Revisiones pronóstico: una introducción práctica.

XXI Reunión de la Red **Cochrane Iberoamericana**

Trusted evidence.
Informed decisions.
Better health.

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La investigación pronostica y su importancia

Pronosticar, en general, significa prever, estimar o predecir la **probabilidad o riesgo** de que ocurra una **condición futura**, a lo largo del tiempo.

En investigación clínico-epidemiológica: probabilidad (o riesgo), de que un individuo desarrolle un estado particular de salud o condición (endpoint), en función de sus características (startpoint), en un periodo de tiempo determinado(futuro).

Predecir

- Aparición de complicaciones médicas
- Efectos secundarios derivados del tratamiento
- Recurrencia
- Curación
- Mortalidad

Decisiones clínicas y de salud pública

- Informar resultados futuros
- Definir estrategias de intervención
- Dirigir tratamiento

Muchos estudios (calidad variable, hallazgos inconsistentes) + **Necesidad RS**

Tipos de investigación pronóstica

Prognosis research strategy (PROGRESS) clasifica la investigación pronóstica en cuatro tipos clave:

a) Tipo I: Pronóstico global, investigación pronostica general (riesgo basal/promedio)

b) Tipo II: Factores pronósticos (medidas asociadas a resultados)

c) Tipo III: Modelos pronósticos (ecuaciones con múltiples factores)

d) Tipo IV: Predictores del efecto del tratamiento (predicen respuesta al tto)

2013. Plos Medicine and BMJ PROGRESS papers

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Desafío(s) práctico(s) en RS de factores pronóstico

Sex as a prognostic factor for mortality in adults with acute symptomatic pulmonary embolism

2025 Mar 20;3(3):CD013835. doi: 10.1002/14651858.CD013835.pub2.

Desafío(s) práctico(s) en RS de factores pronóstico

1. Identificar el problema/ tema y **determinar la pregunta PICO**

Escribir un plan de revisión: protocolo

2. Búsqueda de artículos/estudios

3. **Selección de artículos**

4. Extracción de datos de los estudios

5. Evaluación del riesgo de sesgo

Combinar los datos (síntesis/metaanálisis)

Evaluar la calidad de la evidencia

Discusión y conclusión de los resultados

Desafío(s) práctico(s) en RS de factores pronóstico

1. PICOTS (basado en el CHARMS)

P: población

I: factor pronóstico índice

C: otros factores pronósticos. Referencia/ajuste. **Preselección (consistencia..)**

- Evidencia publicada: modelos predictivos, RS…
- Evidencia clínica
- Universales: edad, raza, socioeconómicos

O: resultados

T: tiempo
- **Medición/evaluación de los factores pronósticos** (ej: valor troponina al ingreso o al alta, medición PCR <2s después del diagnóstico)
- **Durante qué período predicen el resultado** (ej:, 30dias, 48horas, 1 año..)

S: setting, distintos entornos: capacidad pronóstica

Desafío(s) práctico(s) en RS de factores pronóstico

1. PICOTS (basado en el CHARMS)

P: adultos con EP sintomática aguda (pruebas objetivas)

I: Sexo (mujer): variable de interés

C: Ajuste covariables(búsqueda, consenso, sPESI): edad, cáncer (antecedentes, actual), enfermedad cardiopulmonar (antecedentes, actual),FC, PAS, y satO2

O: mortalidad (hospitalaria por todas las causas, todas las causas, hospitalaria relacionada con TEP, relacionada con TEP). No core-outcome set

T: tiempo
- Medición/evaluación de los factores pronósticos: en el momento del diagnostico de TEP
- Durante qué período predicen el resultado: 48h,30 d, 90 d, 1 año, todo el ingreso

S: Cualquiera

Desafío(s) práctico(s) en RS de factores pronóstico

1. PICOTS (basado en el CHARMS)

Population	Adults, hospitalised or not, treated for acute symptomatic pulmonary embolism confirmed by objective testing	
Index prognostic factor	Sex: being a female patient	
Comparator	Covariates: age, history of cancer, current cancer, history of chronic cardiopulmonary disease, current chronic cardiopulmonary disease, heart rate, systolic blood pressure, and O2 saturation	
Outcomes of interest	**Timing - prognostication time**	**Timing - over what period the outcome is predicted**
All-cause hospital mortality	At PE diagnosis	During the hospital stay: the longest follow-up provided by the study authors
		Early hospital mortality (during the first 48 hours)
		At 30 days
All-cause mortality		At 30 days
		At 90 days
		At 1 year
PE-related hospital mortality		During the hospital stay: the longest follow-up provided by the study authors
		Early PE-related hospital mortality (during the first 48 hours)
		At 30 days
PE-related mortality		At 30 days
Setting	Patients with PE managed in any setting. Death can occur at the hospital or not.	

Desafío(s) práctico(s) en RS de factores pronóstico

1. P**IC**O**T**S (basado en el CHARMS) - Diseño de estudio)

Se incluyeron estudios longitudinales, aleatorizados o no aleatorizados:

(i) estudios observacionales (p. ej., estudios de cohorte o de vinculación de bases de datos)

(ii) análisis secundarios de estudios experimentales (aleatorizados o no aleatorizados) que aportaran evidencia sobre el pronóstico.

* Se incluyeron de fase 2, estudios confirmatorios : es decir, investigaciones explicativas cuyo objetivo era **confirmar una asociación independiente** entre un posible factor pronóstico (sexo) y el desenlace de interés.

Desafío(s) práctico(s) en RS de factores pronóstico

2. BÚSQUEDAS: selección amplia términos + filtros para combinarlos

Complicaciones:

- Difícil identificación (estudios pronóstico no bien indexados)
- PICOTS bien definida → ambigüedad términos
- Necesidad de búsquedas amplias (términos investigación de pronóstico + términos específicos del dominio o la enfermedad) → muchos artículos irrelevantes
- Necesidad de filtros metodológicos

Research | Open access | Published: 10 April 2022

Development and evaluation of a search filter to identify prognostic factor studies in Ovid MEDLINE

Elena Stallings, Andrea Gaetano-Gil, Noelia Alvarez-Diaz, Ivan Solà, Jesús López-Alcalde, Daniel Molano & Javier Zamora

BMC Medical Research Methodology **22**, Article number: 107 (2022) | Cite this article

Desafío(s) práctico(s) en RS de factores pronóstico

2. BÚSQUEDAS: selección amplia términos + filtros para combinarlos

1 lung embolism/
2 thromboembolism/
3 exp venous thromboembolism/
4 exp vein thrombosis/
5 ((vein* or ven*) adj thromb*).ti,ab.
6 (blood adj3 clot*).ti,ab.
7 "deep vein thrombosis".ti,ab
8 (lung adj3 clot*).ti,ab.
9 "peripheral vascular thrombosis".ti,ab.
10 "post-thrombotic syndrome".ti,ab.
11 "pulmonary embolism".ti,ab.
12 (pulmonary adj3 clot*).ti,ab.
13 (thrombopro* or thrombotic* or thrombolic* or thromboemboli* or embol* or microembol*).ti,ab.
14 "venous thromboembolism".ti,ab.

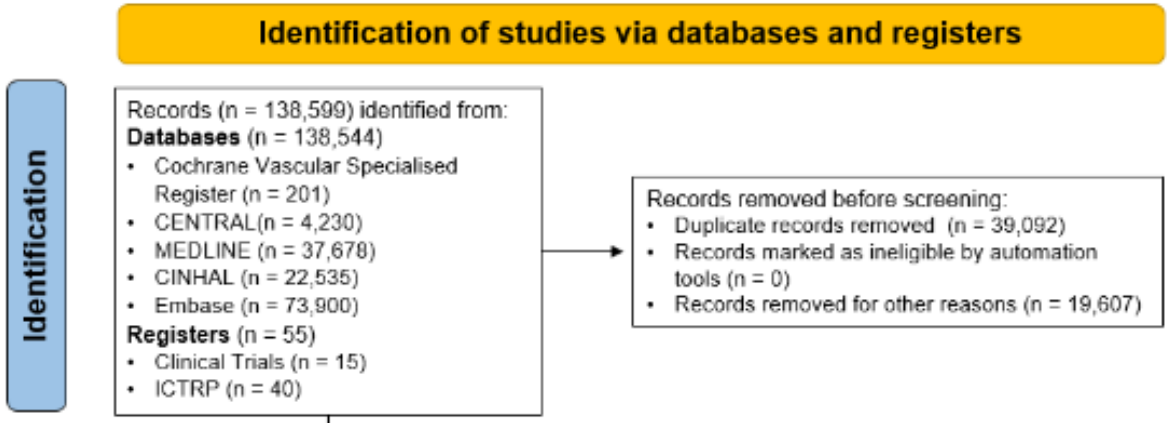
22 female*.ti,ab.
23 gender.ti,ab.
24 girl*.ti,ab.
25 male*.ti,ab.
26 maternal.ti,ab.
27 men.ti,ab.
28 postnatal.ti,ab.
29 pregnan*.ti,ab.
30 sex.ti,ab.
31 women.ti,ab.

34 exp mortality/
35 exp incidence/
36 exp survival analysis/
37 prognos*.ti,ab.
38 predict*.ti,ab.
39 course*.ti,ab.
40 "disease history".ti,ab.

Desafío(s) práctico(s) en RS de factores pronóstico

2. BÚSQUEDAS: selección amplia términos + filtros para combinarlos

Complicaciones:



≈ 140.000 records

Estadio Olímpico Félix Sánchez, con una capacidad **50.000 espectadores conciertos**

✖ 3

Desafío(s) práctico(s) en RS de factores pronóstico

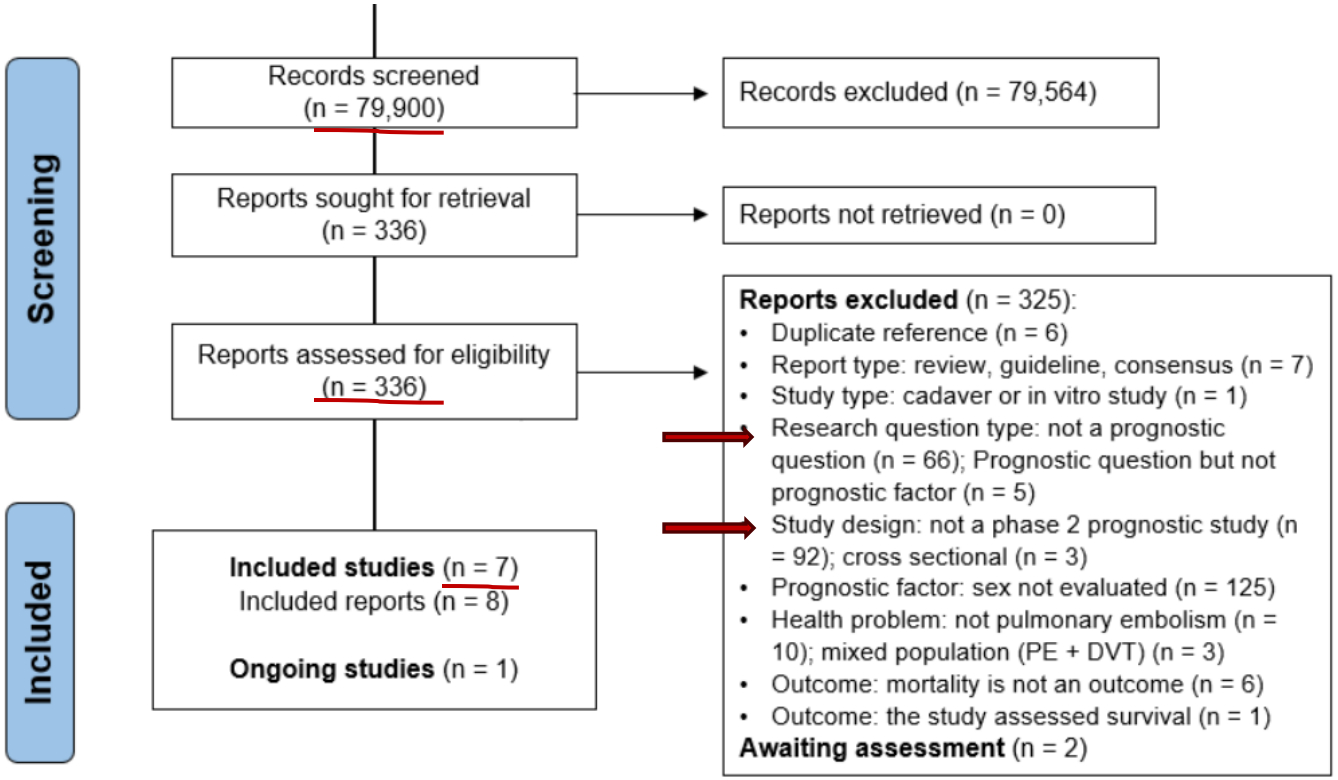
2. SELECCIÓN:

Complicaciones:

- Gran cantidad de registros recuperados (irrelevantes): T&A, FT
- Tiempo
- Heterogeneidad: más desviaciones respecto al PICOTS
- Pocos estudios incluidos
- Conocimiento del tema metodológico (diferenciar fase 1 vs fase 2…)

Desafío(s) práctico(s) en RS de factores pronóstico

3. SELECCIÓN:



Desafío(s) práctico(s) en RS de factores pronóstico

4. EXTRACCIÓN (Basada en la guía CHARMS-PF)

Complicaciones:

- Mal/poca información clave reportada en los estudios incluidos (ej: tiempo aparición síntomas EP – inicio seguimiento)
- Heterogeneidad: medición de factores y resultados (definición), seguimientos, análisis
- Resultados: estandarizar, recalcular

Table 1 | CHARMS-PF checklist of key items to be extracted from primary studies of prognostic factors, based on additions and modifications of the original CHARMS checklist for primary studies of prediction models[15]

Domain and key items	General	Applicability	Risk of bias
Source of data:			
Source of data (eg, cohort, case control, randomised trial, or registry data)	X	X	X
Participants:			
Participant eligibility and recruitment method (eg, consecutive participants, location, number of centres, setting, inclusion and exclusion criteria)	X	X	X
Participant description	X	X	
Details of treatments received (if relevant)		X	X
Study dates	X	X	
Outcomes to be predicted:			
Definition and method for measurement of outcomes		X	X
Was the same outcome definition (and method for measurement) used in all participants?			X
Types of outcomes (eg, single or combined endpoints)?	X	X	
Were the outcomes assessed without knowledge of the candidate prognostic factors (that is, blinded)?			X
Were candidate prognostic factors part of the outcome (eg, when using a panel or consensus outcome measurement)?			X
Time of outcome occurrence or summary of duration of follow-up	X	X	X
Prognostic factors (index and comparator prognostic factors):			
Number and type of prognostic factors (eg, obtained from demographics, patient history, physical examination, additional testing, disease characteristics)	X		X
Definition and method for measurement of prognostic factors		X	X
Timing of prognostic factor measurement (eg, at patient presentation, diagnosis, treatment initiation, at the end of surgery)		X	X
Were prognostic factors assessed blinded for outcome, and for each other (if relevant)?			X
Handling of prognostic factors in the analysis (eg, continuous, linear, non-linear transformations or categorised)			X
Sample size:			
Was a sample size calculation conducted and, if so, how?	X		
Number of participants and number of outcomes or events	X		
Number of outcomes or events in relation to the number of candidate prognostic factors (events per variable)			X
Missing data:			
Number of participants with any missing value (in the prognostic factors and outcomes)	X		X
Number of participants with missing data for each prognostic factor of interest			X
Details of attrition (loss to follow-up) and, for time-to-event outcomes, number of censored observations (ideally in each category for those categorical prognostic factors of interest)			X
Handling of missing data (eg, complete case analysis, imputation, or other methods)			X
Analysis:			
Modelling method (eg, linear, logistic, Cox, parametric survival, competing risks) regression)	X		X
How modelling assumptions were checked; in particular, for time-to-event outcomes and the analysis of hazard ratios, the method for assessing non-proportional hazards (non-constant hazard ratios over time)			X
Method for selection of prognostic factors for inclusion in multivariable modelling (eg, all candidate prognostic factors considered, preselection of established prognostic factors, retain only those significant from univariable analysis)			X
Method for selection or exclusion of prognostic factors (including those of interest and those used as adjustment factors) during multivariable modelling (eg, backward or forward selection, or full model approach including all factors regardless), and criteria used for any selection or exclusion (eg, P value, Akaike information criterion)			X
Method of handling each continuous prognostic factor (eg, dichotomisation, categorisation, linear, non-linear), including values of any cutpoints used and their justification; for non-linear trends, the method of identifying non-linear relationships (eg, splines, fractional polynomials)			X
Results:			
Unadjusted and adjusted prognostic effect estimates (eg, risk ratios, odds ratios, hazard ratios, mean differences) for each prognostic factor of interest, and the corresponding 95% confidence interval (or variance or standard error). Details of any non-linear relationships and whether modelling assumptions hold; in particular, for time-to-event outcomes, any evidence of non-proportional hazards (non-constant hazard ratios) for each prognostic factor of interest	X	X	X
For each extracted adjusted prognostic effect estimate of interest, the set of adjustment factors used	X	X	X
Interpretation and discussion:			
Interpretation of presented results	X	X	
Comparison with other studies, discussion of generalisability, strengths and limitations	X	X	

CHARMS=checklist for critical appraisal and data extraction for systematic reviews of prediction modelling studies. CHARMS-PF enables reviewers to describe, assess (eg, for applicability or risk of bias), and summarise (individually and within a meta-analysis) primary studies.

Desafío(s) práctico(s) en RS de factores pronóstico

5. RIESGO DE SESGO

QUIPS (Quality In Prognosis Studies):

Dominios:

1. Participación
2. Pérdidas
3. Medición factor pronóstico
4. Medición del outcome
5. Ajuste por otros factores pronósticos
6. Análisis estadístico y reporte

Table 2 | QUIPS tool (quality in prognostic factor studies), which can be used to classify risk of bias of prognostic factor studies

Domains	Signalling items	Risk of bias ratings
1. Study participation	(a) Adequate participation in the study by eligible persons (b) Description of the target population or population of interest (c) Description of the baseline study sample (d) Adequate description of the sampling frame and recruitment (e) Adequate description of the period and place of recruitment (f) Adequate description of inclusion and exclusion criteria	High: the relationship between the PF and outcome is very likely to be different for participants and eligible non-participants Moderate: the relationship between the PF and outcome may be different for participants and eligible non-participants Low: the relationship between the PF and outcome is unlikely to be different for participants and eligible non-participants
2. Study attrition	(a) Adequate response rate for study participants (b) Description of attempts to collect information on participants who dropped out (c) Reasons for loss to follow-up are provided (d) Adequate description of participants lost to follow-up (e) There are no important differences between participants who completed the study and those who did not	High: the relationship between the PF and outcome is very likely to be different for completing and non-completing participants Moderate: the relationship between the PF and outcome may be different for completing and non-completing participants Low: the relationship between the PF and outcome is unlikely to be different for completing and non-completing participants
3. Prognostic factor measurement	(a) A clear definition or description of the PF is provided (b) Method of PF measurement is adequately valid and reliable (c) Continuous variables are reported or appropriate cutpoints are used (d) The method and setting of measurement of PF is the same for all study participants (e) Adequate proportion of the study sample has complete data for the PF (f) Appropriate methods of imputation are used for missing PF data	High: the measurement of the PF is very likely to be different for different levels of the outcome of interest Moderate: the measurement of the PF may be different for different levels of the outcome of interest Low: the measurement of the PF is unlikely to be different for different levels of the outcome of interest
4. Outcome measurement	(a) A clear definition of the outcome is provided (b) Method of outcome measurement used is adequately valid and reliable (c) The method and setting of outcome measurement is the same for all study participants	High: the measurement of the outcome is very likely to be different related to the baseline level of the PF Moderate: the measurement of the outcome may be different related to the baseline level of the PF Low: the measurement of the outcome is unlikely to be different related to the baseline level of the PF
5. Adjustment for other prognostic factors	(a) All other important PFs are measured (b) Clear definitions of the important PFs measured are provided (c) Measurement of all important PFs is adequately valid and reliable (d) The method and setting of PF measurement are the same for all study participants (e) Appropriate methods are used to deal with missing values of PFs, such as multiple imputation (f) Important PFs are accounted for in the study design (g) Important PFs are accounted for in the analysis	High: the observed effect of the PF on the outcome is very likely to be distorted by another factor related to PF and outcome Moderate: the observed effect of the PF on outcome may be distorted by another factor related to PF and outcome Low: the observed effect of the PF on outcome is unlikely to be distorted by another factor related to PF and outcome
6. Statistical analysis and reporting	(a) Sufficient presentation of data to assess the adequacy of the analytic strategy (b) Strategy for model building is appropriate and is based on a conceptual framework or model (c) The selected statistical model is adequate for the design of the study (d) There is no selective reporting of results	High: the reported results are very likely to be spurious or biased related to analysis or reporting Moderate: the reported results may be spurious or biased related to analysis or reporting Low: the reported results are unlikely to be spurious or biased related to analysis or reporting

Hayden 2013, Internal Medicine
Riley 2019, BMJ

Desafío(s) práctico(s) en RS de factores pronóstico

5. RIESGO DE SESGO

QUIPS (Quality In Prognosis Studies):

A study should have adjusted for at least four of our covariates of interest to be judged as a low risk of bias for this domain

Table 2 | QUIPS tool (quality in prognostic factor studies), which can be used to classify risk of bias of prognostic factor studies

Domains	Signalling items	Risk of bias ratings
1. Study participation	(a) Adequate participation in the study by eligible persons (b) Description of the target population or population of interest (c) Description of the baseline study sample (d) Adequate description of the sampling frame and recruitment (e) Adequate description of the period and place of recruitment (f) Adequate description of inclusion and exclusion criteria	High: the relationship between the PF and outcome is very likely to be different for participants and eligible non-participants Moderate: the relationship between the PF and outcome may be different for participants and eligible non-participants Low: the relationship between the PF and outcome is unlikely to be different for participants and eligible non-participants
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4. Outcome measurement	(a) A clear definition of the outcome is provided (b) Method of outcome measurement used is adequately valid and reliable (c) The method and setting of outcome measurement is the same for all study participants	High: the measurement of the outcome is very likely to be different related to the baseline level of the PF Moderate: the measurement of the outcome may be different related to the baseline level of the PF Low: the measurement of the outcome is unlikely to be different related to the baseline level of the PF
5. Adjustment for other prognostic factors	(a) All other important PFs are measured (b) Clear definitions of the important PFs measured are provided (c) Measurement of all important PFs is adequately valid and reliable (d) The method and setting of PF measurement are the same for all study participants (e) Appropriate methods are used to deal with missing values of PFs, such as multiple imputation (f) Important PFs are accounted for in the study design (g) Important PFs are accounted for in the analysis	High: the observed effect of the PF on the outcome is very likely to be distorted by another factor related to PF and outcome Moderate: the observed effect of the PF on outcome may be distorted by another factor related to PF and outcome Low: the observed effect of the PF on outcome is unlikely to be distorted by another factor related to PF and outcome
6. Statistical analysis and reporting	(a) Sufficient presentation of data to assess the adequacy of the analytic strategy (b) Strategy for model building is appropriate and is based on a conceptual framework or model (c) The selected statistical model is adequate for the design of the study (d) There is no selective reporting of results	High: the reported results are very likely to be spurious or biased related to analysis or reporting Moderate: the reported results may be spurious or biased related to analysis or reporting Low: the reported results are unlikely to be spurious or biased related to analysis or reporting

Hayden 2013, Internal Medicine
Riley 2019, BMJ

Desafío(s) práctico(s) en RS de factores pronóstico

5. RIESGO DE SESGO

QUIPS (Quality In Prognosis Studies):

Outcome	Study	Risk of bias with the QUIPS tool							Weight in meta-analysis
		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Adjustment for other prognostic factors	Statistical analysis and reporting	Overall Rob	
All-cause hospital mortality	Agarwal 2015	Low	Low	Low	Low	High	Moderate: Low/Mod	High	51%
	Marshall 2017	Moderate	High	Low	Low	High	Moderate: Low/Mod	High	19%
	Pribish 2020	Low	Low	Low	Low	Low	Moderate: Low/Mod	Moderate	Non applicable
	Sedhom 2022	Low	Low	Low	Low	Low	Moderate: Low/Mod	Moderate	30%
All-cause mortality at 30 days	Barrios 2017	Low	Low	Low	Low	Low	Moderate: Mod/Low	Moderate	7%
	Borrero 2007	Low	Moderate	Low	Low	Low	Moderate: Low/Mod	Moderate	93%
PE-related mortality at 30 days	Barrios 2017	Low	Low	Low	Low	Low	Moderate: Mod/Low	Moderate	88%
	Tanabe 2018	Low	Low	Low	Moderate	High	Moderate: Mod/Mod	High	12%

QUIPS tool: Quality in Prognostic Studies tool

Hayden 2013, Internal Medicine
Riley 2019, BMJ

Desafío(s) práctico(s) en RS de factores pronóstico

6. OTROS

Síntesis de evidencia:

- Ausencia información
- Datos inconsistentes
- Disparidad definiciones

GRADE:

- Inicio certeza alta: observacionales (mejor evidencia)

Hayden 2013, Internal Medicine
Riley 2019, BMJ

Desafío(s) práctico(s) en RS de factores pronóstico

RESUMEN/ IDEAS CLAVE

Investigación en factores pronóstico está menos estadarizada que la investigación sobre efecto de intervenciones:

- Busquedas más complejas (no hay filtros) y con más estudios
- Selección más compleja:
  - Necesidad de distinguir estudios confirmatorios (fase 2) de exploratorios (fase 1)
- Riesgo de sesgo más complejo: QUIPS – Dominio relacionado con estudio confirmatorio

Desafío(s) práctico(s) en RS de factores pronóstico

Avances o propuestas para superar los retos

- Clasificación adecuada de estudios pronóstico (indexación)

- Core-outcome sets: consistencia, comparabilidad, estandarizar resultados

- Estandarización de factores clave de ajuste (validez análisis, síntesis de evidencia)

- Uso de IA en búsquedas, selección (proyecto con epistemonikos, eppi reviewer,)

- Estandarización GUÍAS, checklists y herramientas (≈ modelos pronóstico TRIPOD, PROBAST)

MUCHAS GRACIAS POR VUESTRA ATENCIÓN

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