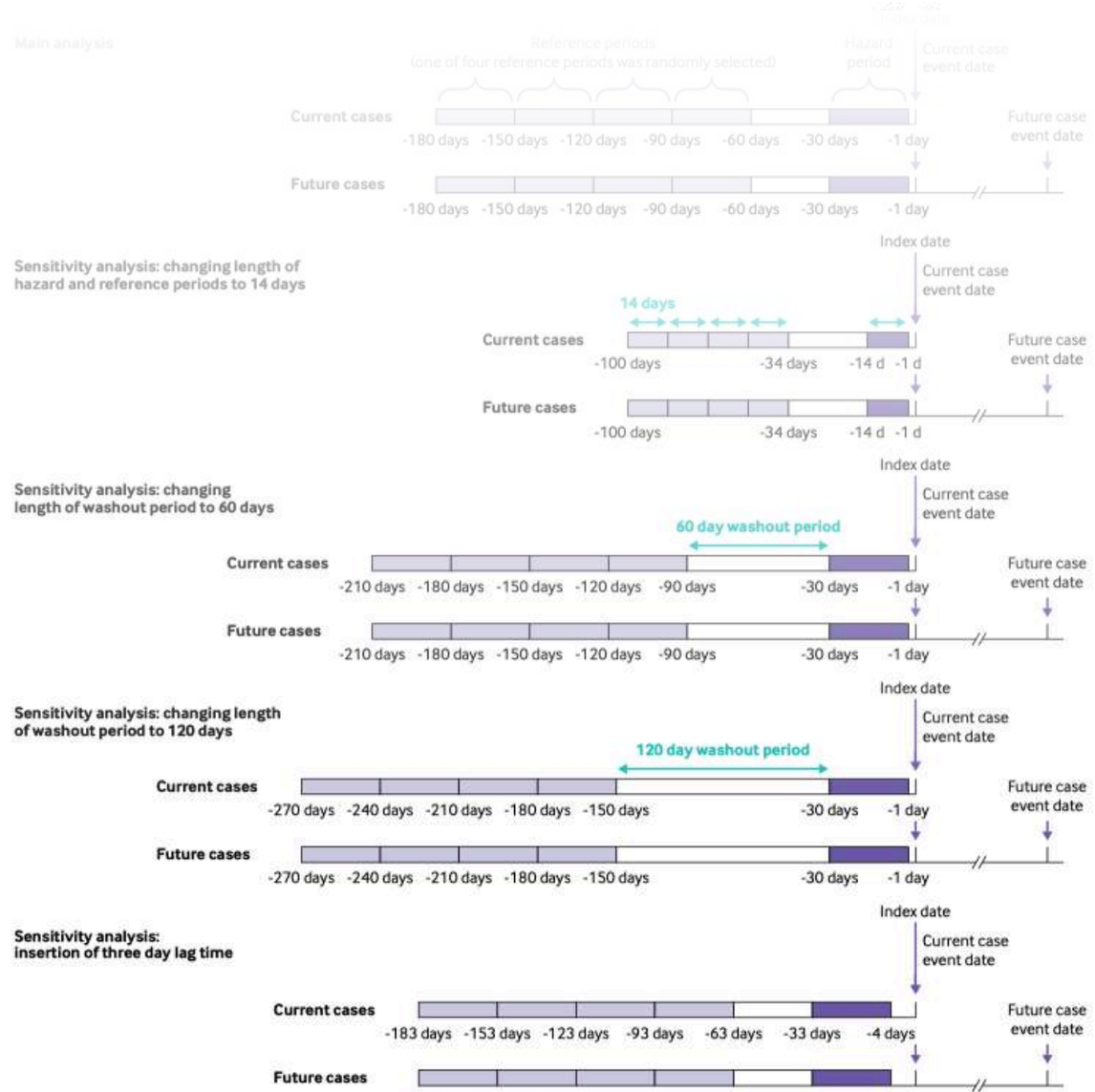

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Taiwán 2011–2018.

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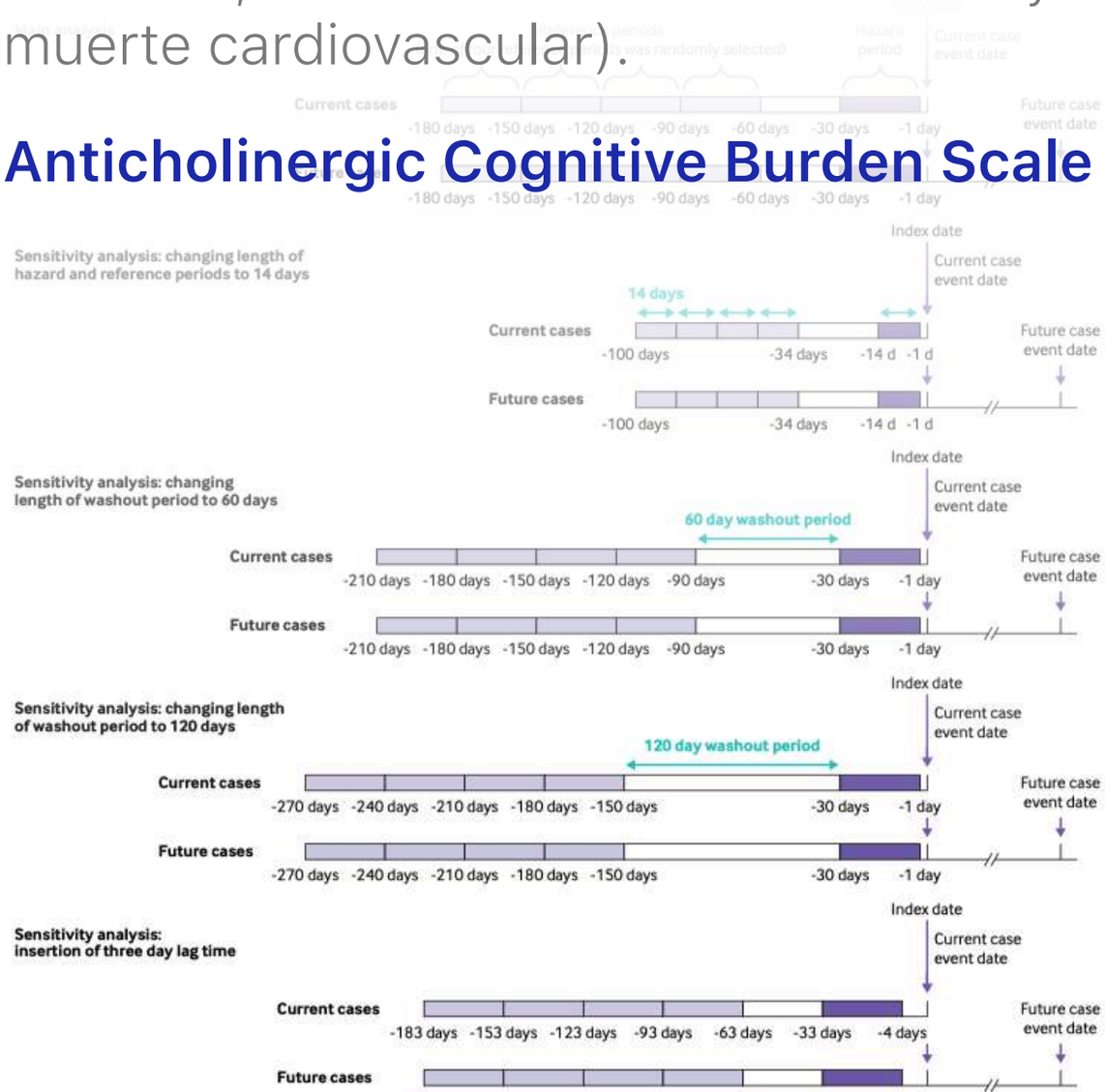
Anticholinergic Cognitive Burden Scale



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Check for updates

Association between recently raised anticholinergic burden and risk of acute cardiovascular events: nationwide case-case-time-control study

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ABSTRACT

OBJECTIVE
To evaluate the association between recently raised anticholinergic burden and risk of acute cardiovascular events in older adults.

DESIGN
Case-case-time-control study (ie, incorporating a case crossover design and a control crossover design consisting of future cases).

SETTING
Taiwan's National Health Insurance Research Database.

PARTICIPANTS
317 446 adults aged ≥65 who were admitted to hospital because of an incident acute cardiovascular event between 2011 and 2018. Acute cardiovascular events included myocardial infarction, strokes, arrhythmias, conduction disorders, and cardiovascular death.

MAIN OUTCOME MEASURES
The anticholinergic burden was measured for each participant by adding up the anticholinergic scores for individual drugs using the Anticholinergic Cognitive Burden Scale. Scores were classified into three levels (0 points, 1-2 points, and ≥3 points). For each participant, anticholinergic burden levels during hazard periods (day −1 to −30 before the cardiovascular event) were compared with randomly selected 30 day reference periods (ie, periods between days −61 and −180). Conditional logistic regression determined odds ratios with 95% confidence intervals to evaluate the association between acute cardiovascular events and recently raised anticholinergic burden.

RESULTS
The crossover analyses included 248 579 current cases. Participants' average age on the index date was 78.4 years (standard deviation 0.01), and 53.4% were men. The most frequently prescribed drugs with anticholinergic activity were antihistamines (68.9%), gastrointestinal antispasmodics (40.9%), and diuretics (33.8%). Among patients with varying levels of anticholinergic burden in different periods, more patients carried higher levels of anticholinergic burden during hazard periods than during reference periods. For example, 17 603 current cases had 1-2 points of anticholinergic burden in the hazard period with 0 points in the reference period, while 8507 current cases had 0 points in the hazard period and 1-2 points in the reference period. In the comparison of 1-2 points versus 0 points of anticholinergic burden, the odds ratio was 1.86 (95% confidence interval 1.83 to 1.90) in the case crossover analysis and 1.35 (1.33 to 1.38) in the control crossover analysis, which yielded a case-case-time-control odds ratio of 1.38 (1.34 to 1.42). Similar results were found in the comparison of ≥3 versus 0 points (2.03, 1.98 to 2.09) and ≥3 versus 1-2 points (1.48, 1.44 to 1.52). The findings remained consistent throughout a series of sensitivity analyses (eg, cut-off points for anticholinergic burden categories were redefined and different scales were used to measure anticholinergic burden).

CONCLUSIONS
An association was found between recently raised anticholinergic burden and increased risk of acute cardiovascular events. Furthermore, a greater increase in anticholinergic burden was associated with a higher risk of acute cardiovascular events.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Previous studies have reported an association between anticholinergic burden and increased cardiovascular risk, but have not considered the potential issue of protopathic bias

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Existe dosis-respuesta entre la **carga anticolinérgica** y el riesgo de **eventos CV agudos** (hasta ×2)

Huang WC, Yang ASH, Tsai DHT, Shao SC, Lin SJ, Lai ECC. Association between recently raised anticholinergic burden and risk of acute cardiovascular events: nationwide case-case-time-control study. BMJ. 27 de septiembre de 2023;e076045

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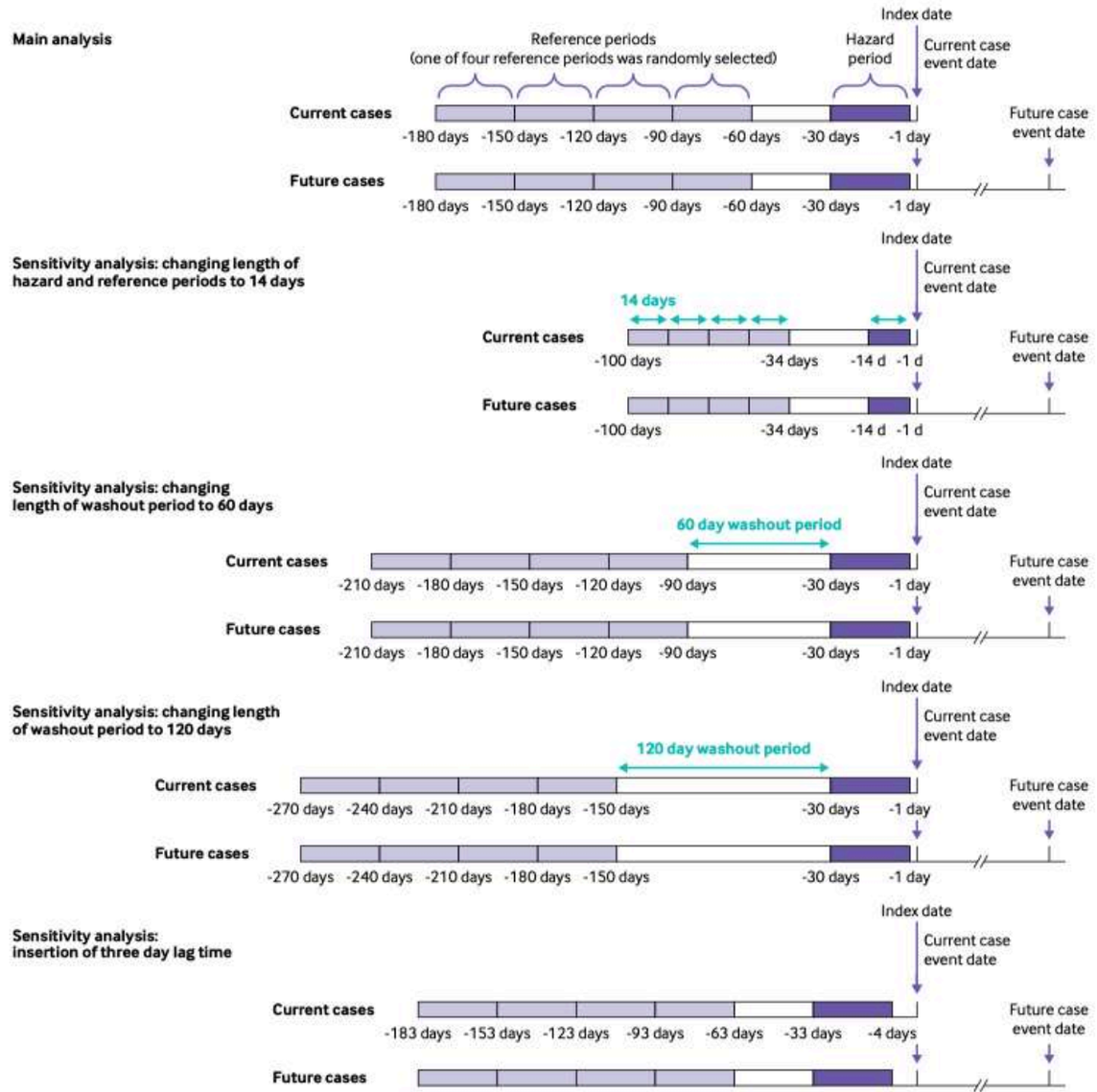

RESEARCH

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ESTABLISHED IN 1812 SEPTEMBER 14, 2023 VOL. 389 NO. 11

Ferric Carboxymaltose in Heart Failure with Iron Deficiency

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ABSTRACT

BACKGROUND

Ferric carboxymaltose therapy reduces symptoms and improves quality of life in patients who have heart failure with a reduced ejection fraction and iron deficiency. Additional evidence about the effects of ferric carboxymaltose on clinical events is needed.

METHODS

In this double-blind, randomized trial, we assigned ambulatory patients with heart failure, a left ventricular ejection fraction of 40% or less, and iron deficiency, in a 1:1 ratio, to receive intravenous ferric carboxymaltose or placebo, in addition to standard therapy for heart failure. Ferric carboxymaltose or placebo was given every 6 months as needed on the basis of iron indexes and hemoglobin levels. The primary outcome was a hierarchical composite of death within 12 months after randomization, hospitalizations for heart failure within 12 months after randomization, or change from baseline to 6 months in the 6-minute walk distance. The significance level was set at 0.01.

RESULTS

We enrolled 3065 patients, of whom 1532 were randomly assigned to the ferric carboxymaltose group and 1533 to the placebo group. Death by month 12 occurred in 131 patients (8.6%) in the ferric carboxymaltose group and 158 (10.3%) in the placebo group; a total of 297 and 332 hospitalizations for heart failure, respectively, occurred by month 12; and the mean (±SD) change from baseline to 6 months in the 6-minute walk distance was 8±60 and 4±59 m, respectively (Wilcoxon–Mann–Whitney P=0.02; unmatched win ratio, 1.10; 99% confidence interval, 0.99 to 1.23). Repeated dosing of ferric carboxymaltose appeared to be safe with an acceptable adverse-event profile in the majority of patients. The number of patients with serious adverse events occurring during the treatment period was

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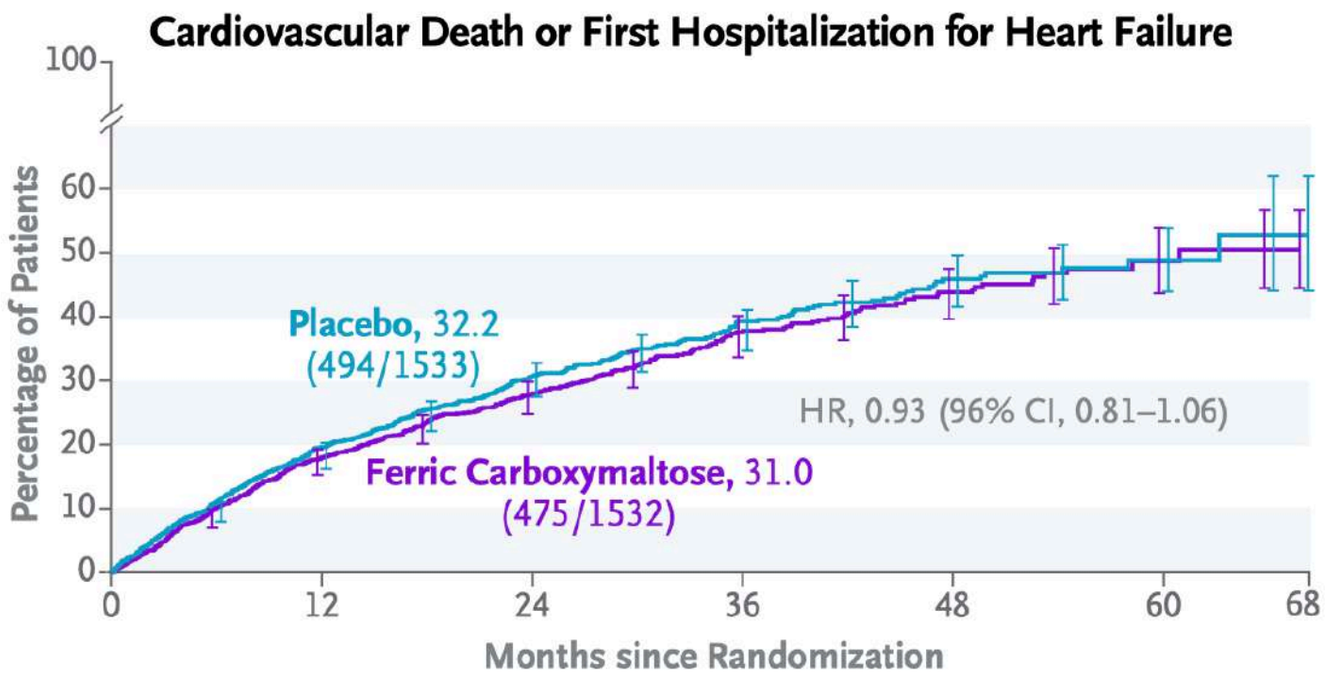
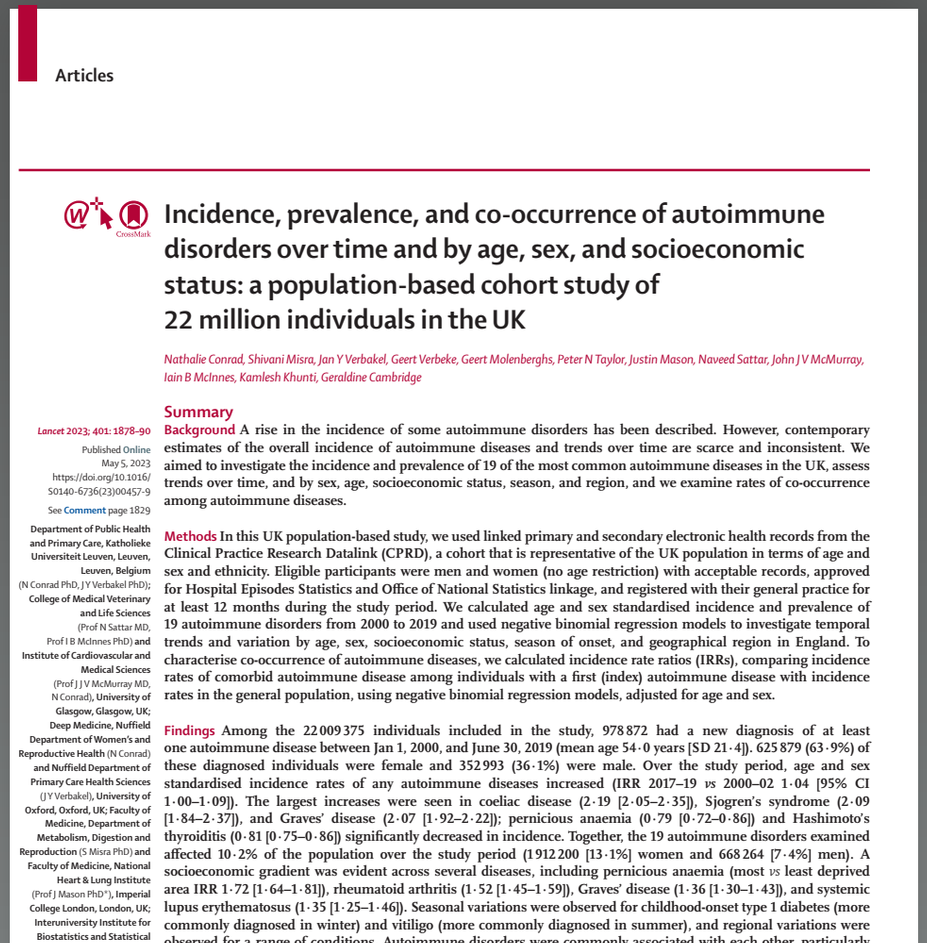


PREGUNTA SORPRESA

Conrad N, Misra S, Verbakel JY, Verbeke G, Molenberghs G, Taylor PN, et al. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. The Lancet. junio de 2023;401(10391):1878-90.



Articles

Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK

Nathalie Conrad, Shivani Misra, Jan Y Verbakel, Geert Verbeke, Geert Molenberghs, Peter N Taylor, Justin Mason, Naveed Sattar, John J V McMurray, Iain B McInnes, Kamlesh Khunti, Geraldine Cambridge

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See Comment page 1829

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Summary

Background A rise in the incidence of some autoimmune disorders has been described. However, contemporary estimates of the overall incidence of autoimmune diseases and trends over time are scarce and inconsistent. We aimed to investigate the incidence and prevalence of 19 of the most common autoimmune diseases in the UK, assess trends over time, and by sex, age, socioeconomic status, season, and region, and we examine rates of co-occurrence among autoimmune diseases.

Methods In this UK population-based study, we used linked primary and secondary electronic health records from the Clinical Practice Research Datalink (CPRD), a cohort that is representative of the UK population in terms of age and sex and ethnicity. Eligible participants were men and women (no age restriction) with acceptable records, approved for Hospital Episodes Statistics and Office of National Statistics linkage, and registered with their general practice for at least 12 months during the study period. We calculated age and sex standardised incidence and prevalence of 19 autoimmune disorders from 2000 to 2019 and used negative binomial regression models to investigate temporal trends and variation by age, sex, socioeconomic status, season of onset, and geographical region in England. To characterise co-occurrence of autoimmune diseases, we calculated incidence rate ratios (IRRs), comparing incidence rates of comorbid autoimmune disease among individuals with a first (index) autoimmune disease with incidence rates in the general population, using negative binomial regression models, adjusted for age and sex.

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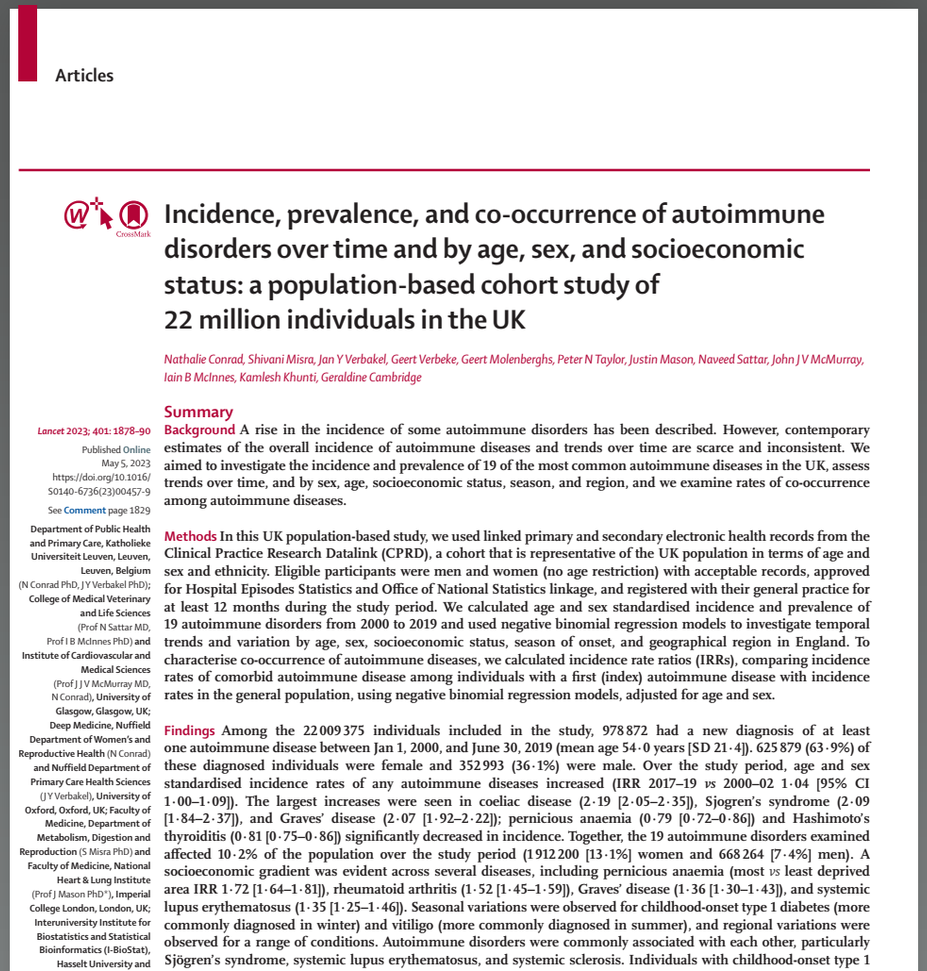
Las enfermedades **autoinmunes** se manifiestan en casi el **10%** de la población y dependen sobre todo de **factores ambientales**.

VERDADERO

FALSO

PREGUNTA SORPRESA

Conrad N, Misra S, Verbakel JY, Verbeke G, Molenberghs G, Taylor PN, et al. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. The Lancet. junio de 2023;401(10391):1878-90.



Articles

Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK

Nathalie Conrad, Shivani Misra, Jan Y Verbakel, Geert Verbeke, Geert Molenberghs, Peter N Taylor, Justin Mason, Naveed Sattar, John J V McMurray, Iain B McInnes, Kamlesh Khunti, Geraldine Cambridge

Lancet 2023; 401: 1878–90

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See Comment page 1829

Department of Public Health and Primary Care, Katholieke Universiteit Leuven, Leuven, Leuven, Belgium (N Conrad PhD, J Y Verbakel PhD); College of Medical Veterinary and Life Sciences (Prof N Sattar MD, Prof I B McInnes PhD) and Institute of Cardiovascular and Medical Sciences (Prof J J V McMurray MD, N Conrad), University of Glasgow, Glasgow, UK; Deep Medicine, Nuffield Department of Women's and Reproductive Health (N Conrad) and Nuffield Department of Primary Care Health Sciences (J Y Verbakel), University of Oxford, Oxford, UK; Faculty of Medicine, Department of Metabolism, Digestion and Reproduction (S Misra PhD) and Faculty of Medicine, National Heart & Lung Institute (Prof J Mason PhD†), Imperial College London, London, UK; Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), Hasselt University and

Summary

Background A rise in the incidence of some autoimmune disorders has been described. However, contemporary estimates of the overall incidence of autoimmune diseases and trends over time are scarce and inconsistent. We aimed to investigate the incidence and prevalence of 19 of the most common autoimmune diseases in the UK, assess trends over time, and by sex, age, socioeconomic status, season, and region, and we examine rates of co-occurrence among autoimmune diseases.

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VERDADERO

MICRORRESUMEN

Incidencia de EAS en 22 millones de pacientes de UK del 2000–2019

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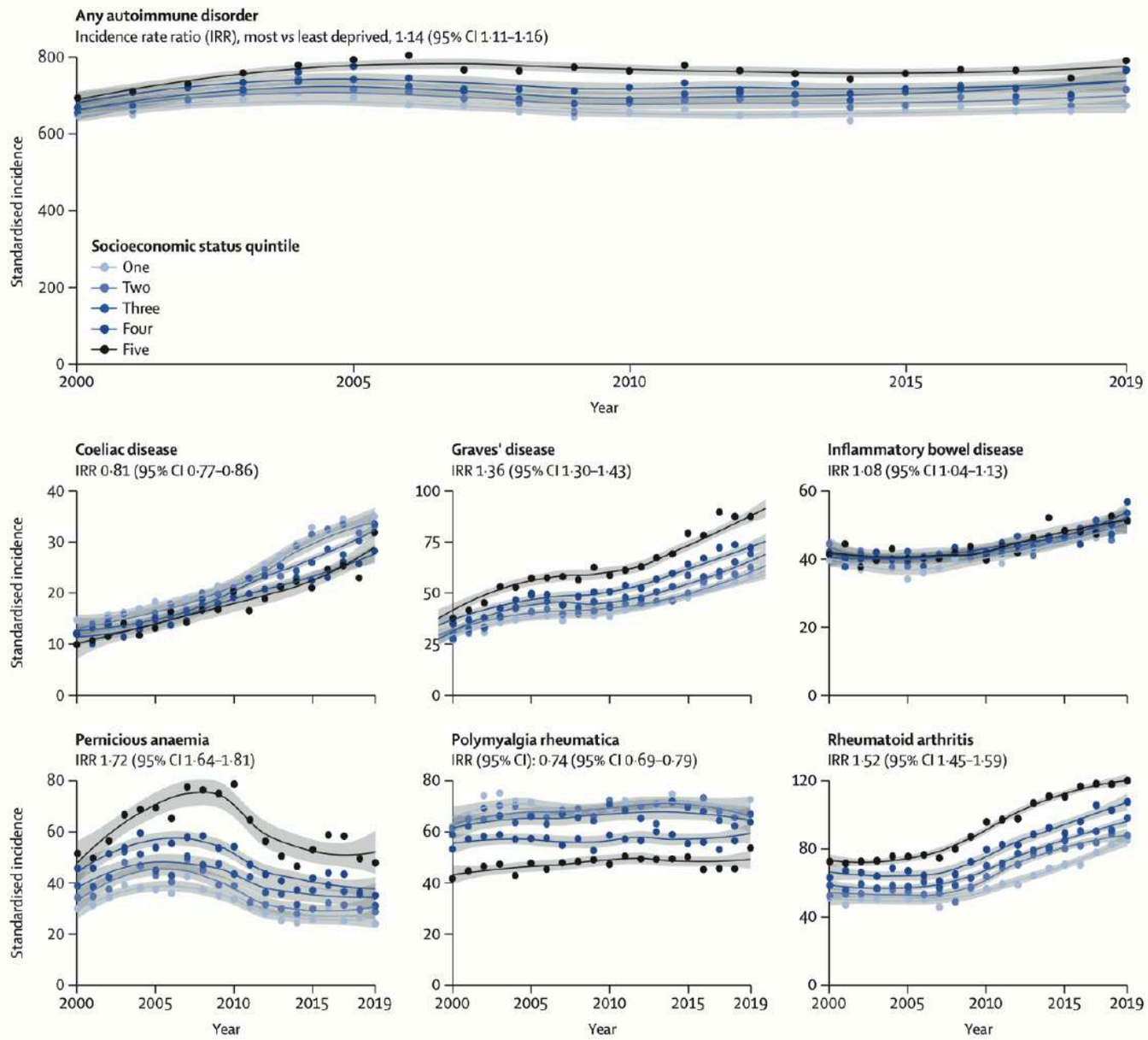
- Pruebas muy robustas de que hay factores **socioeconómicos**, **estacionales** y **regionales** de varias enfermedades autoinmunes — especialmente Graves, la anemia perniciosa, la AR, el LES y la DM1

- Es improbable que tales variaciones puedan atribuirse ~~únicamente a diferencias genéticas~~.



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MICRORRESUMEN

La **PA sistólica** tiene el mayor potencial para la prevención de enfermedades CV

Conrad N, Misra S, Verbakel JY, Verbeke G, Molenberghs G, Taylor PN, et al. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. The Lancet. junio de 2023;401(10391):1878-90.

- 1.518.028 👤 en 112 estudios de **cohortes prospectivos** realizados en 34 países de todo el mundo (Global Cardiovascular Risk Consortium)
- 5 factores de riesgo modificables: índice de masa corporal, presión arterial sistólica, colesterol no HDL, tabaquismo y diabetes.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Global Effect of Modifiable Risk Factors on Cardiovascular Disease and Mortality

The Global Cardiovascular Risk Consortium

ABSTRACT

BACKGROUND
Five modifiable risk factors are associated with cardiovascular disease and death from any cause. Studies using individual-level data to evaluate the regional and sex-specific prevalence of the risk factors and their effect on these outcomes are lacking.

METHODS
We pooled and harmonized individual-level data from 112 cohort studies conducted in 34 countries and 8 geographic regions participating in the Global Cardiovascular Risk Consortium. We examined associations between the risk factors (body-mass index, systolic blood pressure, non–high-density lipoprotein cholesterol, current smoking, and diabetes) and incident cardiovascular disease and death from any cause using Cox regression analyses, stratified according to geographic region, age, and sex. Population-attributable fractions were estimated for the 10-year incidence of cardiovascular disease and 10-year all-cause mortality.

RESULTS
Among 1,518,028 participants (54.1% of whom were women) with a median age of 54.4 years, regional variations in the prevalence of the five modifiable risk factors were noted. Incident cardiovascular disease occurred in 80,596 participants during a median follow-up of 7.3 years (maximum, 47.3), and 177,369 participants died during a median follow-up of 8.7 years (maximum, 47.6). For all five risk factors combined, the aggregate global population-attributable fraction of the 10-year incidence of cardiovascular disease was 57.2% (95% confidence interval [CI], 52.4 to 62.1) among women and 52.6% (95% CI, 49.0 to 56.1) among men, and the corresponding values for 10-year all-cause mortality were 22.2% (95% CI, 16.8 to 27.5) and 19.1% (95% CI, 14.6 to 23.6).

CONCLUSIONS
Harmonized individual-level data from a global cohort showed that 57.2% and 52.6% of cases of incident cardiovascular disease among women and men, respectively, and 22.2% and 19.1% of deaths from any cause among women and men, respectively, may be attributable to five modifiable risk factors. (Funded by the

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Blankenberg can be contacted at s.blankenberg@uke.de or at the University Heart and Vascular Center, Department for Cardiology, Center of Population Health Innovation, University Medical Center Hamburg–Eppendorf, Martinistr. 52, 20246 Hamburg, Germany.

A list of the investigators in the Global Cardiovascular Risk Consortium is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Magnussen, Ojeda, and Leong contributed equally to this article.

This article was published on August 26, 2023, at NEJM.org.

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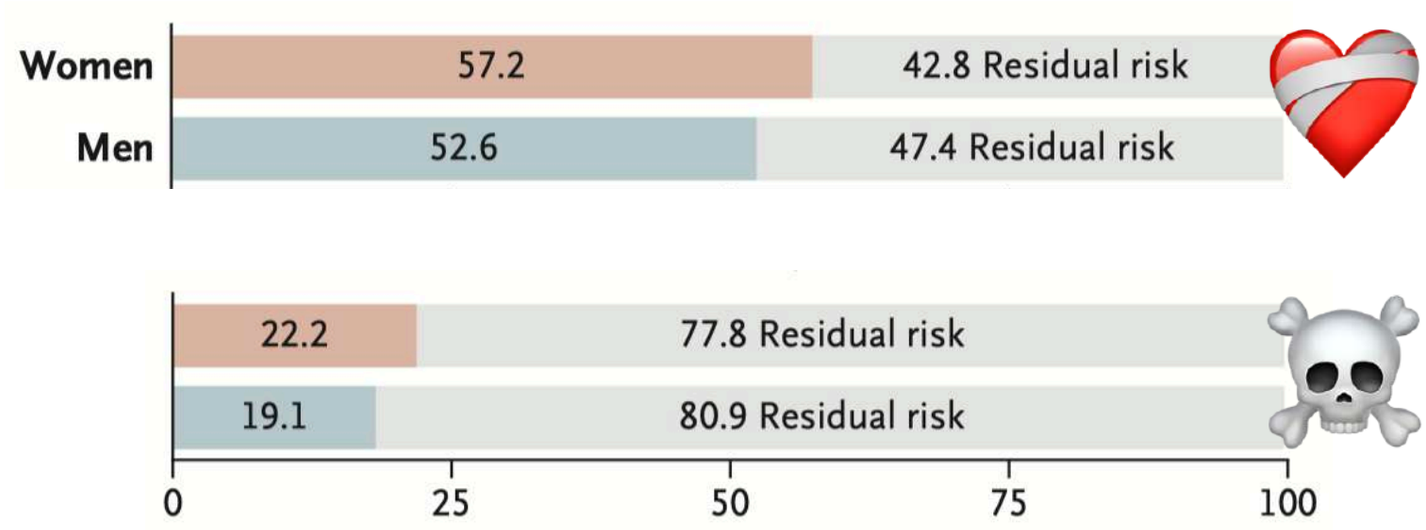
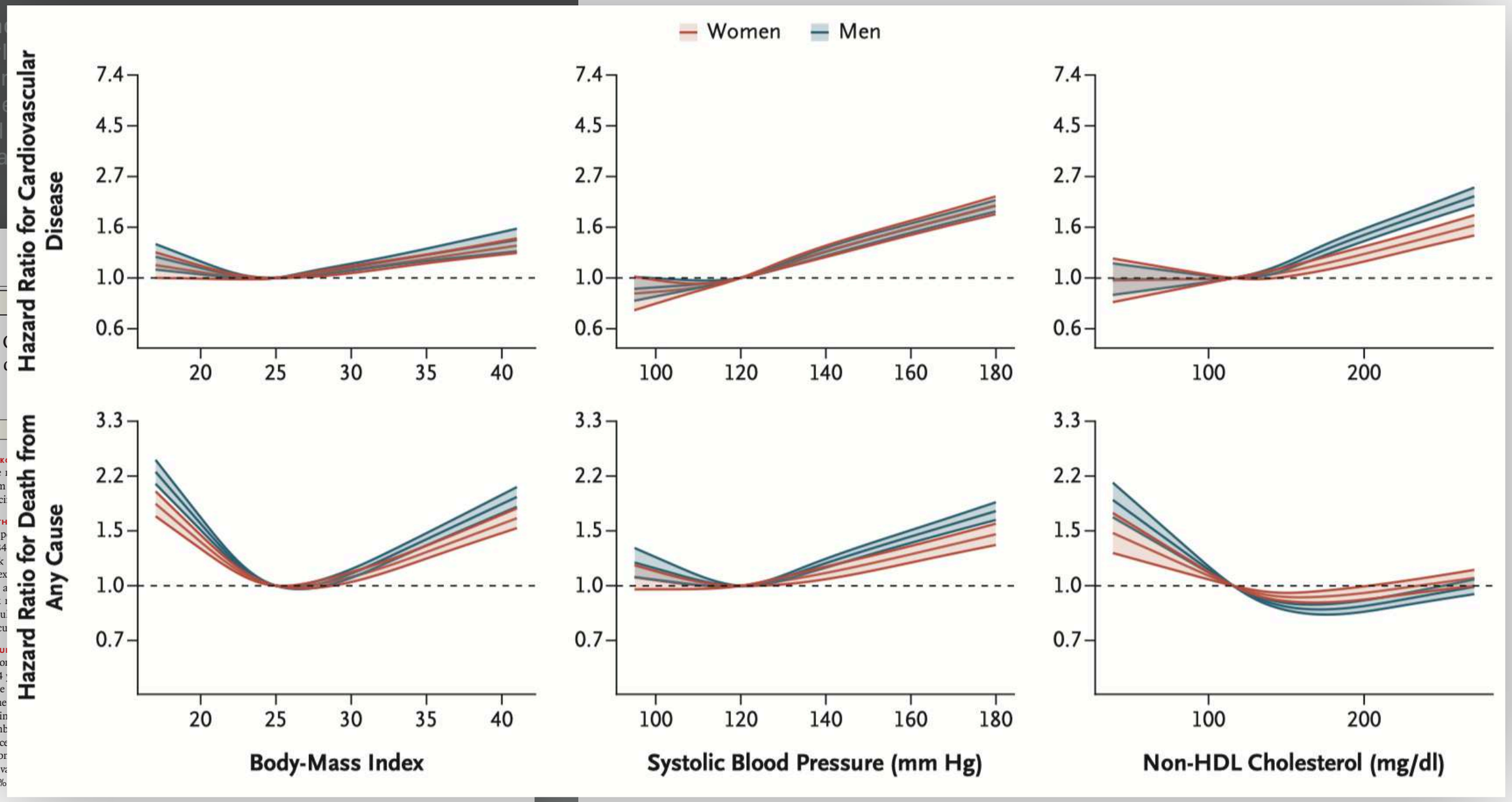
DOI: 10.1056/NEJMoa2206916



MICRORRESUMEN

La **PA sistólica** tiene el mayor potencial para la prevención de enfermedades CV

Figura 1. Asociaciones de los factores de riesgo continuos con la enfermedad cardiovascular y la muerte por cualquier causa. Se muestran los resultados de un análisis global de referencia a 1 año que tuvo en cuenta los efectos no lineales. Se excluyó a los participantes con enfermedad cardiovascular al inicio del estudio. Se utilizó la edad como escala temporal. Los cinco factores de riesgo, junto con el uso de medicación antihipertensiva, se incluyeron como covariables en los modelos [...]



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Consenso 2023 de actuación durante el ingreso hospitalario por IC aguda

J.M. Fernández-Rodríguez, J. Casado, F. Formiga et al., Resumen ejecutivo de la actualización 2023 del consenso de actuación básica durante el ingreso hospitalario por insuficiencia cardiaca aguda, Revista Clínica Española, https://doi.org/10.1016/j.rce.2023.06.001

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www.elsevier.es/rce

ARTÍCULO ESPECIAL

Resumen ejecutivo de la actualización 2023 del consenso de actuación básica durante el ingreso hospitalario por insuficiencia cardiaca aguda

J.M. Fernández-Rodríguez[a,b,*], J. Casado[c], F. Formiga[d], A. González-Franco[e], J.C. Arévalo[f], M. Beltrán[g], J.M. Cerqueiro González[h], P. Llàcer[a,b], L. Manzano[i], J.L. Morales-Rull[j], J. Pérez Silvestre[k] y A. Conde-Martel[l]

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[b] *Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, España*
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[f] *Servicio de Medicina Interna, Hospital Universitario de Badajoz, Badajoz, España*
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[i] *Servicio de Medicina Interna, Hospital Universitario Ramón y Cajal, Departamento de Medicina y Especialidades Médicas, Facultad de Medicina y Ciencias de la Salud, Universidad de Alcalá, IRYCIS, Madrid, España. Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, España*
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[l] *Servicio de Medicina Interna, Hospital Universitario de Gran Canaria Dr. Negrín, Universidad de Las Palmas, Las Palmas de Gran Canaria, España*

Recibido el 31 de mayo de 2023; aceptado el 22 de junio de 2023

PALABRAS CLAVE
Insuficiencia cardiaca aguda;

Resumen La insuficiencia cardiaca aguda (ICA) está asociada a una importante morbimortalidad, constituyendo la primera causa de hospitalización en mayores de 65 años en nuestro país. Las principales recomendaciones recogidas son: 1) al ingreso, se recomienda realizar una evaluación integral, considerando el tratamiento habitual y comorbilidades, ya que condicionan el

Tratamiento VO frente a IV para la endocarditis en pacientes seleccionados

Freling S, Wald-Dickler N, Banerjee J, Canamar CP, Tangpraphaphorn S, Bruce D, et al. Real-World Application of Oral Therapy for Infective Endocarditis: A Multicenter, Retrospective, Cohort Study. Clinical Infectious Diseases. 11 de septiembre de 2023;77(5):672-9.

Clinical Infectious Diseases

MAJOR ARTICLE

Real-World Application of Oral Therapy for Infective Endocarditis: A Multicenter, Retrospective, Cohort Study

Sarah Freling,[1,2] Noah Wald-Dickler,[1,2] Josh Banerjee,[1] Catherine P. Canamar,[1] Soodtida Tangpraphaphorn,[1] Dara Bruce,[3] Kusha Davar,[1] Fernando Dominguez,[1] Daniel Norwitz,[3] Ganesh Krishnamurthi,[1,2] Lilian Fung,[1,2] Ashley Guanzon,[1,4] Emi Minejima,[1,4] Michael Spellberg,[1] Catherine Spellberg,[1] Rachel Baden,[1] Paul Holtom,[1,2] and Brad Spellberg[1]

[1]Department of Medicine and Infectious Diseases, Los Angeles County + University of Southern California Medical Center, Los Angeles, California, USA; [2]Department of Medicine, Keck School of Medicine–University of Southern California, Los Angeles, California, USA; [3]Department of Integrative Anatomical Sciences, Keck School of Medicine–University of Southern California, Los Angeles, California, USA; and [4]Department of Pharmacy, University of Southern California Mann School of Pharmacy and Pharmaceutical Sciences, Los Angeles, California, USA

Background. We sought to compare the outcomes of patients treated with intravenous (IV)-only vs oral transitional antimicrobial therapy for infective endocarditis (IE) after implementing a new expected practice within the Los Angeles County Department of Health Services (LAC DHS).

Methods. We conducted a multicentered, retrospective cohort study of adults with definite or possible IE treated with IV-only vs oral therapy at the 3 acute care public hospitals in the LAC DHS system between December 2018 and June 2022. The primary outcome was clinical success at 90 days, defined as being alive and without recurrence of bacteremia or treatment-emergent infectious complications.

Results. We identified 257 patients with IE treated with IV-only (n = 211) or oral transitional (n = 46) therapy who met study inclusion criteria. Study arms were similar for many demographics; however, the IV cohort was older, had more aortic valve involvement, were hemodialysis patients, and had central venous catheters present. In contrast, the oral cohort had a higher percentage of IE caused by methicillin-resistant *Staphylococcus aureus*. There was no significant difference between the groups in clinical success at 90 days or last follow-up. There was no difference in recurrence of bacteremia or readmission rates. However, patients treated with oral therapy had significantly fewer adverse events. Multivariable regression adjustments did not find significant associations between any selected variables and clinical success across treatment groups.

Conclusions. These results demonstrate similar outcomes of real-world use of oral vs IV-only therapy for IE, in accord with prior randomized, controlled trials and meta-analyses.

Keywords. infective endocarditis; oral stepdown antibiotic therapy.

Three randomized, controlled trials have established that oral transitional therapy for infective endocarditis (IE) is at least as effective as intravenous (IV)-only therapy [1-3]. Indeed, in the largest such trial, oral therapy resulted in significantly better clinical response, lower relapse, and higher survival rates than IV-only therapy out to 5 years of follow-up [4, 5]. Systematic reviews have demonstrated extensive supporting pharmacological and observational data for oral therapy, and meta-analyses of randomized, controlled trials have confirmed that oral therapy is at least as effective as IV-only therapy for this disease [6, 7]. Nevertheless, oral therapy remains rarely used for bacteremia in practice and less so for endocarditis [8, 9].

One potential reason for slow uptake of the use of oral therapy for IE is that data describing practical, real-world outcomes of oral therapy outside the setting of carefully conducted randomized, controlled trials are limited. We recently implemented an evidence-based expected practice [10] defining the scope of oral transitional therapy for IE in the 3 acute care, public hospitals comprising the Los Angeles County Department of Health Services (LAC DHS). We sought to compare the outcomes of patients treated with oral transitional therapy with the outcomes of patients treated with IV-only therapy in a retrospective cohort study.

METHODS

MÁS LECTURAS DE INTERÉS...

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J.M. Fernández-Rodríguez
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Resultados
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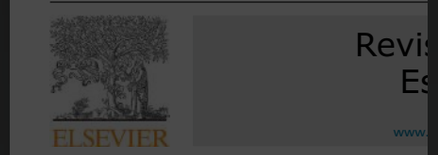
Mejor control glucémico con insulina icodec semanal que con glargina U100/día

Rosenstock J, Bain SC, Gowda A, Jódar E, Liang B, Lingvay I, et al. Weekly Icodec versus Daily Glargine U100 in Type 2 Diabetes without Previous Insulin. N Engl J Med. 27 de julio de 2023;389(4):297-308.



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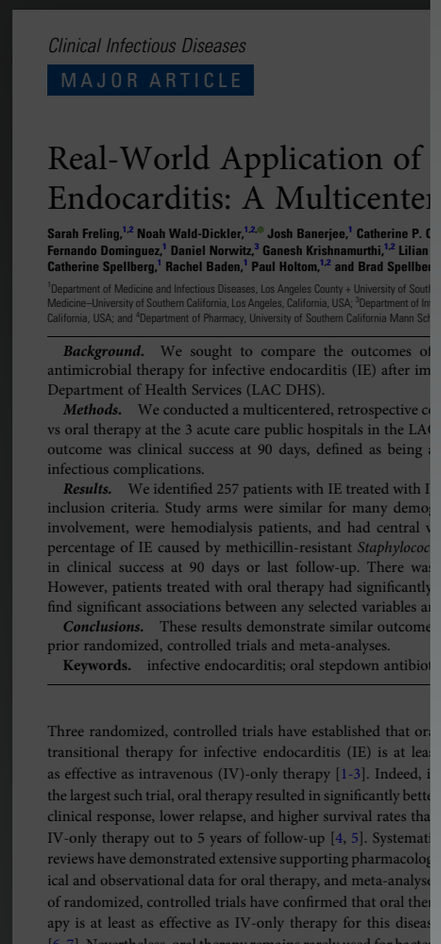

Clinical Infectious Diseases

MAJOR ARTICLE

Real-World Application of
Endocarditis: A Multicente

Sarah Freling,[1,2] Noah Wald-Dickler,[1,2,©] Josh Banerjee,[1] Catherine P. C
Fernando Dominguez,[1] Daniel Norwitz,[3] Ganesh Krishnamurthi,[1,2] Lilian
Catherine Spellberg,[1] Rachel Baden,[1] Paul Holtom,[1,2] and Brad Spellber
[1]Department of Medicine and Infectious Diseases, Los Angeles County + University of Soutl
Medicine–University of Southern California, Los Angeles, California, USA; [2]Department of In
California, USA; and [3]Department of Pharmacy, University of Southern California Mann Sch

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Keywords. infective endocarditis; oral stepdown antibio

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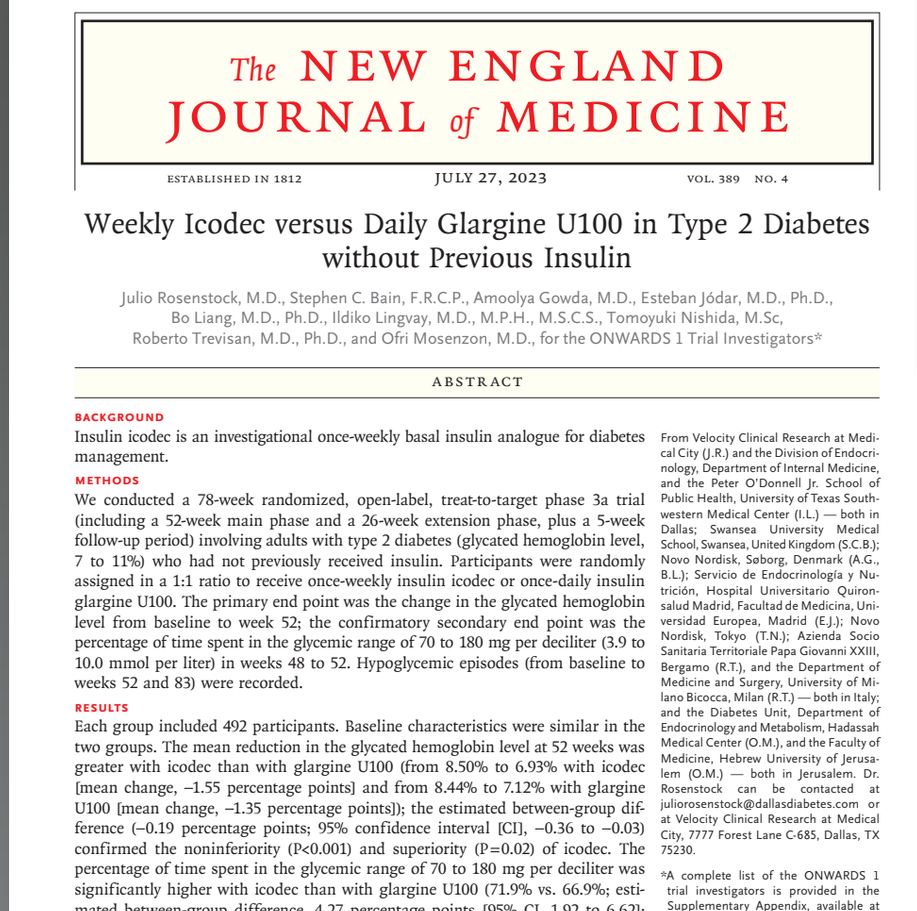

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 27, 2023 VOL. 389 NO. 4

Weekly Icodec versus Daily Glargine U100 in Type 2 Diabetes without Previous Insulin

Julio Rosenstock, M.D., Stephen C. Bain, F.R.C.P., Amoolya Gowda, M.D., Esteban Jódar, M.D., Ph.D., Bo Liang, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Tomoyuki Nishida, M.Sc, Roberto Trevisan, M.D., Ph.D., and Ofri Mosenzon, M.D., for the ONWARDS 1 Trial Investigators*

ABSTRACT

BACKGROUND
Insulin icodec is an investigational once-weekly basal insulin analogue for diabetes management.

METHODS
We conducted a 78-week randomized, open-label, treat-to-target phase 3a trial (including a 52-week main phase and a 26-week extension phase, plus a 5-week follow-up period) involving adults with type 2 diabetes (glycated hemoglobin level, 7 to 11%) who had not previously received insulin. Participants were randomly assigned in a 1:1 ratio to receive once-weekly insulin icodec or once-daily insulin glargine U100. The primary end point was the change in the glycated hemoglobin level from baseline to week 52; the confirmatory secondary end point was the percentage of time spent in the glycemic range of 70 to 180 mg per deciliter (3.9 to 10.0 mmol per liter) in weeks 48 to 52. Hypoglycemic episodes (from baseline to weeks 52 and 83) were recorded.

RESULTS
Each group included 492 participants. Baseline characteristics were similar in the two groups. The mean reduction in the glycated hemoglobin level at 52 weeks was greater with icodec than with glargine U100 (from 8.50% to 6.93% with icodec [mean change, −1.55 percentage points] and from 8.44% to 7.12% with glargine U100 [mean change, −1.35 percentage points]); the estimated between-group difference (−0.19 percentage points; 95% confidence interval [CI], −0.36 to −0.03) confirmed the noninferiority (P<0.001) and superiority (P=0.02) of icodec. The percentage of time spent in the glycemic range of 70 to 180 mg per deciliter was significantly higher with icodec than with glargine U100 (71.9% vs. 66.9%; estimated between-group difference, 4.27 percentage points [95% CI, 1.92 to 6.62]; P<0.001), which confirmed superiority. Rates of combined clinically significant or

From Velocity Clinical Research at Medical City (J.R.) and the Division of Endocrinology, Department of Internal Medicine, and the Peter O'Donnell Jr. School of Public Health, University of Texas Southwestern Medical Center (I.L.) — both in Dallas; Swansea University Medical School, Swansea, United Kingdom (S.C.B.); Novo Nordisk, Søborg, Denmark (A.G., B.L.); Servicio de Endocrinología y Nutrición, Hospital Universitario Quironsalud Madrid, Facultad de Medicina, Universidad Europea, Madrid (E.J.); Novo Nordisk, Tokyo (T.N.); Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo (R.T.), and the Department of Medicine and Surgery, University of Milano Bicocca, Milan (R.T.) — both in Italy; and the Diabetes Unit, Department of Endocrinology and Metabolism, Hadassah Medical Center (O.M.), and the Faculty of Medicine, Hebrew University of Jerusalem (O.M.) — both in Jerusalem. Dr. Rosenstock can be contacted at juliorosenstock@dallasdiabetes.com or at Velocity Clinical Research at Medical City, 7777 Forest Lane C-685, Dallas, TX 75230.

*A complete list of the ONWARDS 1 trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

MÁS LECTURAS DE INTERÉS...

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J.M. Fernández-Rodríguez
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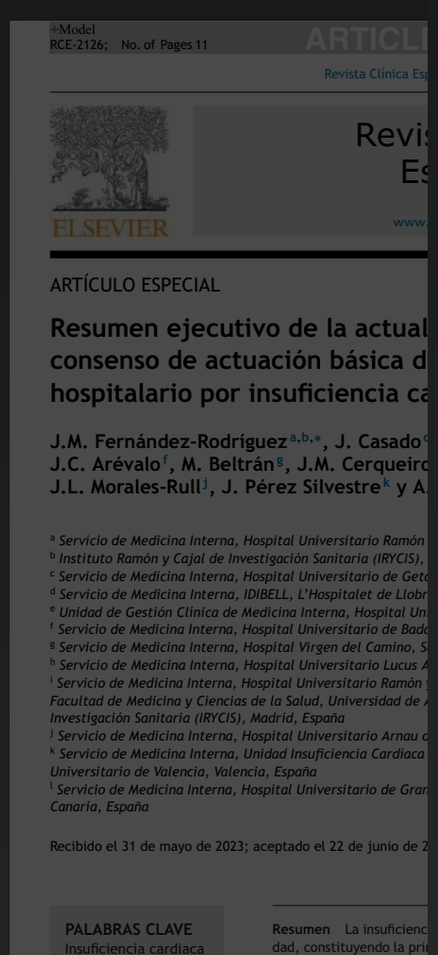
Vaughn VM, Gupta A, Petty LA, Malani AN, Osterholzer D, Patel PK, et al. A Statewide Quality Initiative to Reduce Unnecessary Antibiotic Treatment of Asymptomatic Bacteriuria. JAMA Intern Med. 1 de septiembre de 2023;183(9):933.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Resumen ejecutivo de la actual consenso de actuación básica d hospitalario por insuficiencia ca

J.M. Fernández-Rodríguez[a,b,*], J. Casado[c], J.C. Arévalo[f], M. Beltrán[g], J.M. Cerqueiro[h], J.L. Morales-Rull[j], J. Pérez Silvestre[k] y A.

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[b] Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS),
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Canaria, España

Recibido el 31 de mayo de 2023; aceptado el 22 de junio de 2

PALABRAS CLAVE
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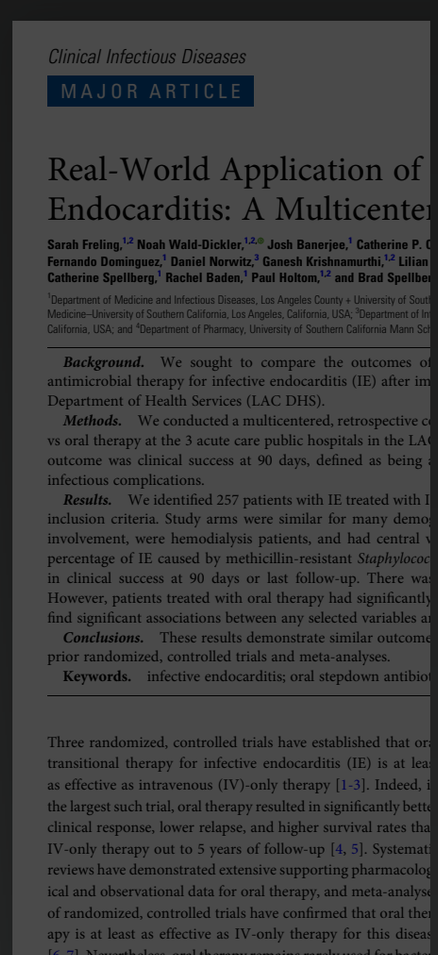
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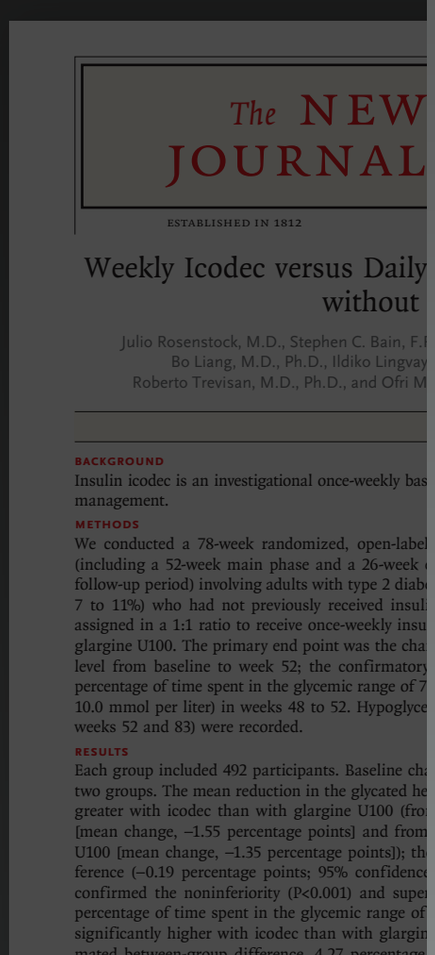
The NEW JOURNAL
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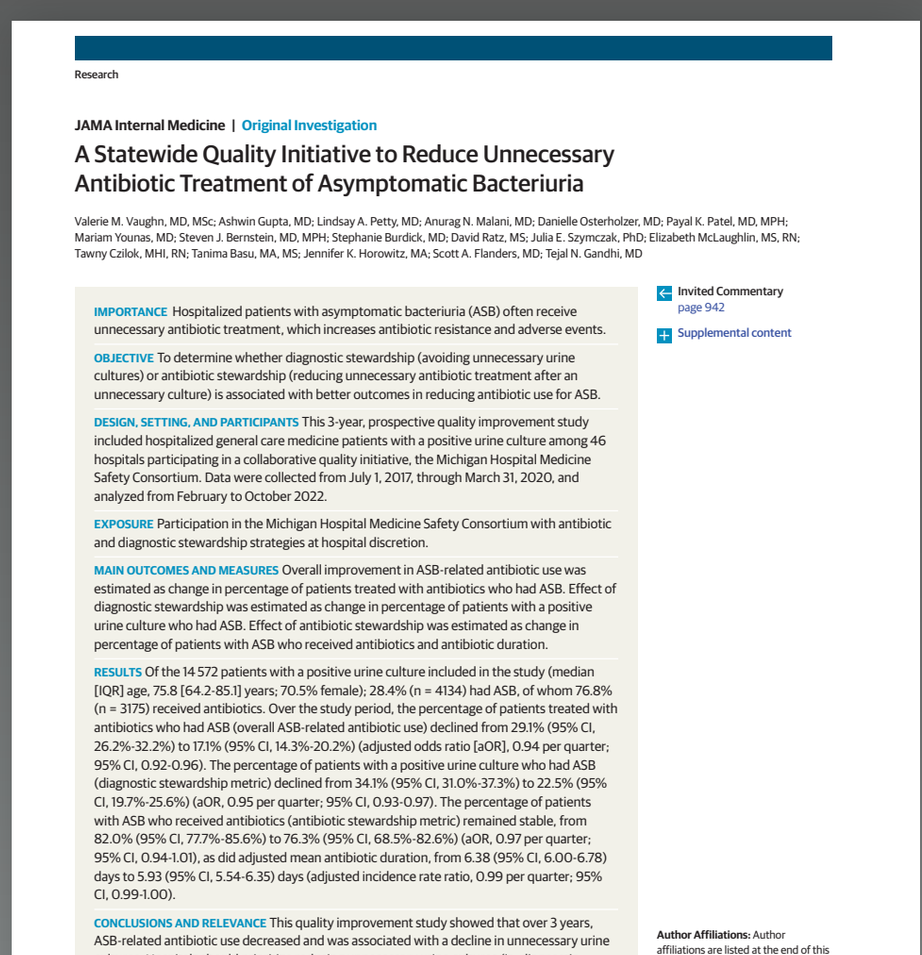
Research

JAMA Internal Medicine | Original Investigation

A Statewide Quality Initiative to Reduce Unnecessary Antibiotic Treatment of Asymptomatic Bacteriuria

Valerie M. Vaughn, MD, MSc; Ashwin Gupta, MD; Lindsay A. Petty, MD; Anurag N. Malani, MD; Danielle Osterholzer, MD; Payal K. Patel, MD, MPH; Mariam Younas, MD; Steven J. Bernstein, MD, MPH; Stephanie Burdick, MD; David Ratz, MS; Julia E. Szymczak, PhD; Elizabeth McLaughlin, MS, RN; Tawny Czilok, MHI, RN; Tanima Basu, MA, MS; Jennifer K. Horowitz, MA; Scott A. Flanders, MD; Tejal N. Gandhi, MD

IMPORTANCE Hospitalized patients with asymptomatic bacteriuria (ASB) often receive unnecessary antibiotic treatment, which increases antibiotic resistance and adverse events.

OBJECTIVE To determine whether diagnostic stewardship (avoiding unnecessary urine cultures) or antibiotic stewardship (reducing unnecessary antibiotic treatment after an unnecessary culture) is associated with better outcomes in reducing antibiotic use for ASB.

DESIGN, SETTING, AND PARTICIPANTS This 3-year, prospective quality improvement study included hospitalized general care medicine patients with a positive urine culture among 46 hospitals participating in a collaborative quality initiative, the Michigan Hospital Medicine Safety Consortium. Data were collected from July 1, 2017, through March 31, 2020, and analyzed from February to October 2022.

EXPOSURE Participation in the Michigan Hospital Medicine Safety Consortium with antibiotic and diagnostic stewardship strategies at hospital discretion.

MAIN OUTCOMES AND MEASURES Overall improvement in ASB-related antibiotic use was estimated as change in percentage of patients treated with antibiotics who had ASB. Effect of diagnostic stewardship was estimated as change in percentage of patients with a positive urine culture who had ASB. Effect of antibiotic stewardship was estimated as change in percentage of patients with ASB who received antibiotics and antibiotic duration.

RESULTS Of the 14 572 patients with a positive urine culture included in the study (median [IQR] age, 75.8 [64.2-85.1] years; 70.5% female); 28.4% (n = 4134) had ASB, of whom 76.8% (n = 3175) received antibiotics. Over the study period, the percentage of patients treated with antibiotics who had ASB (overall ASB-related antibiotic use) declined from 29.1% (95% CI, 26.2%-32.2%) to 17.1% (95% CI, 14.3%-20.2%) (adjusted odds ratio [aOR], 0.94 per quarter; 95% CI, 0.92-0.96). The percentage of patients with a positive urine culture who had ASB (diagnostic stewardship metric) declined from 34.1% (95% CI, 31.0%-37.3%) to 22.5% (95% CI, 19.7%-25.6%) (aOR, 0.95 per quarter; 95% CI, 0.93-0.97). The percentage of patients with ASB who received antibiotics (antibiotic stewardship metric) remained stable, from 82.0% (95% CI, 77.7%-85.6%) to 76.3% (95% CI, 68.5%-82.6%) (aOR, 0.97 per quarter; 95% CI, 0.94-1.01), as did adjusted mean antibiotic duration, from 6.38 (95% CI, 6.00-6.78) days to 5.93 (95% CI, 5.54-6.35) days (adjusted incidence rate ratio, 0.99 per quarter; 95% CI, 0.99-1.00).

CONCLUSIONS AND RELEVANCE This quality improvement study showed that over 3 years, ASB-related antibiotic use decreased and was associated with a decline in unnecessary urine cultures. Hospitals should prioritize reducing unnecessary urine cultures (ie, diagnostic stewardship) to reduce antibiotic treatment related to ASB.

Invited Commentary
page 942

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Contiene esta sesión, los artículos empleados, los descartados por cuestión de tiempo + bonus de revisiones y monográficos encontrados en el proceso de búsqueda bibliográfica.

¡Gracias!