Volumen 11, número 2 de 2024
https://doi.org/10.53853/encr.11.2.862

Decisiones Acertadas
Cuidando desde el conocimiento

REVISTA COLOMBIANA de Endocrinología Diabetes & Metabolismo

Consensus

Choosing Wisely in Endocrinology: Recommendations from an Expert Panel of the Colombian Association of Endocrinology, Diabetes, and Metabolism

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How to cite this article: Palacios-Bayona KL, Castaño-Ceballos PA, Restrepo-Giraldo LM, Builes-Montaño CE, Ramírez-Rincón A, Tovar-Cortes H, *et al*. Choosing Wisely in Endocrinology: Recommendations from an Expert Panel of the Colombian Association of Endocrinology, Diabetes, and Metabolism. Rev Colomb Endocrinol Diabet Metab. 2024;11(2):e862. https://doi.org/10.53853/encr.11.2.862

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E-ISSN: 2805-5853 | L-ISSN: 2389-9786

Submission: 15/Dec/2023 **Acceptance:** 10/May/2024 **Published:** 6/June/2024

Abstract

Context: In 2022, the Colombian Association of Endocrinology, Diabetes, and Metabolism (ACE) joined the Choosing Wisely initiative to prevent low-value medical practices.

Objective: To generate five evidence-based recommendations to decrease inappropriate clinical practices.

Methodology: A reviewing committee was established to identify "do not do" recommendations from ACE members. The most frequent recommendations were pre-selected, and a systematic literature search was conducted. Subsequently iterative rounds were conducted using the Delphi methodology to select the five recommendations that achieved the highest consensus among the panel of experts.

Results: Between October 2022 and April 2023, 117 active ACE members submitted a total of 211 recommendations. Of these, 109 were selected for further analysis. Subsequently, a Delphi panel identified five key recommendations, four of which addressed the excessive use of diagnostic tests, while the remaining one focused on therapeutic intervention.

Conclusions: To avoid unnecessary procedures, routine thyroid ultrasounds should not be performed on the general population or on hypothyroid individuals without changes in their physical examination. Requesting markers of bone turnover in patients with osteoporosis is also discouraged. Additionally, measuring basal insulin and/or post-glucose load in individuals who are overweight, obese, or have signs of insulin resistance is discouraged, along with indiscriminate measurements of vitamin D and unnecessary prescription of vitamin D supplements in the general population. The implementation of these recommendations could lead to a reduction in overdiagnosis and overtreatment of patients with endocrine conditions. This would help to improve resource management, quality of care, and clinical outcomes, benefiting both patients and the healthcare system.

Keywords: Endocrinology, Overdiagnosis, Overtreatment, Health Care Quality, Delivery of Health Care, Diagnostic Tests, Routine, Behavior, Prescriptions.

Highlights

- Do not order routine thyroid ultrasounds in the general population or in patients with hypothyroidism when the physical examination is normal.
- Do not request markers of bone turnover in patients with osteoporosis.
- Do not order basal insulin, post-load glucose, or use the HOMA index to assess insulin resistance in patients who are overweight, obese, or show clinical signs of insulin resistance.
- Do not perform routine measurements of vitamin D (25 [OH] vitamin D) in the general population.
- Do not routinely prescribe vitamin D, except in cases of deficiency (25 [OH] vitamin D < 12 ng/ml), osteomalacia, secondary hyperparathyroidism due to vitamin D deficiency, or in patients with osteoporosis at risk of hypocalcemia.

Decisiones acertadas en Endocrinología: recomendaciones de un panel de expertos de la Asociación Colombiana de Endocrinología, Diabetes y Metabolismo

Resumen

Contexto: en el año 2022 la Asociación Colombiana de Endocrinología, Diabetes y Metabolismo (ACE) se une a la iniciativa Decisiones Acertadas para evitar prácticas médicas excesivas.

Objetivo: generar cinco recomendaciones basadas en evidencia que permitan reconsiderar conductas inapropiadas en la práctica clínica.

Metodología: se estableció un comité revisor que recibió las recomendaciones de "no hacer" de los miembros de la ACE. Se realizó una preselección de las propuestas más frecuentes y se llevó a cabo una búsqueda sistemática de la literatura. Posteriormente, mediante la metodología Delphi, se realizaron rondas de iteración para seleccionar las cinco recomendaciones que lograron mayor consenso entre el panel de expertos.

Resultados: entre octubre de 2022 a abril de 2023, se recibieron propuestas de 117 miembros activos de la ACE. Se recopilaron 211 recomendaciones, de las cuales 109 fueron seleccionadas para su análisis posterior. Tras una evaluación minuciosa, se preseleccionaron

Destacados

- No ordene ecografías tiroideas de rutina en la población general ni en pacientes con hipotiroidismo cuando el examen físico es normal.
- No solicite marcadores de recambio óseo en pacientes con osteoporosis.
- No solicite insulina basal, poscarga de glucosa o utilice el índice HOMA para evaluar resistencia a la insulina en pacientes con sobrepeso, obesidad o signos clínicos de resistencia a la insulina.

las 20 recomendaciones más frecuentes. Luego, el panel Delphi eligió cinco recomendaciones, incluyendo cuatro centradas en el uso excesivo de pruebas diagnósticas y una de intervención terapéutica.

Conclusiones: se recomienda evitar la ecografía tiroidea de rutina en población general o hipotiroidea sin cambios en el examen físico, así como abstenerse de solicitar marcadores de recambio óseo en pacientes con osteoporosis. También se desaconseja la medición de insulina basal y/o poscarga de glucosa en individuos con sobrepeso, obesidad o signos de resistencia a la insulina, junto con mediciones indiscriminadas de vitamina D y la prescripción innecesaria de suplementos de vitamina D en la población general. Al evitar estas prácticas, se prioriza una atención selectiva y centrada en el paciente, lo que reduce el sobrediagnóstico y el sobretratamiento de patologías endocrinas. Estas decisiones mejoran la gestión de recursos, la calidad de la atención y los resultados clínicos, beneficiando tanto a los pacientes como al sistema de salud.

Palabras clave: endocrinología, sobrediagnóstico, sobretratamiento, calidad de la atención de salud, atención a la salud, pruebas diagnósticas de rutina, conducta, prescripciones.

- No realice mediciones rutinarias de vitamina D (25 [OH] vitamina D) en la población general.
- No prescriba vitamina D de forma rutinaria, salvo en casos de deficiencia (25 [OH] vitamina D < 12 ng/ml), osteomalacia, hiperparatiroidismo secundario a deficiencia de vitamina D o en pacientes con osteoporosis y riesgo de hipocalcemia.

Introduction

The widespread adoption of medical technologies, which often results in unnecessary tests, treatments, and procedures that may cause more harm than good, is a global concern (1). In response to this challenge, the Choosing Wisely initiative was launched in 2012 by the American Board of Internal Medicine (ABIM) in the United States, with the aim of advocating for evidence-based and appropriate medical practices (2,3). This initiative has achieved considerable international recognition, with active involvement from Latin American countries including Brazil, Colombia, and Argentina. Particularly noteworthy is Colombia's adoption of the initiative in May 2022 through the Colombian Association of Scientific Societies (ACSC), under the name *Decisiones Acertadas* (4).

Recent research, drawing on Medicare data, has shed light on the substantial contribution of specialists to healthcare spending on services that offer little or no value within healthcare systems (5). This trend is also evident among endocrinologists, who have been found to engage in a high number of unnecessary medical behaviors (6). These findings prompted the Colombian Association of Endocrinology, Diabetes, and Metabolism (ACE) to join the Choosing Wisely initiative in 2022.

This publication outlines five essential strategies put forward by ACE as part of the *Decisiones Acertadas* initiative. These strategies are designed to shift away from practices and interventions that research has shown to be limitedly effective. The findings underscore the importance of decreasing dependence on unnecessary medical technologies and procedures, aiming to improve the quality and safety of patient care in endocrinology.

Methodology

In October 2022, the collaboration between ACSC and ACE initiated the Choosing Wisely initiative in Endocrinology, focusing on a thoroughly reassessing field practices to establish specific improvement goals (Table 1). Utilizing a consensus strategy via two online Delphi method rounds, expert endocrinologists achieved a substantial consensus. This method allowed for an in-depth collection and analysis of specialist opinions (7–9). To minimize the impact of group conformity, participants received the results of the first round anonymously, enabling unbiased feedback and iterative refinement based on previous round outcomes (10).

The formulation of recommendations followed a systematic ten-stage approach:

1. Ethical considerations
2. Establishment of the review committee
3. Receipt and initial assessment of recommendations

4. Comprehensive review and categorization of recommendations
5. Systematic literature review and synthesis of evidence
6. Development and pilot testing of an initial questionnaire
7. Selection of the expert panel
8. Collection of responses and statistical analysis
9. Concluding meeting for dissemination and discussion of results
10. External validation of the final document

Table 1. General and Specific Objectives of the Decisiones Acertadas Initiative in Endocrinology

General objectives
Selecting five "do not" recommendations in Endocrinology clinical practice in Colombia to reduce the use of ineffective or unsafe technologies, thereby improving patient treatment quality and raising standards of care in our specialty.
Specific objectives
To assemble ACE members to start a self-regulatory process targeting the identification of unnecessary and inappropriate medical practices within Colombian endocrinology. To select five "do not" recommendations using a robust and reproducible methodology framework with the aim of serving as a foundation for future efforts to reassess practices in endocrinology. To design and execute a dissemination strategy for the chosen recommendations, tailored to healthcare professionals and the broader public, in order to promote the adoption of these recommendations. To assess the initiative's effectiveness in decreasing the utilization of non-recommended technologies by evaluating its impact on clinical practice. To promote critical thinking within the medical community regarding the selection of diagnostic tests, emphasizing the potential impact on therapeutic decisions and the risks associated with difficult-to-interpret results, with the goal of avoiding unnecessary interventions.

Source: Authors' own elaboration

1. Ethical considerations

This study was classified as risk-free, in accordance with Colombia's Ministry of Health Resolution No. 8430/1993. A Participation Agreement, signed prior to the study, highlighted the protection of participants' dignity and the integrity of data, assuring participants the right to withdraw at any time without repercussions. The research emphasized adherence to inclusion criteria to ensure objectivity and minimize biases, without offering financial compensation. In line with the Helsinki Declaration, the study mandated transparent result disclosure and a commitment to reveal any conflicts of interest or funding sources that might compromise ethical integrity.

2. Establishment of the review committee

The ACE formed a review committee comprising six experienced endocrinologists, three of whom specialized in epidemiology, tasked with evaluating the submitted recommendations. The primary responsibility of this committee was to preliminarily assess the quality and relevance of these recommendations before they were advanced to the expert panel for the consensus process. To safeguard the integrity and clinical pertinence of this process, the committee excluded individuals engaged in non-clinical functions within government health departments, Health Promotion Entities (*Entidades Promotoras de Salud, EPS*),

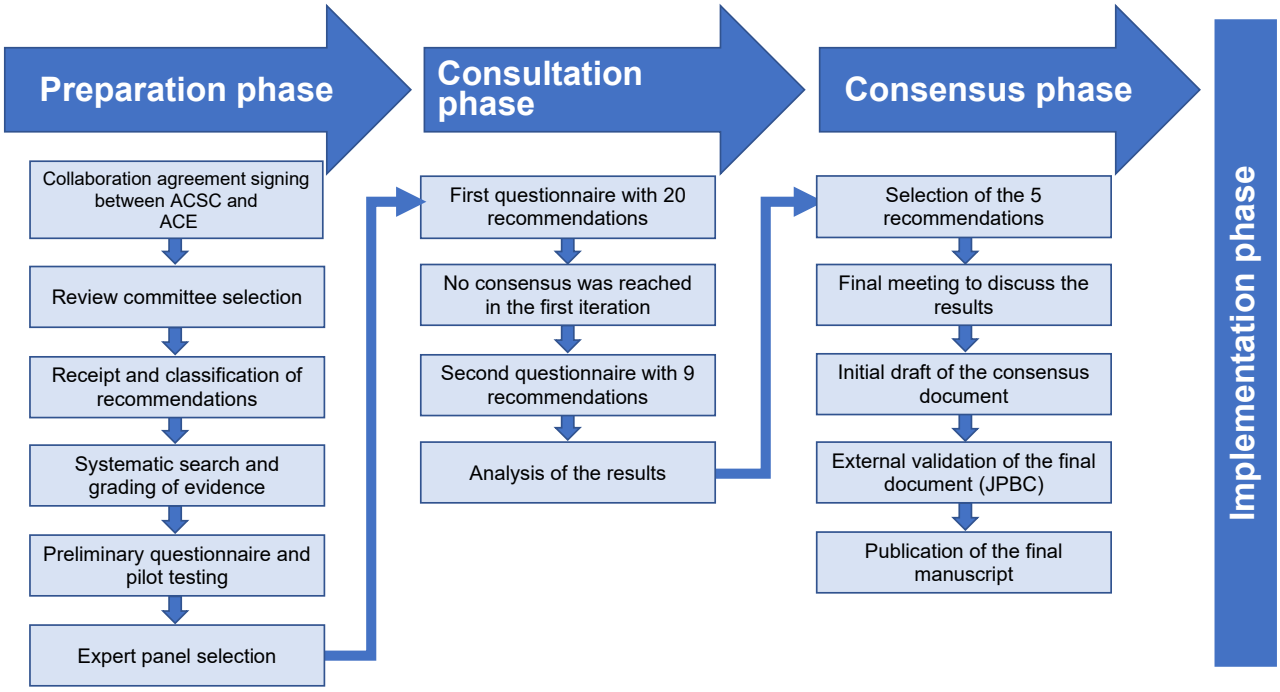

Figure 1. Flowchart of the Delphi Process for Developing Decisiones Acertadas Recommendations in Endocrinology

Source: Authors' own elaboration

payer organizations, or those affiliated with companies involved in the production or distribution of medical technologies. This exclusion was aimed at reducing potential conflicts of interest.

3. Receipt and initial assessment of recommendations

ACE members were invited to submit ideas and recommendations regarding "do not do" actions using the Google Forms platform. They were encouraged to ground their suggestions on uncertainty regarding utility or the lack of conclusive evidence of effectiveness or potential harm. Subsequently, a review was undertaken, applying exclusion criteria to eliminate ambiguous suggestions, opinions lacking scientific support, personal criteria without substantial basis, remarks targeting other specialties, and recommendations to address underuse, such as "Remember to...".

4. Comprehensive review and categorization of recommendations

After applying the exclusion criteria, the review committee performed a detailed evaluation of the remaining recommendations, organizing them into categories like medication classes, diagnostic support, surgical and non-surgical procedures, devices, and others. This classification, determined by the frequency of proposals from ACE members, was designed to enhance understanding and organization.

5. Systematic literature review and synthesis of evidence

A thorough literature review was conducted using PubMed, LILACS, Embase, and Google Scholar, focusing on articles published in English, Spanish, and Portuguese from 2013 to 2023, and augmented by relevant studies provided by the review committee members. The review committee utilized the "Levels of Evidence 2011" framework from the Oxford Centre for Evidence-Based Medicine to assess the evidence backing the shortlisted recommendations. Recommendations were graded with evidence levels from I to V, reflecting the strength and depth of the available research. To avoid information bias, these evidence levels were not initially revealed to the

Delphi panel but were made available during the deliberation rounds upon the panelists' requests.

6. Development and pilot testing of an initial questionnaire

A questionnaire incorporating the first 20 preselected recommendations was crafted and piloted with three endocrinologists, each possessing over five years of clinical experience spanning academia, public hospitals, and private practice, who were not involved in the study. Feedback from this pilot was used to enhance the wording and structure of the questionnaire.

7. Selection of the expert panel

Expert panel participants from various regions of Colombia were selected via convenience sampling, based on criteria including over five years of clinical endocrinology experience with a minimum caseload of 50 patients weekly. Additionally, participants were required to demonstrate engagement in continuous education with relevant certifications, contribute to scientific dialogue through publications and conference participation, and receive peer recognition through awards and endorsements (11,12). To ensure anonymity and impartiality, participants were assigned unique identifiers, P#R#, where "P#" represents the participant number from 1 to 11 and "R#" denotes the region of origin from 1 to 6. This system aimed to minimize bias and foster an environment conducive to the unbiased exchange of professional insights and critiques.

8. Collection of responses and statistical analysis

After the pilot test, the review process continued with a two-round online survey on Google Forms. In the first round, experts rated the relevance of each recommendation on an ordinal Likert scale from 1 (completely disagree) to 9 (completely agree), with 5 indicating neutrality (12,13). A consensus for a recommendation was established at an agreement level of ≥ 70%, with disagreement noted between 31% and 69%, and a consensus against recognized at < 30%. If the first round failed to achieve sufficient consensus, the review committee advanced the top nine recommendations to a second iteration round. During this phase, participants re-evaluated these recommendations, applying the Likert scale for new ratings. This method led to the identification of the final five recommendations that garnered the highest consensus.

9. Concluding meeting for dissemination and discussion of results

A concluding meeting was held to disseminate the study's findings, where detailed results were shared and deliberated with the review committee, peer reviewers, ACE members, and participating scientific societies. This session solidified the consensus and collected further input. Subsequently, an action plan for the implementation and distribution of the recommendations was developed, engaging experts, the scientific community, and the target patient groups in an interactive manner. The final five recommendations, along with contributions from other scientific societies, will be made available on the following website: http://decisionesacertadas.sociedadescientificas.com

10. External validation of the final document

After finalizing the draft containing the top five recommendations, which were collaboratively shaped by all consensus participants, it underwent review by an external expert in shared decision-making and overdiagnosis from the Mayo Clinic (JPBC). This review aimed to validate the quality and relevance of the recommendations.

Results

Between October 2022 and April 2023, ACE conducted the recommendation selection process for the *Decisiones Acertadas* initiative. A reviewing committee, comprised of KLPB, PACC, LMRG, CEBM, ARR, and HV-U, evaluated 211 submissions from 117 active ACE members via Google Forms. After applying exclusion criteria, 109 recommendations were deemed suitable for detailed analysis. Subsequently, the 20 most frequent recommendations were chosen (Table 2), with an analysis conducted on the evidence associated with these recommendations (Table 3).

Table 2. Preliminary Categorization of Recommendations by 117 ACE Participants

INCLUDED RECOMMENDATIONS (N= 109)	
Classification	Number of recommendations
Medications	21
Diagnostic tools	75
Surgical procedures	3
Non-surgical procedures	1
Medical devices	1
Others	8
EXCLUDED RECOMMENDATIONS (N=102)	
Reason for Exclusion	**Number of recommendations**
Ambiguous suggestions	7
Opinions lacking scientific support	5
Personal criteria without substantial basis	1
Remarks targeting other specialties	83
Recommendations to address underuse, for example, "Remember to..."	6

Source: Authors' own elaboration

Table 3. Systematic Search Algorithm in Databases

1. Statement: Do not order routine thyroid ultrasounds in the general population or in patients with hypothyroidism when the physical examination is normal.

PICODT Question: Should thyroid ultrasound be routinely ordered in the general population, patients with Hashimoto's thyroiditis, or patients with abnormal laboratory tests who do not present abnormal findings on physical examination?

- Population: General population, patients with Hashimoto's thyroiditis, and patients with abnormal laboratory tests.
- Intervention: Thyroid ultrasound.
- Comparator: Not performing thyroid ultrasound.
- Outcome: Diagnosis of thyroid cancer, diagnosis of thyroid nodules, fine needle aspiration, thyroidectomy, and radioactive iodine therapy.

- Study design included: Clinical practice guidelines, editorials, narrative reviews, opinion articles, systematic reviews.
- Time (publication of studies): January 2012 to May 2023.

Keywords:

- English: Task forces, advisory committees, ultrasonography, Hashimoto disease, thyroid function test, overdiagnosis, overtreatment, thyroid neoplasms, biopsies, fine needle aspiration, iodine radioisotopes.
- Portuguese: Comitês consultivos, ultrassonografia, doença de Hashimoto, testes de função tireóidea, sobrediagnóstico, sobretratamento, neoplasias da glândula tireoide, biópsia por agulha fina, iodo.
- Spanish: comités consultivos, ecografía, enfermedad de Hashimoto, pruebas de función de la tiroides, sobrediagnóstico, sobretratamiento, neoplasias de la tiroides, biopsia con aguja fina, yodo.

Search strategy*:

- Pubmed: (((((((((task forces[MeSH Terms]) OR (advisory committee[MeSH Terms])) AND (Ultrasonography[MeSH Terms])) AND (hashimoto disease[MeSH Terms])) OR (thyroid function test[MeSH Terms])) AND (Overdiagnosis)) OR (Overtreatments)) OR (thyroid neoplasms[MeSH Terms])) OR (iodine radioisotopes[MeSH Terms])) OR (biopsies, fine needle aspiration[MeSH Terms]). Filters applied: Consensus Development Conference, Editorial, Government Publication, Guideline, Meta-Analysis, Personal Narrative, Practice Guideline, Review, Systematic Review, Humans, English, Portuguese, Spanish, from 2012/1/1 - 2023/5/30.
- EMBASE: (task forces OR advisory committee) AND (Ultrasonography) AND (thyroid function test) AND (Overdiagnosis OR Overtreatments OR thyroid neoplasms OR iodine radioisotopes OR biopsies, fine needle aspiration).
- LILCAS: Ultrasonography [Palavras] and thyroid function test [Palavras] or hashimoto disease [Palavras]

2. Statement: Do not request markers of bone turnover in patients with osteoporosis.

PICODT Question: Should bone turnover markers be requested in patients with osteoporosis to define treatment, monitor the condition, or prior to invasive dental procedures?

- Population: Patients with osteoporosis.
- Intervention: Bone turnover markers.
- Comparator: Not performing bone turnover markers.
- Outcome: Treatment for osteoporosis, monitoring of osteoporosis, and invasive dental procedures.
- Study designs included: Clinical practice guidelines, Expert consensus, Narrative reviews, Opinion articles, Systematic reviews, Case-control studies, Meta-analyses.
- Time (publication dates of studies): January 2005 to May 2023

Keywords:

- English: osteoporosis, osteogenesis, osteocalcin, alkaline phosphatase, bone resorption, hydroxyproline, reference standards.
- Portuguese: osteoporose, osteogênese, osteocalcina, fosfatase alcalina, reabsorção ossea, hidroxiprolina, padrões de referência.
- Spanish: osteoporosis, osteogénesis, osteocalcina, fosfatasa alcalina, resorción ósea, hidroxiprolina, estándares de referencia.

Search strategy *:

- Pubmed: (((((osteoporosis[MeSH Terms]) AND (osteogenesis[MeSH Terms])) OR (osteocalcin[MeSH Terms])) OR (alkaline phosphatase[MeSH Terms])) OR (bone resorption[MeSH Terms])) OR (hydroxyproline[MeSH Terms]). Filters applied: Clinical Trial, Consensus Development Conference, Editorial, Government Publication, Guideline, Meta-Analysis, Personal Narrative, Practice Guideline, Review, Systematic Review, Humans, English, Portuguese, Spanish, from 2005/1/1 - 2023/5/30.
- EMBASE: (osteoporosis) AND (osteogenesis OR osteocalcin OR alkaline phosphatase OR bone resorption OR hydroxyproline)
- LILACS:
  - osteoporosis [Palabras] and osteogenesis [Palabras] or bone resorption [Palabras]
  - osteoporosis [Palabras] and osteocalcin [Palabras] or alkaline phosphatase [Palabras]
  - osteoporosis [Palabras] and bone resorption [Palabras] or hydroxyproline [Palabras]

3. Statement: Do not order basal insulin, post-load glucose, or using the HOMA index to assess insulin resistance in patients who are overweight, obese, or show clinical signs of insulin resistance.

PICODT Question: In patients with overweight, obesity, or clinical signs of insulin resistance, should basal insulin test, glucose post-load insulin test, and/or Homeostasis Model Assessment (HOMA) be requested to evaluate insulin resistance?

- Population: Patients with overweight, obesity, or clinical signs of insulin resistance.
- Intervention: Basal insulin test, glucose post-load insulin test, and/or Homeostasis Model Assessment (HOMA).
- Comparator: Not performing basal insulin test, glucose post-load insulin test, and/or HOMA index.
- Outcome: Insulin resistance.
- Study Designs included: Clinical practice guidelines, Expert consensus, Narrative reviews, Opinion articles, Systematic reviews, Randomized controlled trials, Meta-analyses.
- Time Frame (Publication Dates of Studies): January 2008 to May 2023

Keywords:

- English: mass screening, task forces, overweight, Obesity, insulin resistance,
- Portuguese: programas de rastreamento, sobrepeso, obesidade, resistência à insulina,
- Spanish: tamizaje masivo, sobrepeso, obesidad, resistencia a la insulina,

Search strategy *:

- Pubmed: (((mass screening[MeSH Terms]) AND (overweight[MeSH Terms])) OR (Obesity[MeSH Terms])) AND (insulin resistance[MeSH Terms]). Filters applied: Consensus Development Conference, Editorial, Government Publication, Guideline, Meta-Analysis, Practice Guideline, Randomized Controlled Trial, Review, Systematic Review, Humans, English, Portuguese, Spanish, from 2008/1/1 - 2023/5/30.
- EMBASE: (mass screening OR task forces) AND (overweight OR Obesity) AND (insulin resistance)
- LILACS:
  - overweight [Palabras] or Obesity [Palabras] and insulin resistance [Palabras]
  - mass screening [Palabras] and overweight [Palabras] and insulin resistance [Palabras]
  - mass screening [Palabras] and Obesity [Palabras] and insulin resistance [Palabras]

4. Statement: Do not perform routine measurements of vitamin D (25 [OH] vitamin D) in the general population.

PICODT Question: Should the measurement of 25-hydroxy vitamin D be routinely requested in the general population?

- Population: General population.
- Intervention: Measurement of 25-hydroxy vitamin D.
- Comparator: Not performing measurement of 25-hydroxy vitamin D.
- Outcome: Vitamin D deficiency, vitamin D insufficiency, mortality, risk of fractures, cost-effectiveness.
- Study designs included: Clinical practice guidelines, Narrative reviews, Opinion articles, Systematic reviews, Cost-effectiveness evaluation.
- Time Frame (Publication Dates of Studies): January 2013 to May 2023

Keywords:

- English: mass screening, task forces, Vitamin D, vitamin d deficiencies.
- Portuguese: programas de rastreamento, Vitamina D, deficiência de Vitamina D.
- Spanish: tamizaje masivo, Vitamina D, deficiencia de Vitamina D.

Search strategy *:

- Pubmed: ((mass screening[MeSH Terms]) AND (Vitamin D[MeSH Terms])) OR (vitamin d deficiency[MeSH Terms]). Filters applied: Consensus Development Conference, Editorial, Government Publication, Guideline, Meta-Analysis, Personal Narrative, Practice Guideline, Systematic Review, Humans, English, Portuguese, Spanish, from 2013/1/1 - 2023/5/30.
- EMBASE: (mass screening) AND (Vitamin D OR vitamin d deficiencies)
- LILACS: mass screening [Palabras] and Vitamin D [Palabras] or vitamin d deficiency [Palabras]

5. Statement: ***Do not routinely prescribe vitamin D, except in cases of deficiency (25 [OH] vitamin D < 12 ng/ml), osteomalacia, secondary hyperparathyroidism due to vitamin D deficiency, or in patients with osteoporosis at risk of hypocalcemia.***

PICODT Question: What are the indications for initiating supplementation of 25-hydroxy vitamin D?

- Population: Patients requiring initiation of supplementation with 25-hydroxy vitamin D.
- Intervention: Supplementation with 25-hydroxy vitamin D.
- Comparator: Not supplementing with 25-hydroxy vitamin D.
- Outcome: Osteomalacia, secondary hyperparathyroidism due to vitamin D deficiency, Osteoporosis.
- Study designs included: Randomized controlled trial, systematic review, meta-analysis, Narrative reviews, Opinion articles.
- Time (Publication Dates of Studies): January 2017 to May 2023

Keywords:

- English: cholecalciferol, calcifediol, vitamin d deficiency, hyperparathyroidism, Osteoporosis.
- Portuguese: colecalciferol, calcifediol, deficiência de vitamina D, osteomalacia, hiperparatireoidismo, osteoporose
- Spanish: colecalciferol, calcifediol, deficiencia de vitamina D, osteomalacia, hiperparatiroidismo, osteoporosis

Search strategy *:

- Pubmed: ((((cholecalciferol[MeSH Terms]) OR (calcifediol[MeSH Terms])) AND (vitamin d deficiency[MeSH Terms])) OR (hyperparathyroidism[MeSH Terms])) OR (osteoporosis[MeSH Terms]). Filters applied: Consensus Development Conference, Editorial, Government Publication, Guideline, Meta-Analysis, Practice Guideline, Review, Systematic Review, Humans, English, Portuguese, Spanish, from 2017/1/1 - 2023/5/30.
- EMBASE: (cholecalciferol OR calcifediol) AND (vitamin d deficiency OR hyperparathyroidism OR osteoporosis)
- LILACS:
  - cholecalciferol [Palabras] or calcifediol [Palabras] and vitamin d deficiency [Palabras]
  - cholecalciferol [Palabras] or calcifediol [Palabras] and hyperparathyroidism [Palabras]
  - cholecalciferol [Palabras] or calcifediol [Palabras] and osteoporosis [Palabras]

Note: *It wasn't necessary to include keywords in languages other than English in the search formulas. This is because, within the filters applied in each of the search engines, the search is delimited to the three corresponding languages (English, Spanish, and Portuguese). Therefore, the articles found in the search correspond solely and exclusively to these three languages.

Source: Authors' own elaboration

The expert panel for the Delphi process comprised 11 endocrinologists (Table 4), representing diverse regions of the country: Atlantic Coast (SEGB), Central Region (AMSO, HTC), Coffee Region (AMS), Northwestern Region (ARG, CABB), Northeastern Region (LPPS, JAMM, JBPB), and Southwest Region (KRE, DNPG). Anonymity of interventions and panelists was maintained until the second round of iteration. During the initial iteration round, one panelist requested a synthesis of evidence related to insulin measurement, while three others requested information related to vitamin D. The selection of recommendations in the first Delphi round was based on group median and arithmetic mean scores, as well as agreement levels on an 8 and 9-point Likert scale (Table 5). Since all 20 recommendations received a group median of 9, the reviewing committee chose 9 recommendations for the second iteration (Table 6). The top 5 recommendations with the highest percentage of agreement among participants were then selected.

Table 4. Expert Panel Composition (P#R#): Participants Identified by Participant Number and Region of Origin

Participant	Practice >5 years; >50 patients/week	Highly skilled	Previous contributions	Peer recognition
P1R1	Yes	Yes	Conference speaker, national publication	Positive referrals from other endocrinologists
P2R2	Yes	Yes	Conference speaker, national/ international publication	Committee of experts

P3R2	Yes	Yes	Conference speaker, national/ international publication	Committee of experts
P4R3	Yes	Yes	Conference speaker, national publication	Positive referrals from other endocrinologists
P5R4	Yes	Yes	Conference speaker, national/ international publication	Committee of experts, ACE 2016 Academic Excellence Award
P6R4	Yes	Yes	Conference speaker, national/ international publication	Committee of experts, ACE 2014 Academic Excellence Award
P7R5	Yes	Yes	Conference speaker, continuing medical education	Positive referrals from other endocrinologists
P8R5	Yes	Yes	Conference speaker, national publication	Positive referrals from other endocrinologists
P9R5	Yes	Yes	Conference speaker, national publication	Positive referrals from other endocrinologists
P10R6	Yes	Yes	Conference speaker, national publication	Committee of experts
P11R6	Yes	Yes	Conference speaker, national/ international publication	Committee of experts

Source: Authors' own elaboration

Table 5. Initial Iteration Results of the Twenty Initial Questions

Statement	Mean	Median	Agreement (%)
Do not order routine thyroid ultrasounds in the general population or in patients with hypothyroidism when the physical examination is normal.	8.9	9.0	100
Do not request markers of bone turnover in patients with osteoporosis.	8.7	9.0	90.9
Do not perform routine measurements of vitamin D (25 [OH] vitamin D) in the general population.	8.4	9.0	90.9
Do not order basal insulin, post-load glucose, or use the HOMA index to assess insulin resistance in patients who are overweight, obese, or that show clinical signs of insulin resistance.	8.7	9.0	90.9

Do not routinely prescribe vitamin D, except in cases of deficiency (25 [OH] vitamin D < 12 ng/ml), osteomalacia, secondary hyperparathyroidism due to vitamin D deficiency, or in patients with osteoporosis at risk of hypocalcemia.	8.7	9.0	100
Do not order bone densitometry in women under 65 years of age or men under 70 years of age who do not present risk factors for osteoporosis.	8.7	9.0	100
Do not order continuous glucose monitoring in patients on oral or injectable antidiabetic treatment with low risk of hypoglycemia.	8.5	9.0	90.9
Do not prescribe medication for patients with prediabetes without first implementing lifestyle changes.	8.4	9.0	81.8
Do not routinely prescribe levothyroxine in individuals with subclinical hypothyroidism. Based on evidence from observational studies, its use may be considered in individuals under 65 years with persistently elevated TSH levels (e.g., >7 mIU/L), or in individuals over 65 years with TSH >10 mIU/L, or in the context of assisted reproductive therapies with TSH > 4 mIU/ml.	8.3	9.0	72.7
Do not prescribe antiresorptive agents without clear indication, for example in patients with low bone mass without criteria for initiation, and in patients <50 years old (only with alteration in the Z-score).	8.9	9.0	100
Do not prescribe medications such as ibandronate if there are more appropriate alternatives available for the management of osteoporosis.	8.9	9.0	100
Do not order FSH, LH, or estradiol in women who are receiving exogenous sex hormones (oral contraceptives, injectable contraceptives, subdermal implants, hormone replacement therapy).	9.0	9.0	100
Do not order routine petrosal sinus sampling in all patients with Cushing's disease.	7.8	9.0	81.8
Do not order basal growth hormone (basal GH) for the study of acromegaly or under suspicion of autonomous growth hormone secretion.	9.0	9.0	100
Do not prescribe osteoporosis therapy without clarifying if there is an underlying secondary cause.	8.6	9.0	90.9

Do not order fine-needle aspiration biopsy (FNAB) for thyroid nodules < 1 cm or in patients with poor life expectancy.	8.7	9.0	90.9
Do not order thyroid ultrasound at intervals of less than one year for low-risk thyroid nodules, according to the ATA/TIRADS classification.	8.9	9.0	100
Do not order free testosterone to investigate hypogonadism in men or hyperandrogenism or hypoactive sexual desire disorder in women.	8.3	9.0	72.7
Do not order plasma catecholamines, urine catecholamines, chromogranin A, vanillylmandelic acid, or homovanillic acid in patients suspected of pheochromocytoma or paraganglioma. Instead of these tests, request fractionated metanephrines and normetanephrines in urine or plasma.	8.7	9.0	90.9
Do not order a pooled prolactin test when suspecting hyperprolactinemia.	9.0	9.0	100

Source: Authors' own elaboration

Table 6. Results of the Second Iteration of the Nine Preselected Questions

Statement	Mean	Median	% Agreement
Do not order routine thyroid ultrasounds in the general population or in patients with hypothyroidism when the physical examination is normal.	8.9	9.0	100
Do not request markers of bone turnover in patients with osteoporosis.	8.7	9.0	100
Do not perform routine measurements of vitamin D (25 [OH] vitamin D) in the general population.	8.5	9.0	87.5
Do not order basal insulin, post-load glucose, or use the HOMA index to assess insulin resistance in patients who are overweight, obese, or that show clinical signs of insulin resistance.	8.4	9.0	87.5
Do not routinely prescribe vitamin D, except in cases of deficiency (25 [OH] vitamin D < 12 ng/ml), osteomalacia, secondary hyperparathyroidism due to vitamin D deficiency, or in patients with osteoporosis at risk of hypocalcemia.	8.5	9.0	88.8

Do not order continuous glucose monitoring in patients on oral or injectable antidiabetic treatment with low risk of hypoglycemia.	7.8	8.0	66.7
Do not prescribe medication for patients with prediabetes without first implementing lifestyle changes.	7.4	8.0	66.7
Do not routinely prescribe levothyroxine in individuals with subclinical hypothyroidism. Based on evidence from observational studies, its use may be considered in individuals under 65 years with persistently elevated TSH levels (e.g., >7 mIU/L), or in individuals over 65 years with TSH >10 mIU/L, or in the context of assisted reproductive therapies with TSH > 4 mIU/ml.	8.0	8.0	55.5
Do not prescribe osteoporosis therapy without clarifying if there is an underlying secondary cause.	7.6	8.0	62.5

Source: Own elaboration

Recommendations from the Experts

1. Do not order routine thyroid ultrasounds in the general population or patients with hypothyroidism when the physical examination is normal.

Results of the second iteration: Median of 9.0 and 100% agreement rate.

Justification: The recommendation against routine thyroid ultrasounds in patients without detectable abnormalities during clinical examination is grounded in the phenomenon of overdiagnosis in thyroid cancer. This has led to a significant increase in the detection of small tumors, particularly those measuring less than 1 cm, without a corresponding rise in mortality rates (14–16). Consequently, unnecessary treatments such as fine needle aspirations, thyroidectomies, and radioactive iodine therapies have become prevalent (17,18). However, these interventions not only lack significant impact on recurrence or mortality rates (19) but also have the potential to negatively impact the long-term well-being of patients (20,21).

Studies indicate that patients may experience emotional responses similar to those observed with other malignancies, despite low-risk thyroid cancer typically having a less aggressive clinical course (22–26). Additionally, it is crucial to consider the additional economic burden, as managing thyroid cancer entails substantial costs in the Colombian context (27). Therefore, it is imperative to refrain from indiscriminate thyroid ultrasounds and instead utilize them judiciously for cases with suitable indications (18). This recommendation does not apply to patients with high-risk conditions, such as mutations in the RET gene for multiple endocrine neoplasia type 2 (MEN 2), patients with three or more family members with thyroid carcinoma, and patients with prior neck radiation (28–30).

2. Do not request markers of bone turnover in patients with osteoporosis.

Results of the second iteration: Median of 9.0 and 100% agreement rate.

Justification: The recommendation against using bone turnover markers in patients with osteoporosis, whether to assess treatment efficacy and adherence or before undergoing invasive dental procedures, is based on various factors. These factors include the variability in bone turnover marker results (31,32), lack of standardization in their measurement (31), and weak correlation with fracture risk and mandibular osteonecrosis (33,34). Additionally, research suggests that these markers lack reliable predictive ability in the context of invasive dental procedures (35,36).

A meta-analysis of seven observational studies revealed that a serum type 1 collagen C-terminal telopeptide (sCTX) cutoff point of 150 pg/mL had a sensitivity of 57% (95% CI: 41-71%) and a specificity of 72% (95% CI: 64-79%). The positive likelihood ratio (LR+) was 2 (95% CI: 1.3-3.1), the negative likelihood ratio (LR-) was 0.6 (95% CI: 0.4-0.9), and the diagnostic odds ratio (DOR) was 3.4 (95% CI: 1.5-7.7). These findings suggest that as a preoperative marker, sCTX is not adequate for predicting the risk of developing drug-related osteonecrosis of the jaws (36).

Despite this recommendation, it's crucial to acknowledge that it contradicts certain guidelines for postmenopausal osteoporosis management (37–39). Although some guidelines classify certain recommendations related to bone turnover markers as A or B, suggesting their use for assessing therapeutic compliance and efficacy of osteoporosis treatment, the evidence supporting this is limited. Hence, it's essential to consider these factors when making clinical decisions and to recognize the challenges in practically applying biochemical bone turnover markers in our specific context.

3. Do not order basal insulin, post-load glucose, or use the HOMA index to assess insulin resistance in patients who are overweight, obese, or show clinical signs of insulin resistance.

Results of the second iteration: Median of 9.0 and 87.5% agreement rate.

Justification: Various indices, such as Homeostasis Model Assessment (HOMA), Quantitative Insulin Sensitivity Check Index (QUICKI), Matsuda Index, and Insulin Secretion-Sensitivity Index-2 (ISSI-2), are utilized in clinical research to quantify insulin resistance, adjusting for variables like age, sex, and ethnicity (40–43). Elevated levels of these indices in research settings have been linked to clinical conditions like abdominal obesity, low HDL levels, hypertriglyceridemia, hyperglycemia, fatty liver, polycystic ovary syndrome, and hypertension (40,41,44,45). However, certain limitations exist in their clinical application:

- Lack of universal validation for clinical use (40).
- Variability in insulin measurement due to lack of standardization in immunoassay tests (42,46).
- Inconsistencies in reference intervals among laboratories (42,46).
- Potential inaccuracies due to changes in beta cell function over time (40).
- The post-load glucose insulin test may overestimate insulin resistance in as many as 25% of individuals evaluated (40,47).
- Low intraindividual reproducibility has been observed in insulin measurement (46).

These limitations in the clinical application of basal and post-load insulin support the recommendation to avoid their use in overweight, obese, or clinically insulin-resistant patients (48). Consequently, the presence of insulin resistance is typically inferred from clinical criteria like the presence of metabolic syndrome and insulin resistance syndrome (49).

Throughout this research, some experts discussed the potential utility of triglyceride levels as indirect markers of insulin resistance, either individually or in conjunction with glucose or HDL cholesterol. It was suggested that in patients with prediabetes and triglycerides equal to or greater than 150 mg/dL, there might be a higher probability of insulin resistance (50). Additionally, it was noted that the triglyceride-glucose index exhibited a more robust correlation with adiponectin levels in individuals with insulin resistance compared to other indirect indices such as HOMA-IR and QUICKI (51). Among Caucasians, an elevated

triglyceride-HDL ratio, notably surpassing 3.0 for men and 2.5 for women, has been correlated with insulin resistance (52,53). However, these indices discussed by certain study participants did not undergo a Delphi process or systematic searches, unlike the focused analysis conducted for basal and post-load insulin levels in assessing insulin resistance. Consequently, due to this consensus, a routine recommendation for evaluating insulin resistance based on triglyceride levels or related indices cannot be established.

4. Do not perform routine measurements of vitamin D (25 [OH] vitamin D) in the general population.

Results of the second iteration: Median of 9.0 and 87.5% agreement rate.

Justification: Vitamin D has been associated with various effects, both skeletal and extra-skeletal, as evidenced by preclinical and observational studies. However, findings from randomized clinical trials like VITAL, ViDA, and D2d suggest that vitamin D supplementation in individuals with 25-hydroxyvitamin D (25OHD) levels at or above 20 ng/ml does not significantly impact cancer prevention, cardiovascular events, falls, or the onset of type 2 diabetes mellitus (54–58). Additionally, over 60 Mendelian randomization studies, designed to mitigate confounding biases, have yielded null effects regarding the association between genetically reduced 25OHD levels and disease risk (59).

Conversely, correcting severe vitamin D deficiency, defined as a serum 25OHD concentration below 12 ng/ml, has shown benefits. Thus, specific high-risk groups, such as those with limited sun exposure, malabsorption syndromes, or undergoing osteoporosis treatments that may predispose to hypocalcemia, may benefit from assessing their vitamin D levels. In such cases, measuring 25-hydroxyvitamin D levels can offer both cost-effectiveness and clinical relevance.

4.1. Fractures. Over the past two decades, placebo-controlled prospective studies with follow-ups of up to 5.3 years have not been able to demonstrate the efficacy of high doses of vitamin D, administered annually, quarterly, or monthly, as well as low daily doses, in preventing fractures (55,56,60–68) (Table 7). Furthermore, two studies using single high doses of vitamin D reported significant increases in fracture incidents. The first study, which administered 300,000 IU of vitamin D2 annually via intramuscular injections over three years, observed a substantial increase in hip fractures among women (hazard ratio [HR] 1.82; 95% confidence interval [CI] 1.12–2.99), but not among men (61). The second study, which administered an annual oral dose of 500,000 IU of cholecalciferol, noted an overall increase in fractures (HR 1.26; 95% CI 1.00–1.59), attributed to falls (62).

Table 7. Fracture Incidence in Placebo-Controlled Clinical Trials of Vitamin D

Study, year, reference	Location	Intervention	Participants detail	Baseline vitamin D levels	Post-treatment vitamin D levels	Follow-up period	Hazard Ratio for fractures
Bolus studies involving large single doses							
Smith *et al.*, 2007 (61)	England	300,000 IU I.M. vitamin D2 injection annually over 3 years	9,440 people (4,354 men, 5,086 women) aged 75 years	22.4 ng/mL	29.6 ng/mL	3 years	Hip fracture: Women 1.82 (95% CI 1.12–2.99), Men 1.22 (95% CI 0.52–1.97)

Sanders *et al.*, 2010 (62)	Australia	Single annual dose of 500,000 IU cholecalciferol orally	2,256 community-dwelling women aged ≥70 years at high risk of fracture	22.4 ng/mL	30 ng/mL	3-5 years	Fracture: 1.26 (95% CI, 1.00-1.59; P = .047)
High-dose vitamin D studies: monthly vs. every four months administration							
Waterhouse *et al.*, 2023 (63) (D-Health trial)	Australia	60,000 IU oral cholecalciferol every month	20,326 adults aged 60-84 years, with 45.7% (9,295) women and a mean age of 69.3 years (SD 5.5)	31 ng/mL	46 ng/mL	5.1 years	Fracture risk overall HR 0·94 [95% CI 0·84-1·06]
Trivedi *et al.*, 2003 (64)	UK	100,000 IU oral cholecalciferol every four month	2,686 participants (2,037 men, 649 women), aged 65-85, from the general community	21.2 ng/mL	29.6 ng/mL	5 years	Any first fracture: Total 0.78 (95% CI 0.61-0.99); Men 0.83 (95% CI 0.61-1.03); Women 0.68 (95% CI 0.46-1.01)
Lyons *et al.*, 2007 (65)	UK	100,000 IU oral ergocalciferol (vitamin D_2) every four months	3,440 individuals (2,624 women and 816 men) residing in residential or care homes	21.6 ng/mL	32 ng/mL	3 years	First fracture: 0.95 (95% CI 0.79-1.15)
Khaw *et al.*, 2017 (ViDA trial) (54)	New Zealand	Starting with 200,000 IU of vitamin D3, then monthly doses of 100,000 IU	5,110 healthy volunteers aged 50-84, with 42% women (2,139) and 58% men (2,969)	25.2 ng/mL	46.8-52.8 ng/mL	3.4 years	Any first fracture: 0.98 (95% CI 0.92-1.06)
Studies using oral daily doses							
Lips *et al.*, 1996 (66)	Netherlands	400 IU daily	2,578 persons (1,916 women, 662 men) aged ≥70 years	10 ng/mL	24.8 ng/mL	3.5 years	Hip fracture: 1.09 (95% CI 0.73-1.63), Peripheral fracture: 0.92 (0.66-1.27)

Meyer *et al.*, 2002 (67)	Norway	400 IU daily	1,144 residents from 51 nursing homes	20 ng/mL	25.6 ng/mL	2 years	Hip fracture: 1.18 (95% CI 0.81–1.71), Peripheral fracture: 1.03 (0.75–1.40)
Grant *et al.*, 2005 (68)	UK	800 IU daily	5,292 participants aged ≥70 years, ambulatory before a low-trauma fracture	15 ng/mL	24.8 ng/mL	5 years	Secondary prevention of low-trauma fractures: 0.99 (95 CI 0.86–1.15)
Bischoff-Ferrari *et al.*, 2020 (60) (DO-HEALTH trial)	Switzerland, France, Germany, Portugal, Austria	2,000 IU daily	2,157 adults aged ≥70 years, no major health events in 5 years prior	22 ng/mL	37.6 ng/mL	3 years	Nonvertebral fractures: 1.03 (95 CI 0.75–1.43)
LeBoff *et al.*, 2022 (55) (VITAL trial)	USA	2,000 IU daily	25,871 participants, comprising men over 50 and women over 55, including 5,106 Black individuals	30 ng/mL	41.2 ng/mL	5.3 years	0.98 (95% CI 0.89-1.08)

Source: Authors' own elaboration

Recent large-scale clinical trials, such as the VITAL trial and the D-Health study, have highlighted the ineffectiveness of vitamin D alone in reducing fracture risks (55,63). In the VITAL trial, supplementation with cholecalciferol did not significantly reduce the risk of fractures (total, non-vertebral, and hip) compared to placebo among healthy middle-aged and older adults not selected for vitamin D deficiency, low bone mass, or osteoporosis (55). Notably, a subgroup of 401 participants with serum 25(OH)D levels below 12 ng/mL, showed a lower fracture rate compared to those with higher levels. In the D-Health study, large monthly doses of 60,000 IU did not significantly alter the general fracture risk (63).

In addition, the co-administration of vitamin D with calcium has proven beneficial, reducing the risk of hip fractures (relative risk [RR] 0.61-0.84) and all fractures (RR 0.74-0.95), according to a recent umbrella review of meta-analyses of randomized controlled trials of vitamin D (69). However, this reduction in fracture risk was not seen in studies that only assessed community-dwelling individuals or those receiving only vitamin D compared to a placebo or control, indicating that the benefits of vitamin D and calcium supplementation on fracture prevention are primarily limited to institutionalized populations (69).

4.2. Falls. In five clinical trials spanning 2 to 5 years (54,62,70–72) (Table 8), various doses

of vitamin D were investigated. Despite higher serum 25(OH)D concentrations in the treatment group compared to the placebo group (39 ng/mL versus 27 ng/mL), no significant differences in fall incidence were observed between the groups.

Table 8. Falls Incidence in Placebo-Controlled Clinical Trials of Vitamin D

Study	Location	Intervention	Participants detail	Baseline vitamin D levels	Post-treatment vitamin D levels	Follow-up period	Hazard Ratio for falls
Sanders *et al.*, 2010 (62)	Australia	Single annual dose of 500,000 IU of cholecalciferol	2256 community-dwelling women, aged 70 or older, at high fracture risk	19.6 ng/mL	22 -29.6 ng/mL	3.5 years	1.15; 95% CI 1.02-1.30; P = .03
Khaw *et al.*, 2017 (ViDA trial) (54)	New Zeland	Starting with 200,000 IU of vitamin D3, then monthly doses of 100,000 IU	5,110 healthy volunteers aged 50-84, with 42% women (2,139) and 58% men (2,969)	25.2 ng/mL	46.8-52.8 ng/mL	3.4 years	0·99 (95% CI 0·92-1·07; P=0·82)
Waterhouse *et al.*, 2021 (70) (D-Health Trial)	Australia	60,000 IU oral cholecalciferol every month	21,315 participants aged 60-84 years, including 9,780 women (46%) and 11,530 men (54%)	31.2 ng/mL	46 ng/mL	4.3 years	1.02, 95% CI 0.95-1.10
LeBoff *et al.*, 2020 (71) (VITAL trial)	USA	2,000 IU daily	25,871 adults, men aged 50+ and women aged 55+ (mean age: 67.1 years), with no history of cancer or cardiovascular disease at baseline	30.8 ng/mL	41.2 ng/mL	5.3 years	0.97; 95% CI, 0.90-1.05, P = .50
Appel *et al.*, 2021 (72)	USA	1,000 IU daily	688 participants aged 70+, at high fall risk, with serum 25-hydroxyvitamin D levels of 10-29 ng/mL.	26.8 ng/mL	33.2 ng/mL	2 years	0.94 [95% CI, 0.76 to 1.15]; P = 0.54

Source: Authors' own elaboration

4.3. Cancer. Clinical trials using low daily doses ranging from 2000 to 4000 IU or high doses of 100,000 IU of oral cholecalciferol every four months did not demonstrate a reduction in cancer incidence over a follow-up period of up to 5.3 years (56,57,64,73–75). For instance, in the FIND study (74), which included 2,495 participants, supplementation with either 1600 IU daily or 3200 IU daily for 5 years did not decrease the incidence of invasive cancer (1600 IU/d [HR: 1.14; 95% CI: 0.75–1.72; P = 0.55] and 3200 IU/d [HR: 0.95; 95% CI: 0.61–1.47; P = 0.81]). Additionally, the D-Health trial (75), using monthly doses of 60,000 IU of cholecalciferol, did not impact cancer mortality, consistent with previous findings from Mendelian randomization studies (59) (Table 9). Further analysis of the VITAL study, a large-scale randomized clinical trial, revealed a decreased cancer risk among individuals with a normal BMI (less than 25 kg/m^2), although this analysis was not adjusted for multiple comparisons. Additionally, this analysis revealed a potential reduction in cancer risk among African Americans, alongside an observed increase in cancer mortality starting from the fourth year of follow-up (57). These findings suggest that extending the follow-up period beyond four years could yield modest mortality benefits.

Table 9. Cancer Incidence in Placebo-Controlled Clinical Trials of Vitamin D

Study	Location	Intervention	Participants detail	Baseline vitamin D levels	Post-treatment vitamin D levels	Follow-up period	Hazard Ratio for cancer
Trivedi *et al.*, 2003 (64)	UK	100,000 IU oral cholecalciferol every four month	2,686 participants (2,037 men, 649 women), aged 65-85, from the general community	21.2 ng/mL	29.6 ng/mL	5 years	1.09 (0.86 to 1.36); P = 0.47
Scragg *et al.*, 2018 (ViDA trial) (56)	New Zeland	Starting with 200,000 IU of vitamin D3, then monthly doses of 100,000 IU.	5110 adult community residents aged 50 to 84 years	25.2 ng/mL	30.8 ng/mL	3.3 years	1.01 (95% CI, 0.81-1.25; P = .95).
Manson *et al.*, 2019 (57) (VITAL trial)	USA	2,000 IU daily	25,871 participants, men ≥50 and women ≥55, cancer-free (except non-melanoma skin cancer) and without cardiovascular disease at baseline	30.8 ng/mL	41.2 ng/mL	5.3 years	0.96; 95% CI, 0.88 to 1.06; P = 0.4

Chatterjee *et al.*, 2021 (73)	USA	4,000 IU daily	2385 participants (mean age: 60 years, mean 25-hydroxyvitamin D: 28 ng/mL) with prediabetes, overweight/obesity, and no cancer history in the past 5 years	28 ng/mL	54 ng/mL	2-4 years	1.07 (95% CI 0.70, 1.62)
Virtanen *et al.*, 2022 (74) (FIND Trial)	Finland	1600 IU daily or 3200 IU daily	2,495 male participants aged 60+ years and post-menopausal females aged 65+ years, without prior CVD or cancer	29.2 ng/mL	40 - 48 ng/mL	5 years	Invasive cancer 1600 IU/d (HR: 1.14; 95% CI: 0.75-1.72; P = 0.55), and 3200 IU/d (HR: 0.95; 95% CI: 0.61-1.47; P = 0.81)
Neale *et al.*, 2022 (75) (D-Health Trial)	Australia	60,000 IU oral cholecalciferol every month	21,315 participants aged 60-84 years	31.2 ng/mL	46 ng/mL	5 years	Cancer mortality: 1.15 (95% CI 0.96 to 1.39; P = 0.13)

Source: Authors' own elaboration

4.4. Cardiovascular events. The VITAL, FIND, and ViDA clinical trials failed to demonstrate a reduction in major cardiovascular events with vitamin D supplementation (Table 10) (56,57,74). However, in the D-Health trial (76), the vitamin D group showed a lower incidence of these events compared to the placebo group (HR: 0.91, 95% CI 0.81-1.01), particularly among participants taking cardiovascular medications at baseline (HR: 0.84, 95% CI: 0.74-0.97; P for interaction=0.12). Additionally, the vitamin D group exhibited lower rates of myocardial infarction (HR: 0.81, 95% CI: 0.67-0.98) and coronary revascularization (HR: 0.89, 95% CI: 0.78-1.01). While no differences were noted in stroke rates (HR: 0.99, 95% CI: 0.80-1.23), these findings suggest a potential cardiovascular benefit from vitamin D supplementation, albeit with a small absolute risk difference and a confidence interval consistent with no effect.

Table 10. Cardiovascular Events Incidence in Placebo-Controlled Clinical Trials of Vitamin D

Study	Location	Intervention	Participants detail	Baseline vitamin D levels	Post-treatment vitamin D levels	Follow-up period	Hazard Ratio for cardiovas-cular events
Trivedi *et al.*, 2003 (64)	UK	100,000 IU oral cholecalciferol every four month	2,686 participants (2,037 men, 649 women), aged 65-85, from the general community	21.2 ng/mL	29.6 ng/mL	5 years	Men 0.91 (0.76 to 1.09), P = 0.30 Women 0.89 (0.63 to 1.27), P = 0.52
Manson *et al.*, 2019 (57) (VITAL trial)	USA	2,000 IU daily	25,871 participants, men ≥50 and women ≥55, cancer-free (except non-melanoma skin cancer) and without cardiovascular disease at baseline	30.8 ng/mL	41.2 ng/mL	5.3 years	0.97; 95% CI, 0.85 to 1.12; P = 0.69
Virtanen *et al.*, 2022 (74) (FIND Trial)	Finland	1600 IU daily or 3200 IU daily	2,495 male participants aged 60+ years and post-menopausal females aged 65+ years, without prior CVD or cancer	29.2 ng/mL	40 - 48 ng/mL	5 years	1600 IU/d (HR: 0.97; 95% CI: 0.63–1.49), and 3200 IU/d (HR: 0.84; 95% CI: 0.54– 1.31)
Scragg *et al.*, 2018 (56) (ViDA trial)	New Zeland	Starting with 200,000 IU of vitamin D3, then monthly doses of 100,000 IU	5110 adult community residents aged 50 to 84 years	25.2 ng/mL	30.8 ng/mL	3.3 years	1,02 (95% CI, 0.87–1.20)
Thompson *et al.*, 2023 (76) (D-health trial)	Australia	60,000 IU oral cholecalciferol every month	21,315 participants aged 60-84 years	31.2 ng/mL	46 ng/mL	5 years	Major cardiovascular events: 0.91, 95% CI 0.81 to 1.01. Participants taking cardiovascular drugs at baseline (0.84, 0.74 to 0.97; P for interaction =0.12)

Source: Authors' own elaboration

4.5. Diabetes. In the Tromsø and D2d studies, the administration of 20,000 IU of cholecalciferol weekly for five years and 4,000 IU daily for four years, respectively, did not significantly prevent the transition from prediabetes to type 2 diabetes (Table 11) (58,77). However, detailed analysis of a subset of 103 D2d participants with initial 25-hydroxyvitamin D levels below 12 ng/mL showed a hazard ratio of 0.38 (95% CI, 0.18-0.80) in the vitamin D supplemented group, suggesting a protective effect in those with severe deficiency (58). Moreover, a recent meta-analysis involving data from three clinical trials reported a 15% decrease in the risk of progressing from prediabetes to diabetes (58,77–79). Nonetheless, the benefits from lifestyle modifications and metformin, which decrease the progression rates by 58% and 31% respectively, are more substantial (80). Thus, the slight benefits derived from vitamin D supplementation do not support its widespread recommendation as a preventive measure for diabetes progression.

Table 11. Diabetes Incidence in Placebo-Controlled Clinical Trials of Vitamin D

Study	Location	Intervention	Participants detail	Baseline vitamin D levels	Post-treatment vitamin D levels	Follow-up period	Hazard Ratio for diabetes
Jorde *et al.*, 2016 (77) (Tromsø trial)	Norway	20,000 IU of oral cholecalciferol weekly	511 participants (mean age 62 years, 314 males) diagnosed with prediabetes through oral glucose tolerance testing	24 ng/mL	48.8 ng/mL	5 years	0.90; 95% CI 0.69 –1.18, Cox regression, P = .45, intention to treat analysis
Pittas *et al.*, 2019 (58) (D2d trial)	USA	4,000 IU daily	2423 adults fulfilling at least two of three glycemic criteria for prediabetes (fasting plasma glucose 100-125 mg/dL; postprandial plasma glucose 140-199 mg/dL; glycated hemoglobin 5.7-6.4%)	30.8 ng/mL	41.2 ng/mL	2-4 years	0.97; 95% CI, 0.85 to 1.12; P = 0.69

Kawahara *et al.*, 2022 (79) (DPVD Trial)	Japan	Eldecalcitol 0.75 µg daily	1256 participants, with a mean age of 61.3 years and 59.1% women, who had impaired glucose tolerance as defined by a 75g oral glucose tolerance test and glycated hemoglobin level	20.9 ng/mL	Without changes	2.9 years	0.69, 95% CI, 0.51 to 0.95; P = 0.020

Source: Authors' own elaboration

4.6 Other outcomes. During the final consensus meeting, various outcomes were assessed, including asthma (81,82), respiratory infections (83,84), COVID-19 infection (85,86), autoimmune diseases (87), and infertility (88). Like the previously analyzed outcomes, a potential benefit for individuals with severe vitamin D deficiency was identified. However, it is critical to acknowledge that these outcomes did not undergo a systematic literature review or application of the Delphi method, therefore the conclusions do not completely encompass these results.

5. Do not routinely prescribe vitamin D, except in cases of deficiency (25 [OH] vitamin D < 12 ng/ml), osteomalacia, secondary hyperparathyroidism due to vitamin D deficiency, or in patients with osteoporosis at risk of hypocalcemia.

Results of the second iteration: Median of 9.0 and 88.8% agreement rate.

Justification: Clinical trials have shown that vitamin D supplementation does not provide significant benefits to individuals with levels above 20 ng/mL but does offer more reliable and positive results for those below 12 ng/mL. Thus, there is insufficient evidence to advocate for routine vitamin D supplementation across the general population. Recommendations should be specifically directed toward high-risk groups, including individuals with 25-hydroxyvitamin D levels below 12 ng/mL at risk of osteomalacia, those with secondary hyperparathyroidism due to vitamin D deficiency, or osteoporosis patients susceptible to medication-induced hypocalcemia (59,89,90).

During the consensus discussions, the precise definition of vitamin D deficiency was debated. Although there is consensus that levels below 12 ng/mL denote deficiency and levels above 30 ng/mL denote sufficiency, the classification for levels between 12 and 30 ng/mL remains ambiguous (91). Factors such as racial (50) and age-related differences (51), variable sun exposure (51), differences in fat distribution, pregnancy (92,93), protein carriers, (94,95) and, the lack of standardized assays (96,97), contribute to this uncertainty. These factors hinder the ability to establish a clear consensus on what constitutes deficiency within this range.

Further deliberations emphasized the need to update existing management guidelines based

on our study's findings and a thorough literature review (98,99). A proposal was made to redefine the criteria for vitamin D insufficiency and deficiency to avoid unnecessary supplementation in cases where it is not clearly indicated. This change would allow for a more personalized and evidence-based approach to managing vitamin D levels in patients with endocrine disorders, thereby enhancing patient care and outcomes.

Discussion

This study established five "do not" recommendations to enhance medical care for patients with endocrine disorders in Colombia. These recommendations were unveiled during a webinar introducing the second cohort of "*Decisiones Acertadas*", accessible on the Colombian Association of Scientific Societies' YouTube channel. This marked the inception of disseminating the study's findings and implementing recommendations in clinical practice, with the overarching goal of improving decision-making in endocrinology for the benefit of patients.

One of the key recommendations emphasizes avoiding routine thyroid ultrasounds in patients without detectable anomalies during clinical examination. This aligns with similar guidance from other Choosing Wisely initiatives, such as those in the United States, Canada, Australia, Italy, and Brazil (100). In Colombia, where thyroid cancer prevalence is notable (101–103) and many diagnosed lesions are smaller than 1 centimeter (25), evidence suggests overdiagnosis (25,104,105) and unnecessary aggressive treatment for low-risk thyroid lesions (106). Implementing this recommendation could substantially influence clinical practice in the country. Local studies on cost-effectiveness and quality of life are crucial for assessing its implementation.

Furthermore, consensus participants unanimously agreed to avoid the use of bone turnover markers in the context of osteoporosis. Notably, this recommendation has not been identified in other Choosing Wisely initiatives worldwide. This absence could be attributed to the discrepancy with current management guidelines, which allow clinicians to decide on the use of these markers for monitoring and assessing treatment adherence, despite their diagnostic limitations (37–39). Given the high prevalence of osteoporosis in Colombia, further research is needed to evaluate the potential impact of incorporating these markers into our clinical practice.

Another one of the recommendations was to avoid ordering basal insulin, glucose post-load tests, or HOMA index measurements in overweight, obese, or clinically insulin-resistant patients. This guideline mirrors the emphasis placed on it by the Choosing Wisely initiative in Australia, highlighting the lack of standardization and the significant costs associated with these tests, as discussed in our consensus. With approximately 9 out of every 100 Colombians affected by diabetes mellitus (107,108) and more than half of the Colombian adult population being overweight or obese (109), this recommendation gains further significance given the target population. To reduce the unnecessary use of these tests, conducting local studies to understand the frequency and reasons behind their request in our clinical setting is essential.

Finally, experts have recommended avoiding routine measurement of vitamin D levels in the general population due to lack of evidence supporting widespread supplementation (89). These recommendations align with the Choosing Wisely initiatives in Canada and Australia, reinforcing the findings reported in this consensus. A study conducted in the Colombian population (90) revealed that more than 80% of the requests for the 25-hydroxyvitamin D test yielded values above 15 ng/mL, with the majority of patients in this group showing no abnormalities in the phosphocalcic profile. This underscores the perception of overutilization of this test and the surplus of subsequent treatment. Additionally, the study raised the possibility of changing the "sufficiency" cutoff point from 30 to 20 ng/ml, which would significantly increase the proportion of the population classified as normal, from 25% to 78.8%. Therefore, refraining from routinely requesting the 25-hydroxyvitamin D test and instead concentrating on directing

supplementation in the risk groups identified by consensus would assist in mitigating the influx of unnecessary requests for vitamin D and decreasing associated overtreatment.

The identification of these five "do not" recommendations in the context of endocrinology in Colombia marks a significant step forward in the pursuit of more effective and rationalized medical care. However, the real challenge lies in the effective implementation of these recommendations in daily clinical practice (6,110). To address this challenge, three key strategies are proposed:

1. Medical staff education: Initiating a training program that includes lectures and practical workshops, available both in-person and online, to ensure accessibility and wide dissemination of knowledge among healthcare professionals.
2. Patient education: Developing informational resources and tools for shared decision-making, aimed at instructing patients about the risks and benefits of tests and treatments, thus encouraging active participation in their medical care.
3. Integration into digital medical records: Incorporating alerts in the electronic medical records of some healthcare providers to discourage these five unrecommended practices and to evaluate their effectiveness as a de-implementation strategy.

This collaborative approach among healthcare professionals, patients, and healthcare systems is essential for advancing towards clinical practices that prioritize efficiency, safety, and patient well-being, grounded in the best available evidence.

Conclusion

This article presents the results of the *Decisiones Acertadas* initiative in Endocrinology, led by the ACSC. Our goal was to identify inappropriate practices and provide "do not" recommendations to avoid ineffective, unsafe, or unnecessary diagnostic tests, treatments, and procedures. Recommendations include refraining from routine thyroid ultrasound and avoiding the use of bone turnover markers in osteoporosis patients. It is also discouraged to measure basal insulin and/or glucose post-load in individuals with overweight, obesity, or clinical signs of insulin resistance, as well as routinely measuring 25 (OH) vitamin D levels and prescribing vitamin D supplements in the general population. By adhering to these recommendations, endocrinology professionals can deliver more efficient, effective, and safe care, ensuring optimal patient management based on the strongest scientific evidence.

Limitations

Despite efforts to ensure broad representation of endocrinologists nationwide in the expert panel, it's crucial to acknowledge potential underrepresentation from certain regions and varying perspectives from experts with different contexts and experience levels. Moreover, the Delphi method's nature imposes limitations on fully capturing intricacies and complex contexts in responses.

Another limitation is the exclusive focus on adult patients in deriving recommendations from the Delphi method. Thus, it's essential to acknowledge that these recommendations may not directly apply to other populations, such as children or pregnant women, who may have distinct clinical requirements.

These limitations underscore the importance of interpreting the recommendations within their context and considering additional evidence sources and expert viewpoints across diverse populations and clinical contexts. Moreover, it is advisable for scientific societies to establish self-regulatory initiatives addressing specific population needs and enriching the evidence base in endocrinology.

Ethical statement

This study was classified as risk-free in accordance with Colombia's Ministry of Health Resolution No. 8430/1993 and followed the Helsinki Declaration.

Authors' contributions

Karen Lorena Palacios-Bayona, Pablo Alberto Castaño-Ceballos, Lina Marcela Restrepo-Giraldo, Carlos Esteban Builes-Montaño, Alex Ramírez-Rincón: Conceptualization, formal analysis, investigation, methodology, validation, writing – original draft; Henry Tovar-Cortes, Katherine Restrepo-Erazo, Margarita Sierra-Osorio, Sonia Esperanza Gómez-Benjumea, Lina Patricia Pradilla-Suarez, Doly Nubia Pantoja-Guerrero, Alejandro Román-González, Hernando Vargas-Uricoechea, Carlos Alfonso Builes-Barrera, José Alfonso Mora-Morantes, Juan Bernardo Pinzón-Barco, Alejandro Marín-Sánchez: Data curation, formal análisis, investigation, validation, writing – review & editing.

Funding

The Colombian Association of Endocrinology funded the systematic literature search and offered methodological guidance for conducting the Delphi panel.

Conflicts of interest

Carlos E. Builes Montaño has received consulting or speaker fees from Sanofi, Novo Nordisk, Novartis, Boehringer Ingelheim, Redordati Rare Diseases, Abbott and Amryt.

No other authors of this consensus declare conflicts of interest and did not receive any compensation for their participation.

Acknowledgments

The authors gratefully acknowledge the Colombian Association of Endocrinology, Diabetes, and Metabolism for their support in the *Decisiones Acertadas* initiative, aimed at improving management standards for patients with endocrine disorders in Colombia. Special thanks to Neurobusiness® for their assistance in conducting the systematic literature search for the final recommendations and guiding the Delphi panel development. Furthermore, we extend our appreciation to Dr. Juan Pablo Brito-Campana for his meticulous review of the manuscript.

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