



Healthcare informatics approaches to reduce missed opportunities in diagnosis of pancreatic cancer

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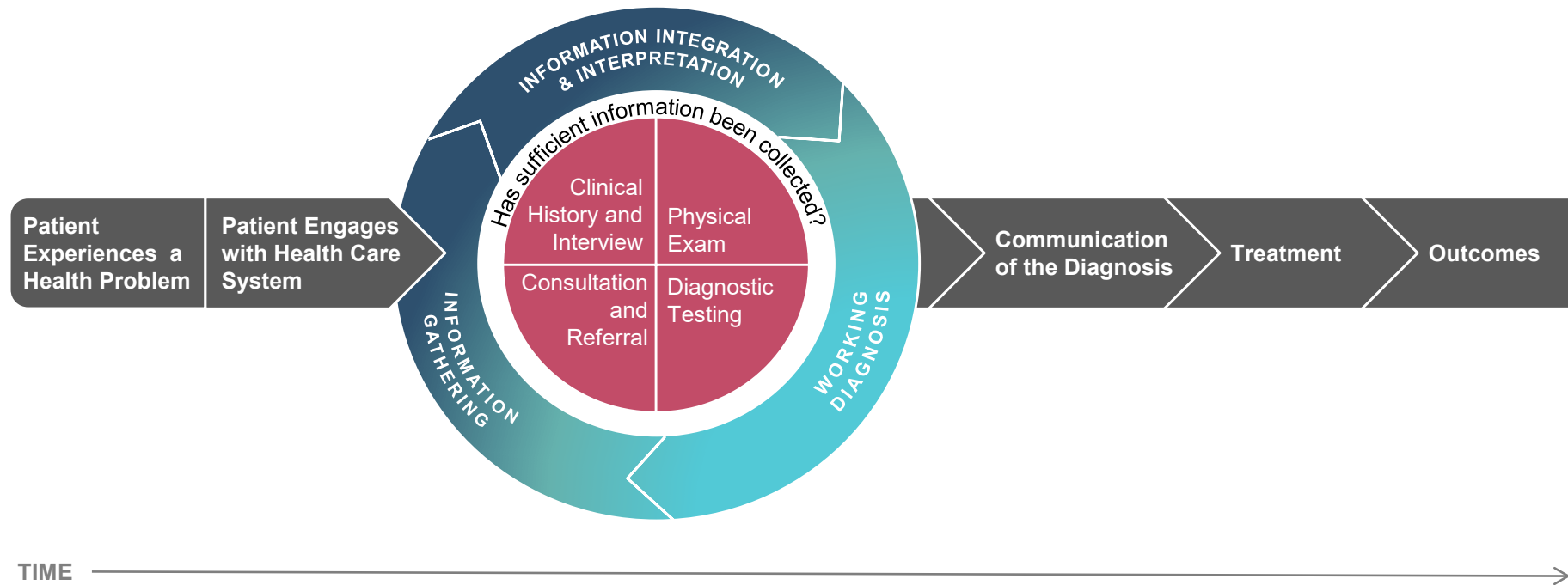
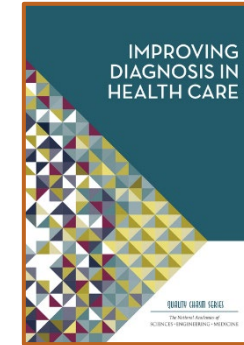
Background: Pancreatic Cancer (PaCa)

- PaCa is the third leading cause of cancer death in the U.S. and projected to rise to number two by 2030^{1,2}
- Early diagnosis offers the best chance of survival, yet <30% of patients are diagnosed at an early stage¹
- Efforts to improve diagnostic timing are needed¹

1. Siegel RL, et al. Cancer statistics, 2019. CA Cancer J Clin 2019;69:7-34.

2. Chari ST, et al. Pancreas 2015;44:693-712.

Model of the Diagnostic Process



Significance of Studying the Diagnostic Process Among PaCa Patients

- The National Academies of Sciences, Engineering, and Medicine's report on "Improving Diagnosis in Health Care" recommends that healthcare organizations have programs in place to¹ :
 - Monitor the diagnostic process
 - Identify, learn from, and reduce diagnostic delay
- Among the top 5 cancer killers, pancreatic cancer is the only cancer without a clear systematic approach to early diagnosis²

1. Committee on Diagnostic Error in Health Care, Board on Health Care Services, <http://www.ncbi.nlm.nih.gov/books/NBK338596/>.
2. US Preventive Services Task Force, JAMA 2019;322:438-444.

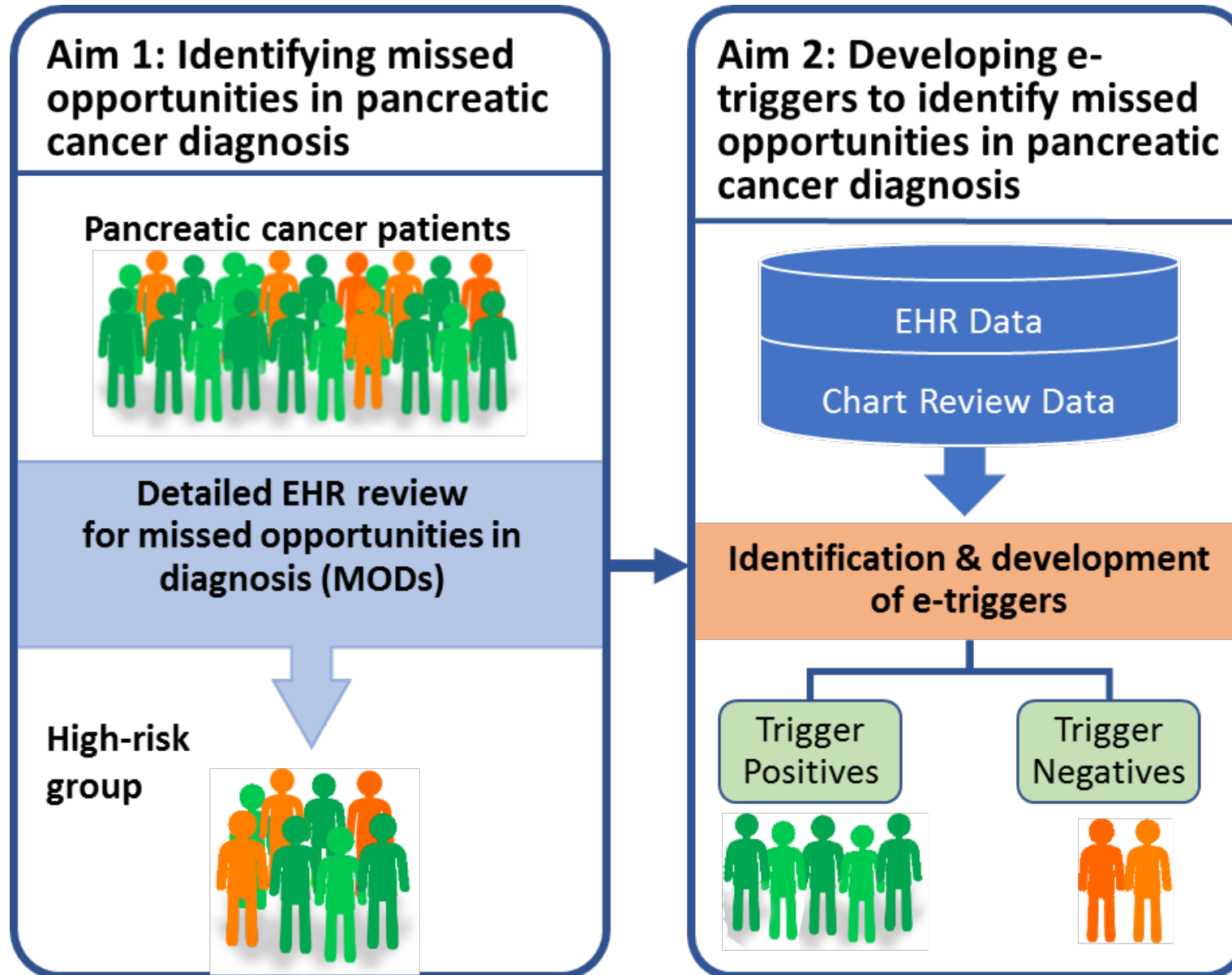
Background:

Diagnostic Delays in PaCa

- Over 30% of PaCa patients are initially misdiagnosed → average delay >4 months¹
- Significant association between shorter delays in diagnosis and better clinical outcomes (e.g., stage, survival)²
- Patient delay of ≤30 days and diagnostic delay of ≤60 days were significant predictors of potentially life-saving surgery³
- Data support that even relatively short delays can impact outcomes^{2,3}

1. Swords DS, et al. J Gastrointest Surg Off J Soc Surg Aliment Tract 2015;19:1813-1821.
2. Lukács G, et al. Cancer Manag Res 2019;11:9849-9861.
3. Deshwar AB, et al. Ann Pancreat Cancer 2018;1.

VA HSR&D CDA Aims



Pilot Work Within the National VA

Stage and treatment among PaCa cases

- VA Cancer Care Registry, ~10,000 veterans, diagnosed 2010-2018
 - Only 31% were diagnosed at early stage (AJCC stage I-II)
 - Only 54% received any cancer-specific treatment
 - Only 15% underwent surgical resection

Within the national VA we do not have earlier stage of PaCa diagnosis or better treatment rates than in the private sector, despite better and more equitable access to care

Pilot Work Within the Houston VA

Diagnostic delays and emergency presentations

- 243 veterans diagnosed between 2007-2019 with at least 2 years of Houston VA healthcare utilization
- 24% (57/243) experienced diagnostic delays \geq 60days
- 67% (162/243) had emergency presentations

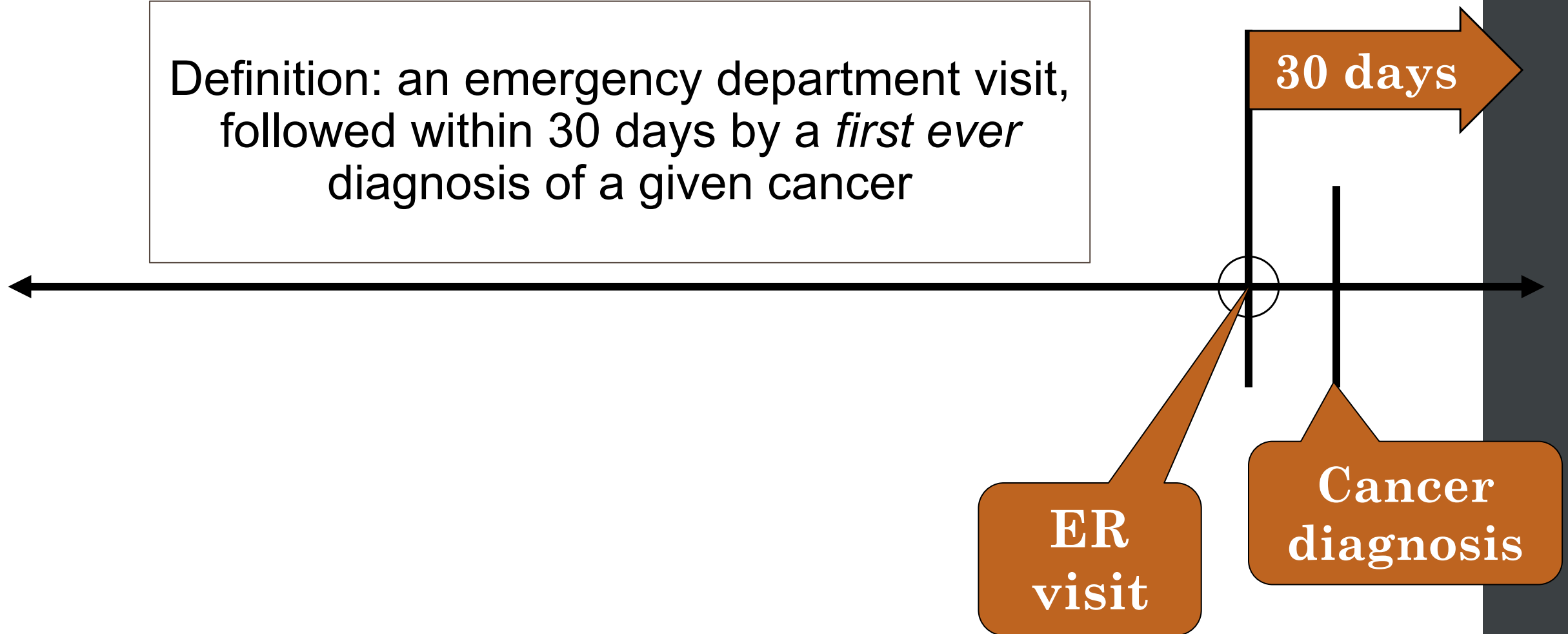
Pilot Work Within the Houston VA

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Emergency Cancer Presentation

Definition: an emergency department visit, followed within 30 days by a *first ever* diagnosis of a given cancer



Why Studying Emergency Presentations is Important

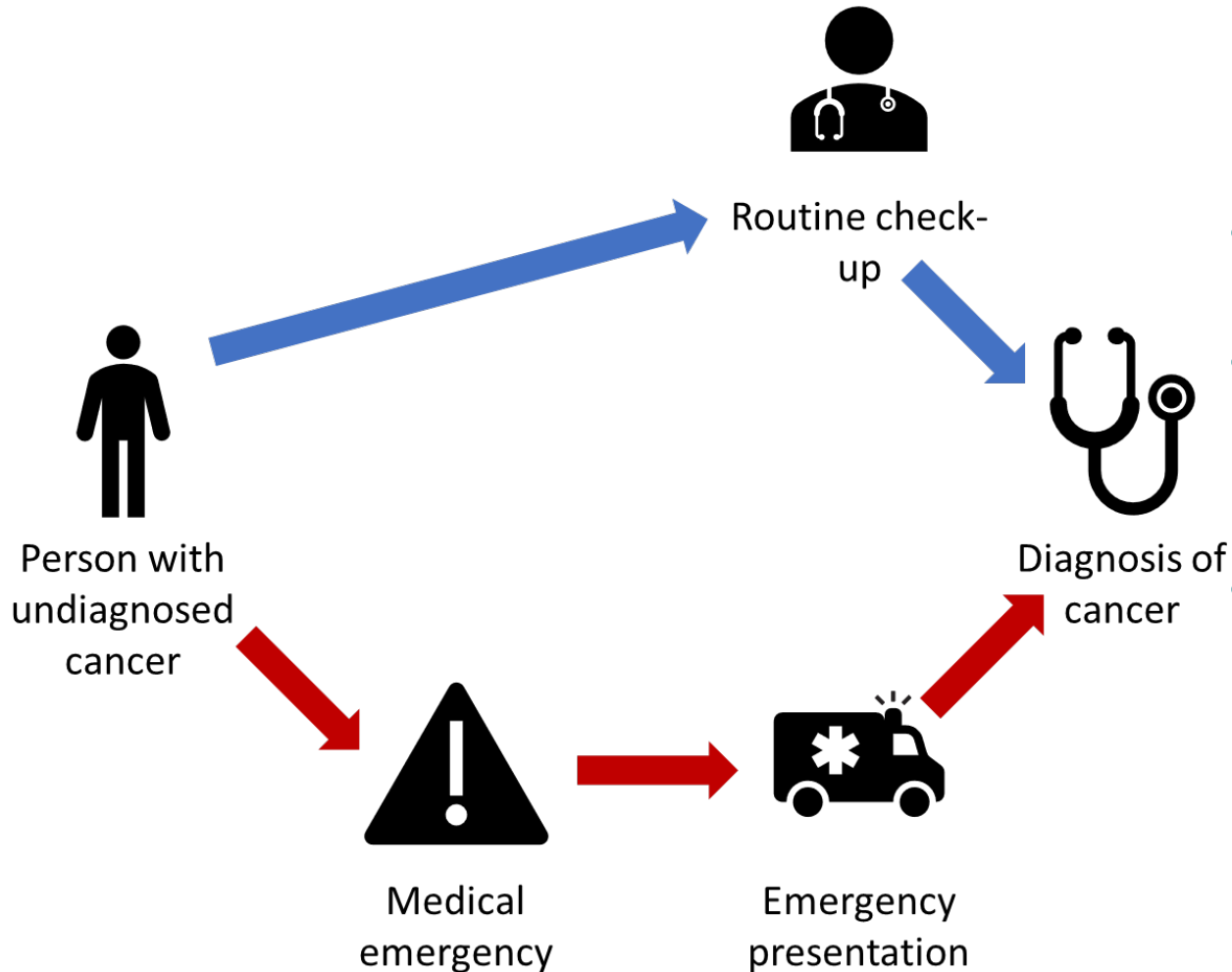
- Common: N~850,000 cancer cases, EP rates 24-42%^{1,2}
- ~34-60% of PaCa cases in European studies³
- Associated with more advanced stage and worse survival, even when adjusted for stage²
- Used as a cancer care quality indicator in Europe^{1,2}
- Little data regarding EPs in U.S. populations

1. Ellis-Brookes, Br J Cancer. 2012.

2. Zhou Y., *Nat Rev Clin Oncol*, 14 (2017), 45-56

3. M cPhail S. *Lancet Oncol* 2022;23:587-600

Emergency Presentation (EP)



- Greater patient/system burden
- May indicate problems at the health system-level
- May be preventable

Major Research Efforts

Study emergency presentations (EPs) of pancreatic cancer

Develop an algorithm to automate the detection of EPs

Study non-EP related diagnostic delays

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A Study of PaCa Emergency Presentations in the Houston VA

- **Objectives:**

- To describe the characteristics of EPs among PaCa patients
- To evaluate the associations between EPs and cancer stage, treatment and survival

- **Methods:**

- Retrospective cohort study
- Structured EHR review to identify EPs: new PaCa dx made within 30day of an ED visit in which a cancer was suspected
- Logistic regression and Cox hazards models for outcomes

- **Results:** N=243, 67% EPs

Outcome of Cancer Treatment in Houston VA

- ✓ Patients diagnosed through EPs were 74% less likely to receive cancer treatment

	Model 1* Adjusted OR (95% CI)	Model 2† Adjusted OR (95% CI)
EP Status		
No EP	-ref-	-ref-
Yes EP	0.27 (0.14-0.53)	0.26 (0.13-0.54)

**Adjusted for race, age, sex, BMI, tobacco and alcohol use, diabetes status, Deyo-Charlson comorbidity score, year of cancer diagnosis*

†Additionally adjusted for AJCC cancer stage

Outcome of Survival in Houston VA

- ✓ Patients diagnosed through EPs had 73% higher mortality risk
- ✓ 47% higher mortality risk after additionally adjusting for stage and treatment

	Model 1* Adjusted HR (95% CI)	Model 2^ Adjusted HR (95% CI)
EP Status		
No EP	-ref-	-ref-
Yes EP	1.73 (1.29-2.34)	1.47 (1.09-1.99)

**Adjusted for race, age, sex, BMI, tobacco and alcohol use, diabetes status, Deyo-Charlson comorbidity score, year of diagnosis*

^Additionally adjusted for AJCC cancer stage and cancer treatment

Summary of Emergency Presentation Study in Houston VA

- Emergency presentations among PaCa patients are:
 - Common (66.7% of cohort)
 - Independently associated with lower likelihood of receiving cancer treatment as well as decreased survival
- We are the first to show within a U.S. population that PaCa EPs are associated with worse clinical outcomes, independent of stage at diagnosis

Lessons Learned

- We found this study to be very labor intensive as it required manual record review to identify EP cases
- We wanted a way to study EPs on a larger scale within the national VA network with efficient EP case identification
- Automating the detection of EPs through an algorithm applied to the EHR would allow us to do so

Major Research Efforts

Study emergency presentations (EPs) of pancreatic cancer

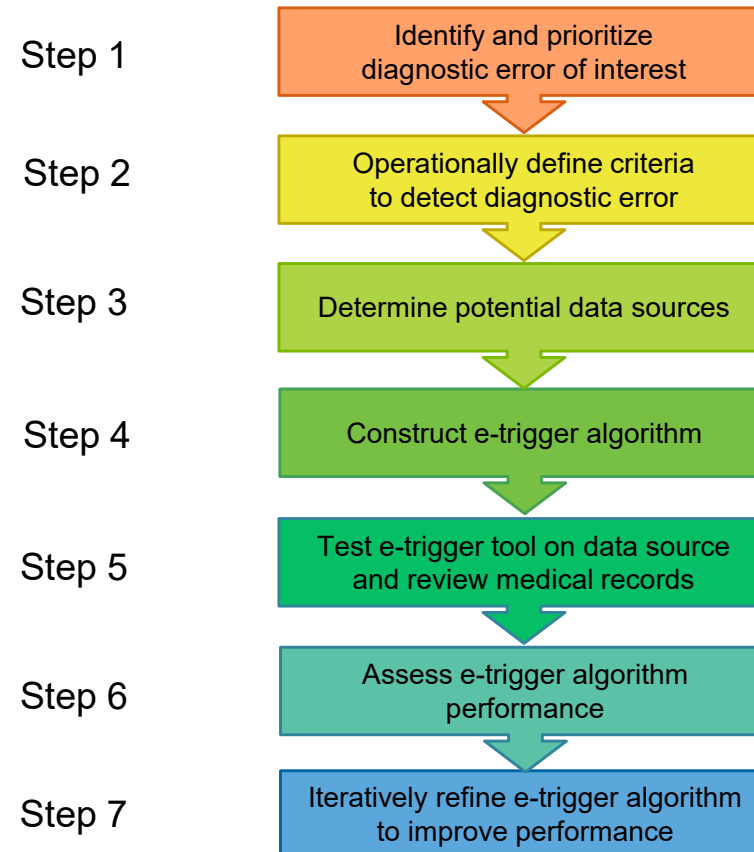
Develop an algorithm to automate the detection of EPs

Study non-EP related diagnostic delays

Electronic (e-) Trigger/ Algorithm Development

Safer Dx Trigger Tools Framework

- Used 7 steps of Safer Dx Trigger Tools Framework



E-Trigger Development

Step 1


An orange rectangular box with a thin black border. Inside the box, the text "diagnostic outcome of interest" is centered. Below the box is a large orange arrow pointing downwards, indicating a flow or transition to the next step.

diagnostic outcome
of interest

E-Trigger Development

Step 1

Identify and prioritize
diagnostic outcome
of interest



Emergency presentations among PaCa patients in the VA

E-Trigger Development

Step 1

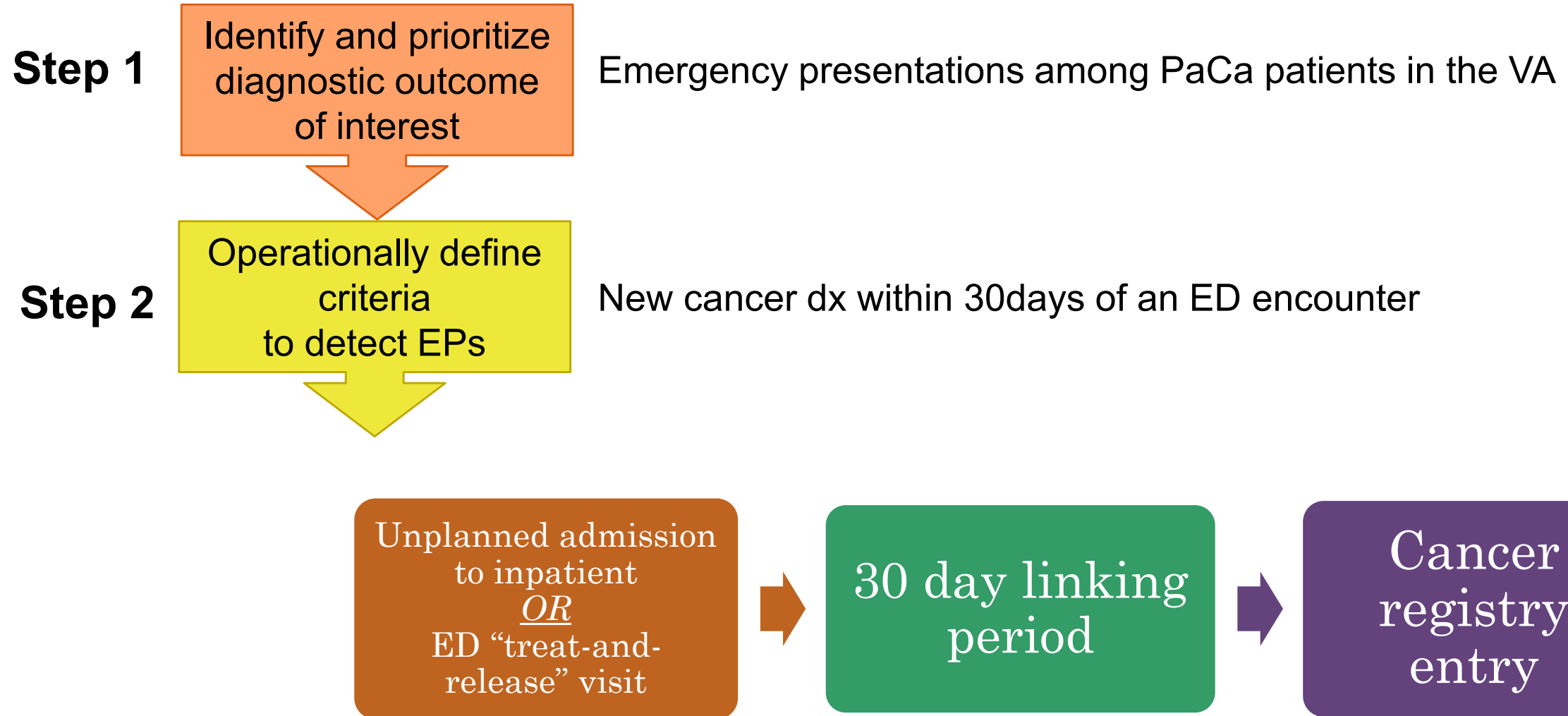
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Emergency presentations among PaCa patients in the VA

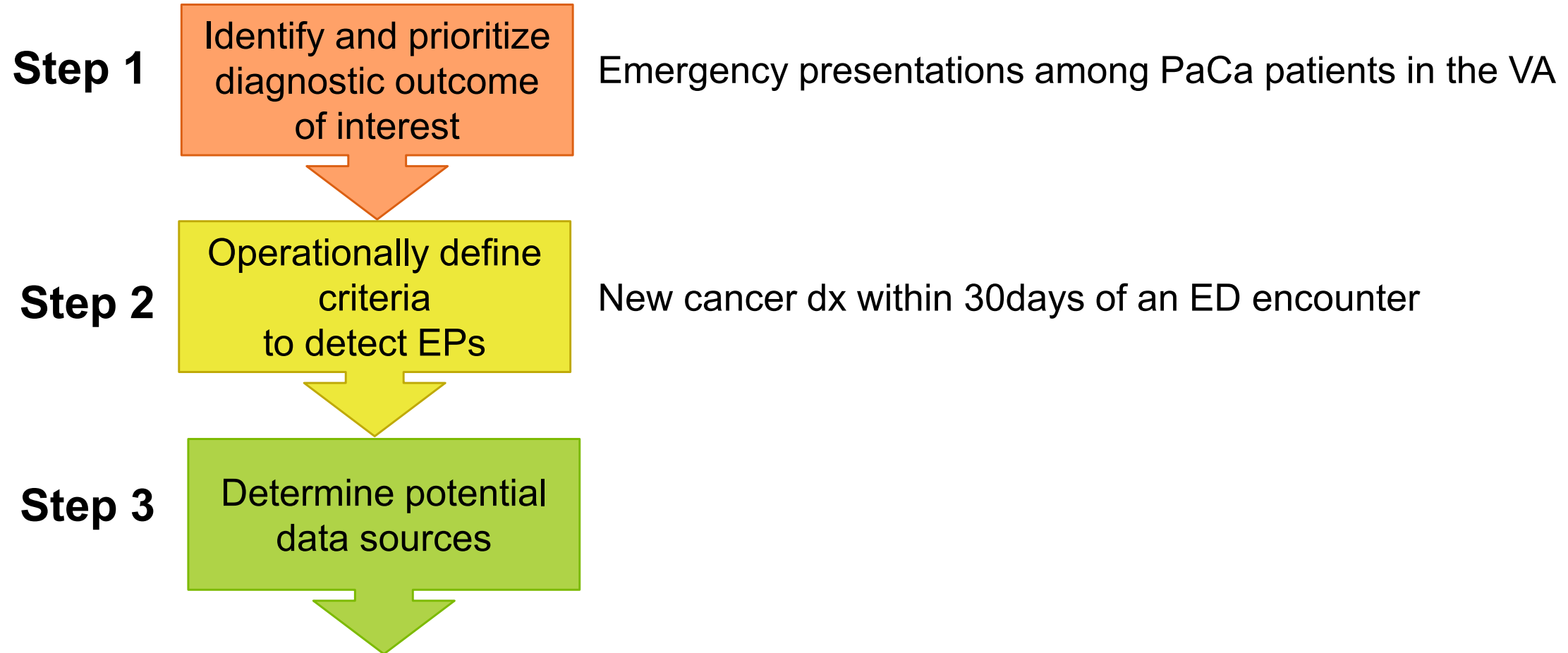
Step 2

Operationally define
criteria
to detect EPs

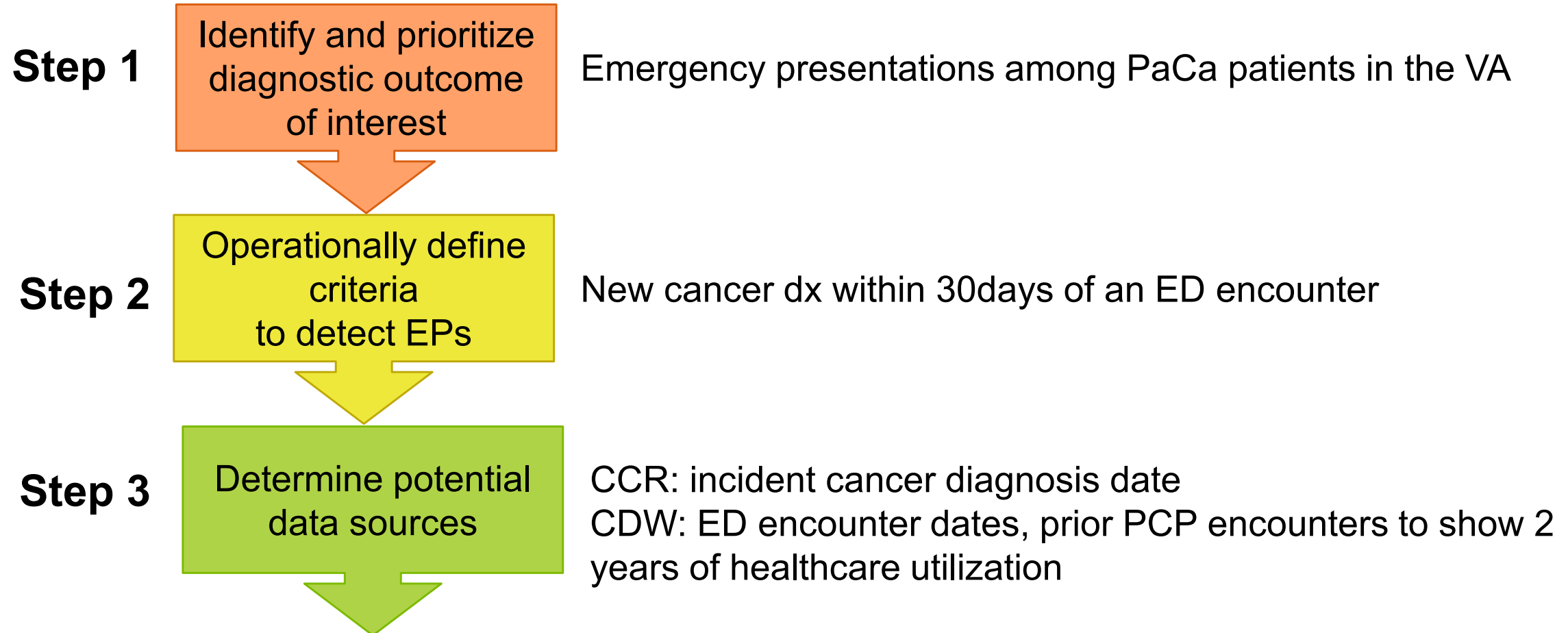
E-Trigger Development



E-Trigger Development



E-Trigger Development



E-Trigger Development

Step 4



Construct e-trigger
algorithm

E-Trigger Development

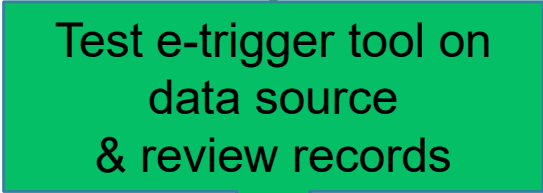
Step 4

Construct e-trigger
algorithm

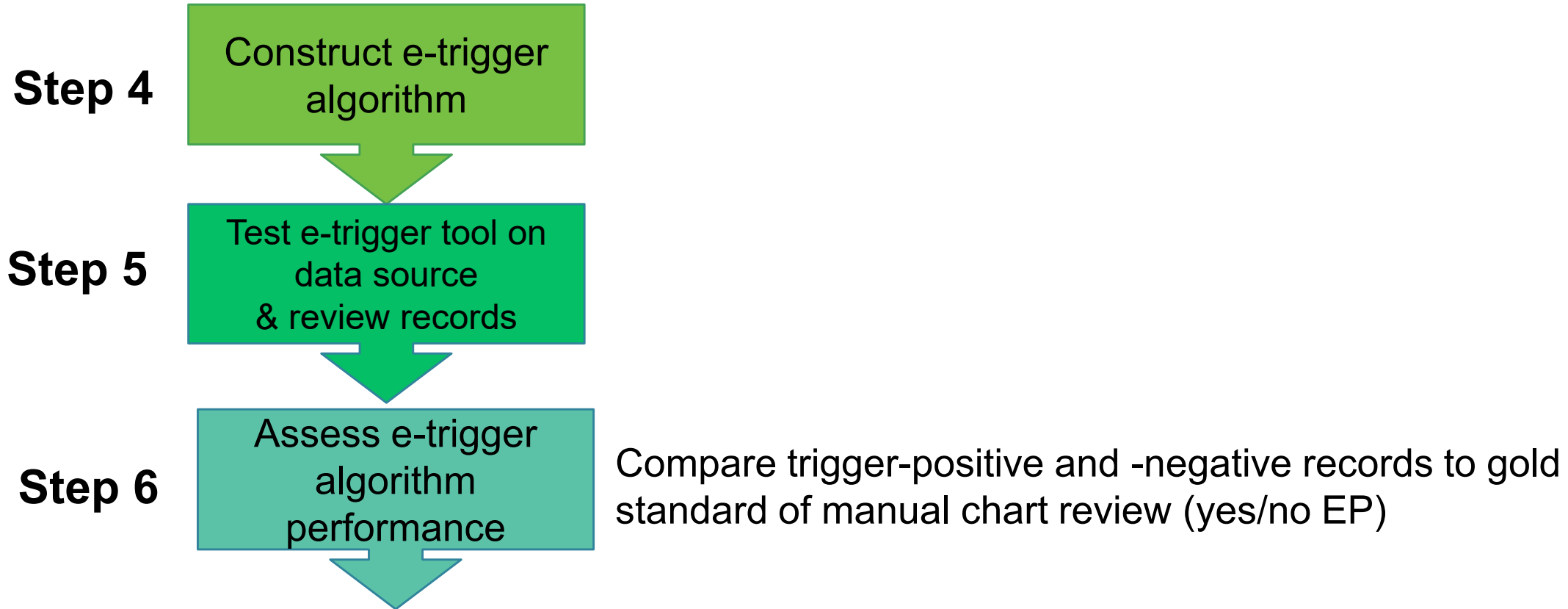


Step 5

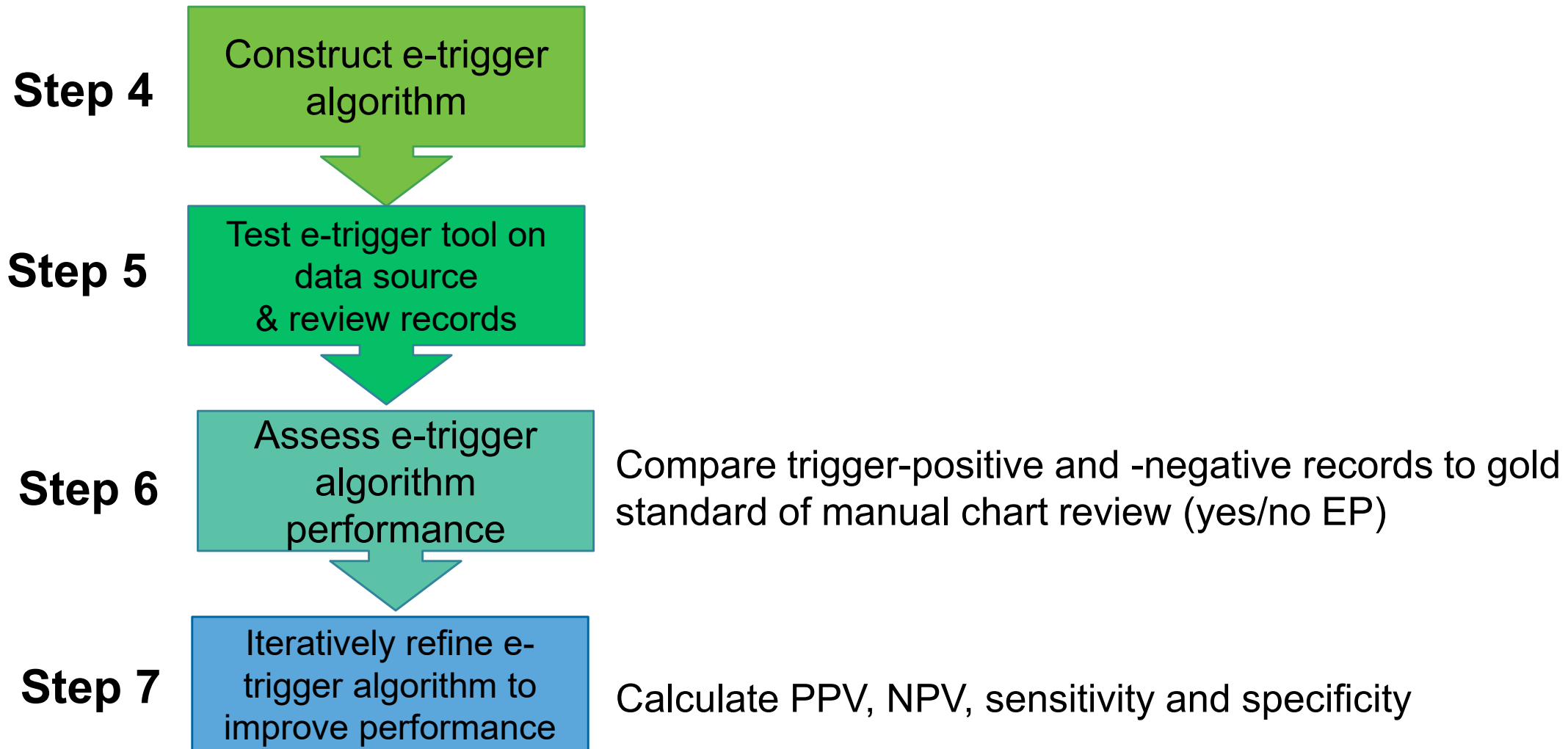
Test e-trigger tool on
data source
& review records



E-Trigger Development



E-Trigger Development



Emergency Presentation e-Trigger Developed in Houston Cohort

- We developed and validated a pancreatic cancer EP yes/no e-trigger within a Houston VA cohort (N=243, 2007-2019)
- The finalized automated e-trigger had the following performance characteristics:

PPV (95% CI)	NPV (95% CI)	Sensitivity	Specificity
89.5% (85.5-93.5)	80.5% (75.0-85.4)	90.6%	78.5%

Next Steps: Extension to National VA

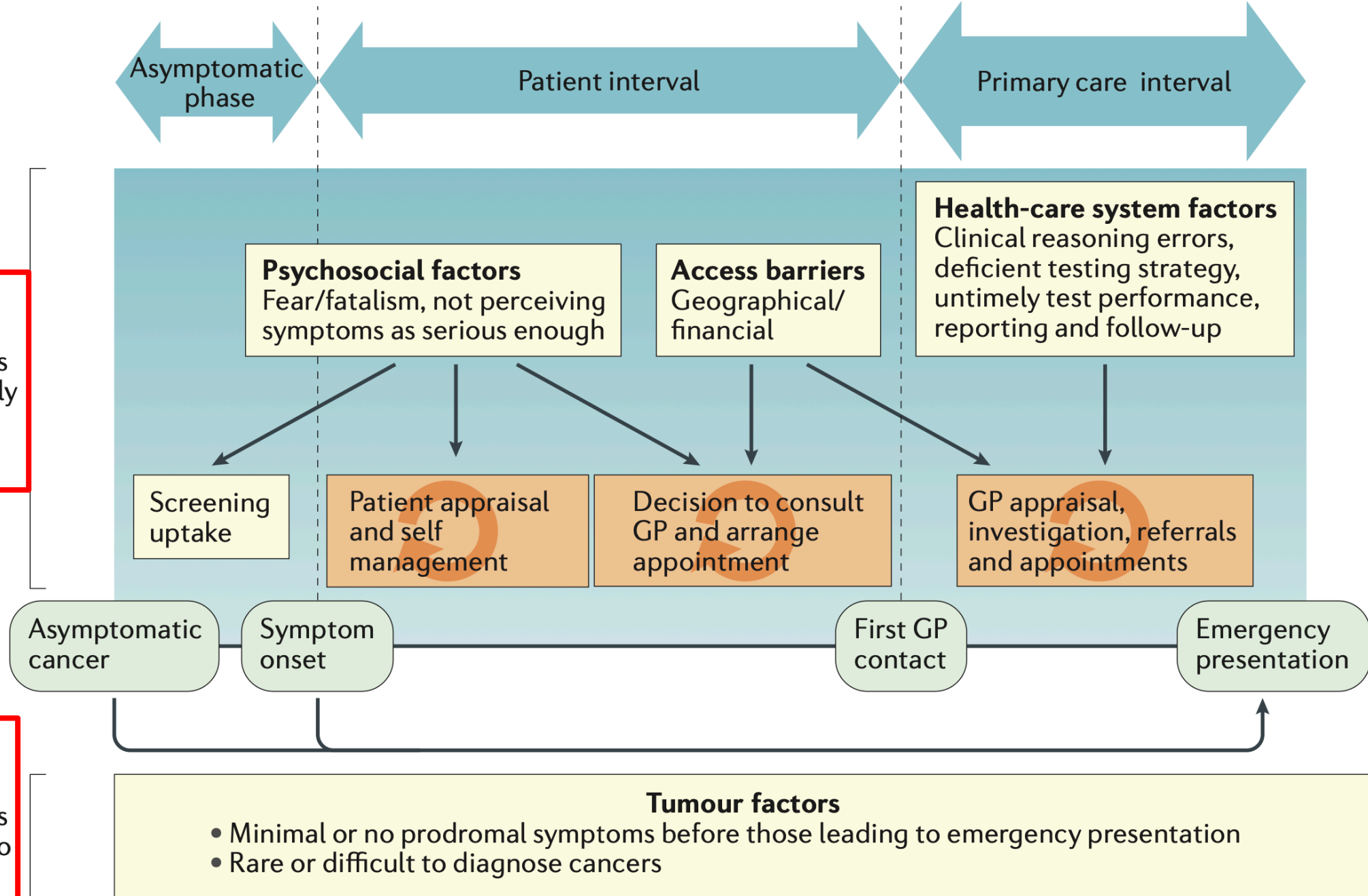
- Applied our e-trigger in the national VA from 2007-2019
 - 11,525 incident PaCa cases → **49.9% EPs** (5751/11525)
- Factors associated with EPs:
 - Race coded as non-Hispanic Black (adjusted OR 1.16; 95% CI 1.04-1.29)
 - Stage IV disease (adjusted OR 1.84; 95% CI 1.65-2.06)
- 1-year mortality was 77.3% for EPs vs. 59.5% for no EPs
 - Cox model: adjusted hazards ratio of 1.58 (95% CI 1.51-1.66)
 - Adjusted for age, race, sex, rurality, stage

Next Steps: Extension to National VA

- We need to validate the e-trigger performance in national VA data through select chart reviews of trigger-positive and –negative charts
- Once we have our finalized trigger, will study the association between EPs and stage, treatment and survival
- Enhancement of our e-trigger to include potentially preventable EPs

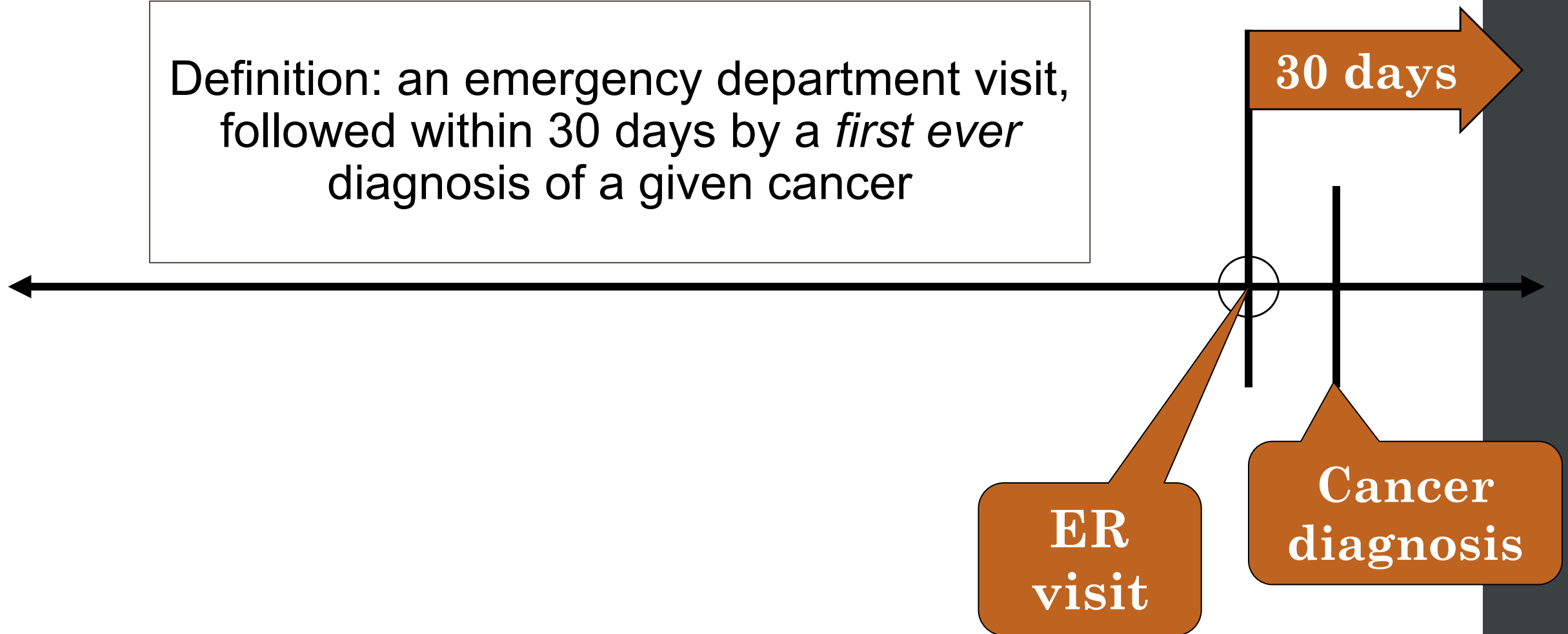
Emergency presentations are potentially avoidable

Emergency presentations are unlikely to be avoidable

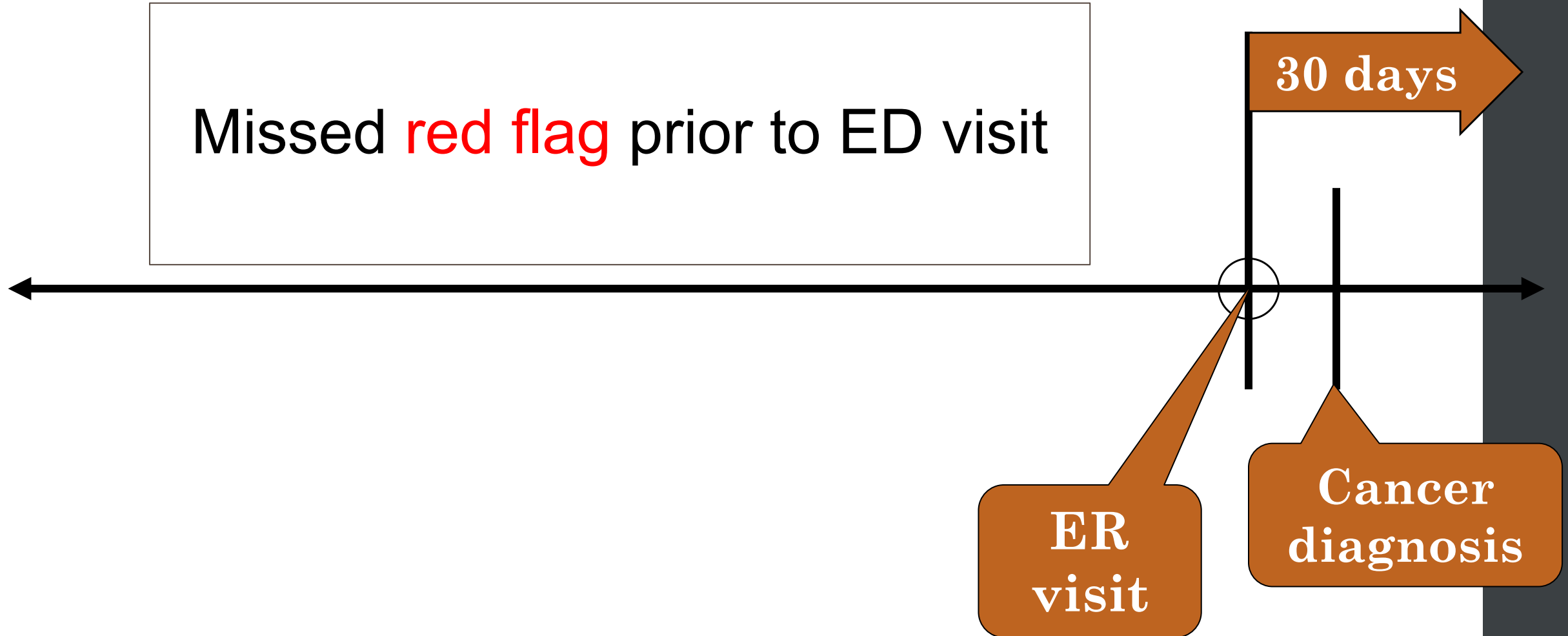


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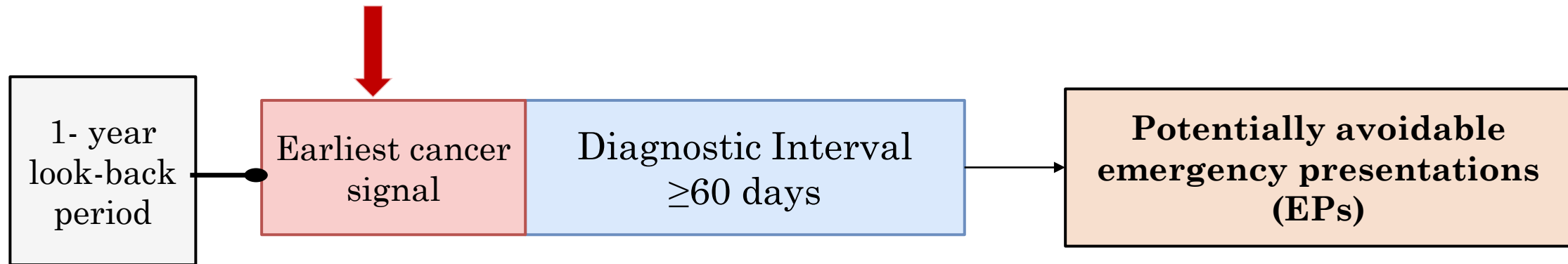
Emergency Cancer Presentation



Potentially Avoidable EPs: Input from Expert Panel

Pancreatic Ca Red Flags

1. New-onset jaundice
2. Cachexia
3. ≥ 1 cancer-associated symptom + any weight loss



Work in Progress Houston Cohort: Potentially Preventable EPs

Red Flag	Jaundice	Cachexia	Significant weight loss + ≥ 1 ssx
Overall cohort (N=64)	33 (41.2%)	32 (50.0%)	33 (51.6%)
Diagnostic delay ≥ 60 d (N=64)	3 (4.7%)	4 (6.3%)	14 (21.9%)
Among Yes EPs (N=44)	29 (65.9%)	23 (52.3%)	23 (52.3%)
Potentially avoidable EPs (N=44)	3 (6.8%)	3 (6.8%)	10 (22.7%)

2 measures we will develop: $\frac{EP_{Avoidable}}{PaCa_{All}}$ $\frac{EP_{Avoidable}}{EP_{All}}$

Summary of Progress on e-Trigger

We have already developed a PaCa emergency presentations e-trigger

- Developed and validated in a Houston cohort (N=243)
- Working on external validation in a national cohort(N=11,525)

Enhancement to a “potentially avoidable” emergency presentation e-trigger is underway

- Operationalized 3 red flags/ missed signals among PaCa emergency presenters
- Preliminarily looked at avoidable EP rates in pilot study

Implications for Clinical Practice

- After project completion, we expect this e-trigger can be applied automatically, at large scale, in the national VA
- Our e-trigger address both diagnostic process and cancer outcomes
- An EP measure can help assess quality of cancer diagnosis (already adopted in U.K.)
- High signal strength for potentially avoidable EPs

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Study non-EP related diagnostic delays

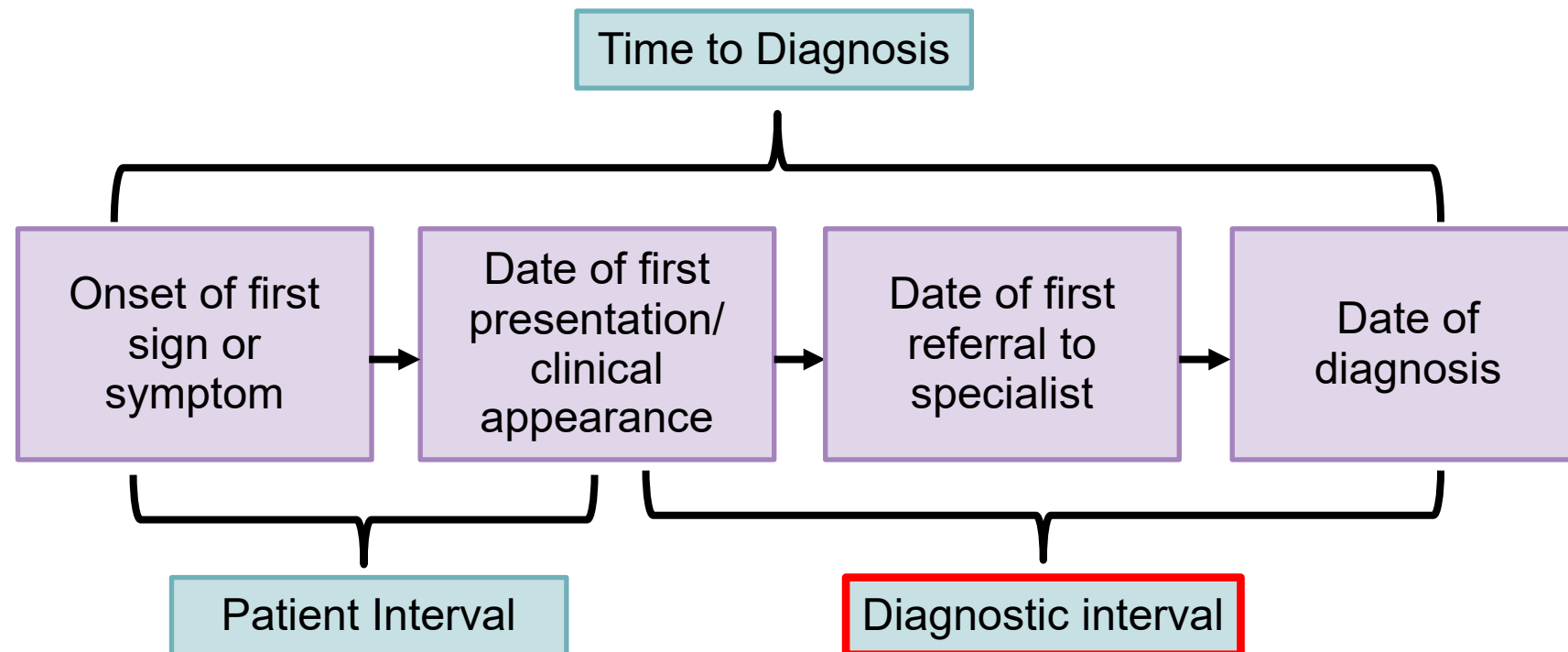
Potentially Avoidable Diagnostic Delays

- Instances in which *post-hoc* judgement indicates that alternative decisions or actions could have led to a timelier diagnosis
- Can occur outside of the context of EPs
- **Diagnostic interval** can serve as a surrogate marker for care delay

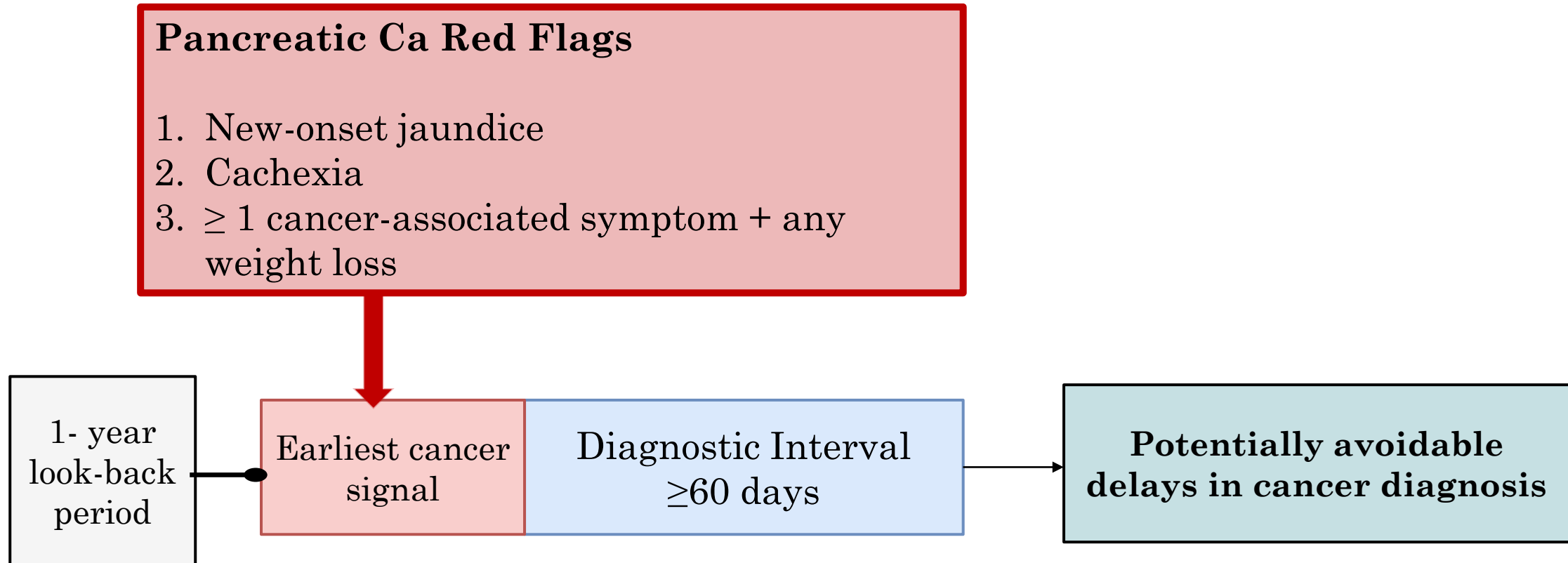
Singh H, Sittig DF. Advancing the science of measurement of diagnostic errors in healthcare: the Safer Dx framework. *BMJ Qual Saf* 2015;24:103-110.

Singh H. Editorial: Helping health care organizations to define diagnostic errors as missed opportunities in diagnosis. *Jt Comm J Qual Patient Saf* 2014;40:99-101.

Defining the Diagnostic Interval



Potentially Avoidable Diagnostic Delays: Input from Expert Panel



Preliminary Results: Avoidable Diagnostic Delays in Houston Cohort

Red Flag	Jaundice	Cachexia	Significant weight loss + ≥ 1 ssx
Overall cohort (N=64)	33 (41.2%)	32 (50.0%)	33 (51.6%)
Potentially avoidable diagnostic delay ≥ 60d (N=64)	3 (4.7%)	4 (6.3%)	14 (21.9%)

$$\frac{Delays_{Avoidable}}{PaCa_{All}} = 5 - 22\%$$

Next Steps: Identify Contributing Factors Related to Avoidable Delays

Patient Related	Patient-provider Encounter	Diagnostic Tests
<ol style="list-style-type: none"> 1. Delay in seeking care 2. Lack of adherence to appointments 3. Other 	<ol style="list-style-type: none"> 1. Problems with history. 2. Problems with physical exam. 3. Problems ordering diagnostic tests. 4. Failure to review previous documentation 5. Problems with data integration and interpretation 6. Other 	<ol style="list-style-type: none"> 1. Ordered test not performed at all. 2. Ordered tests not performed correctly. 3. Performed tests not interpreted correctly. 4. Misidentification. 5. Other
Follow-up/ Tracking		Referrals
<ol style="list-style-type: none"> 1. Problems w/ timely FU of abnormal test results. 2. Problems w/ scheduling appropriate, timely FU visits. 3. Problems w/ diagnostic specialties returning test results. 4. Problems w/ reviewing test results. 5. Problems w/ documenting response to test results. 6. Problems w/ monitoring patients thru FU. 7. Other 		<ol style="list-style-type: none"> 1. Problem initiating referral. 2. Lack of appropriate actions on requested consultation. 3. Communication breakdown from consultant to referring provider. 4. Other

Summary of Work

- ~70% of PaCa patients are diagnosed with late-stage disease within the national VA
- ~50-60% experience EPs, which are associated with worse outcomes
 - Developed an automated algorithm for EP case identification for larger scale study
- We have shown ~25% of PaCa patients have diagnostic delays ≥ 60 days irrespective of EP status
 - Working on identifying potentially avoidable delays and contributing factors

Summary of Work

- There are several clinically detectable signals of undiagnosed PaCa, potentially allowing for earlier diagnosis with appropriate tools
- Identifying and reducing diagnostic delays can lead to improved patient-centered care, a high-priority area for the VA
- Measurement is the first step to understanding and reducing diagnostic delays in cancer care
- E-trigger tools can help identify patients who have potential opportunities for an earlier cancer diagnosis that may be missed during routine care



Contact Info:

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Symptoms of PaCa

(*>15% frequency depending on study*)

Initial cancer sign or symptom*
Jaundice
Cachexia/ Significant weight loss
Abdominal or dyspepsia
Appetite loss/ anorexia
Nausea or vomiting
Change in bowel habits (diarrhea or constipation)
Back pain (<i>or flank pain</i>)
New-onset diabetes or hyperglycemia
Fatigue (<i>or malaise or general weakness</i>)

**Each patient can have more than one cancer sign or symptom*

RAND/UCLA Appropriateness Method (RAM) Level of Agreement on Proposed PaCa “Red Flags”

“Red Flag”	Inappropriate			Uncertain			Appropriate		
	1	2	3	4	5	6	7	8	9

A priori: if >75% agreement by the panel that a proposed “red flag” was appropriate (score range 7-9) then was included for study