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Robotic-Assisted Surgery for Esophageal Cancer: Analysis of Short & Long-Term Outcomes

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VA Evidence Synthesis Program overview

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- Established in 2007
- Provides tailored, timely, and accurate evidence syntheses of VA-relevant, Veteran-focused healthcare topics. These reports help:
  - Develop clinical policies informed by evidence;
  - Implement effective services and support VA clinical practice guidelines and performance measures; and
  - Set the direction for future research to address gaps in clinical knowledge.
- Four ESP Centers across the US:
  - Directors are VA clinicians, recognized leaders in the field of evidence synthesis, and have close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration
- ESP Coordinating Center in Portland:
  - Manages national program operations and interfaces with stakeholders
  - Produces rapid products to inform more urgent policy and program decisions

To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers.

The program solicits nominations for review topics several times a year via the program website.

ESP Center locations

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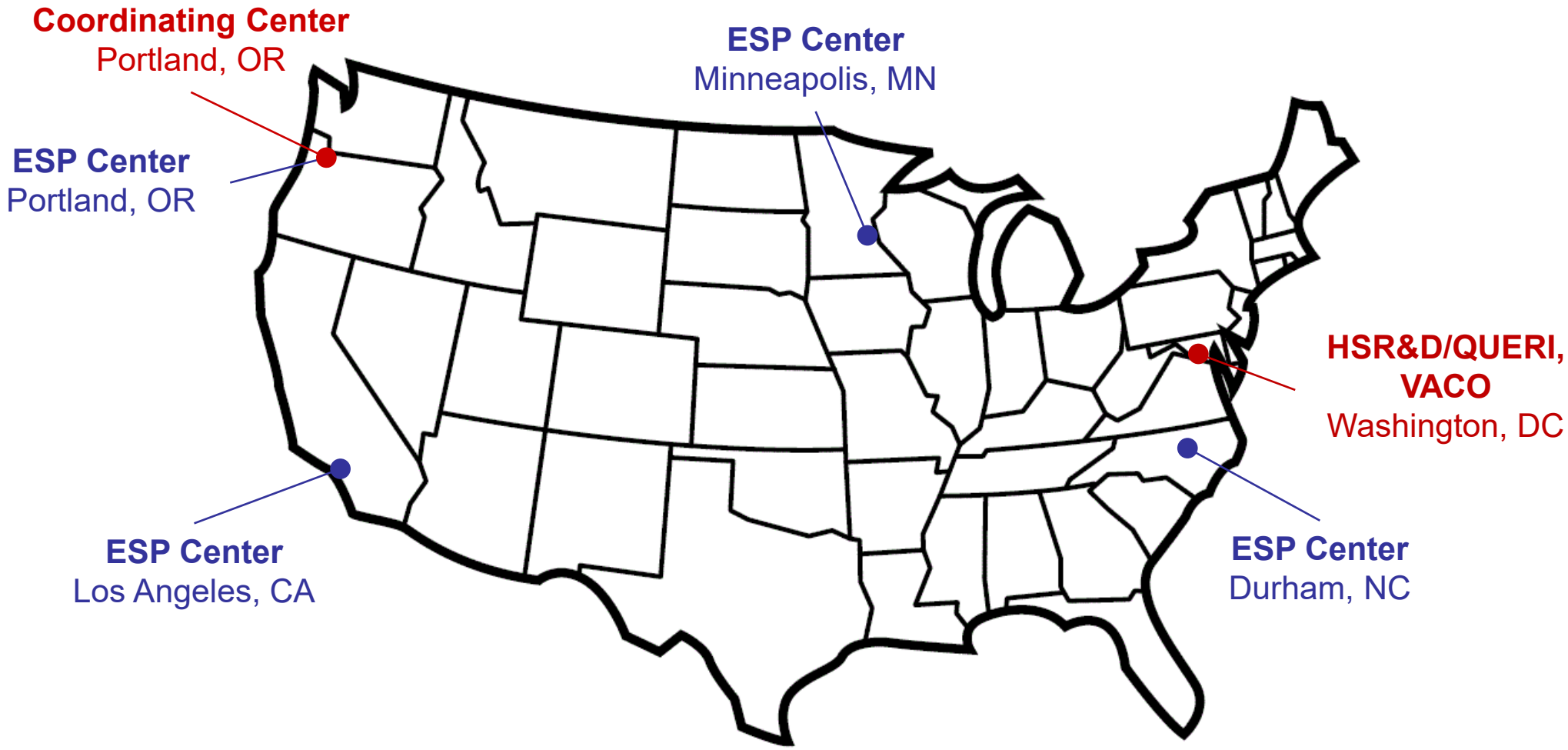

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The review team developed the report's scope, study questions, and methodology in consultation with the Operational Partners, ESP Coordinating Center, and technical expert panel (TEP). The authors gratefully acknowledge Roberta Shanman, Jon Bergman, and the following individuals for their contributions:

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Disclosure

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This report is based on research conducted by the Evidence Synthesis Program (ESP) Center located at the **West Los Angeles VA Medical Center, Los Angeles, CA**, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (*e.g.*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

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March 2021

Full-length report available on ESP website:
http://www.hsrd.research.va.gov/publications/esp/reports.cfm

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Esophageal Cancer Awareness Month

- Esophageal cancer makes up **1%** of all cancer diagnoses in the U.S.
- About **19,260** patients will be diagnosed in 2021
- About **15,530** esophageal cancer-related deaths
- **20%** 5-year survival

American Cancer Society; 2021 Cancer Statistics

Background

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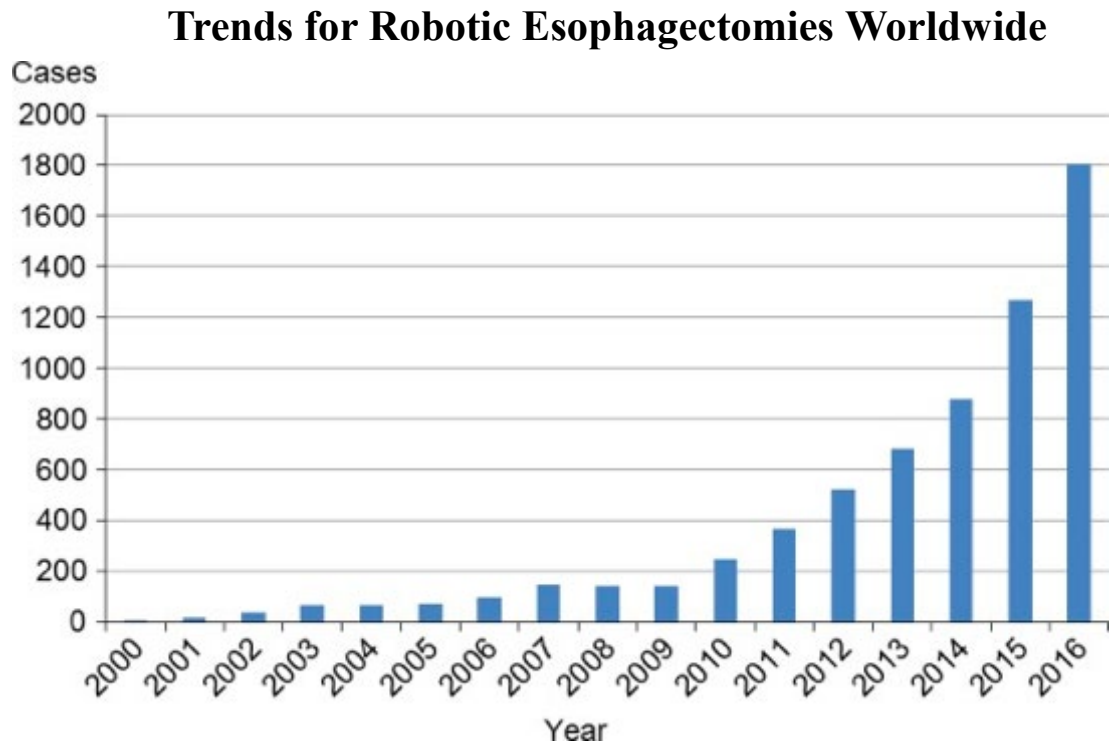
- Nine-fold increase in robot-assisted minimally invasive esophagectomy (RAMIE) from 2009-2016

- Open esophagectomy and thoraco-laparoscopic esophagectomy are the most common approaches. It is unclear how RAMIE compares to these other techniques.



Seto (2017); *Ann Gastroenterol Surg*

FDA warning 2019

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Caution When Using Robotically-Assisted Surgical Devices in Women's Health including Mastectomy and Other Cancer-Related Surgeries: FDA Safety Communication

- Benefits and risks are not established, and long-term clinical and oncologic outcomes are questioned
- Robotic platform requires economic investment and unclear whether improvements in outcomes outweigh costs (cost-effectiveness questions remain).

Key questions

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1) What is the clinical effectiveness of robotic-assisted esophagectomy compared to open or thoracoscopic/laparoscopic esophagectomy for cancer?

2) What is the cost-effectiveness of robotic-assisted esophagectomy compared to open or thoracoscopic/laparoscopic esophagectomy for cancer?

Selection of Studies

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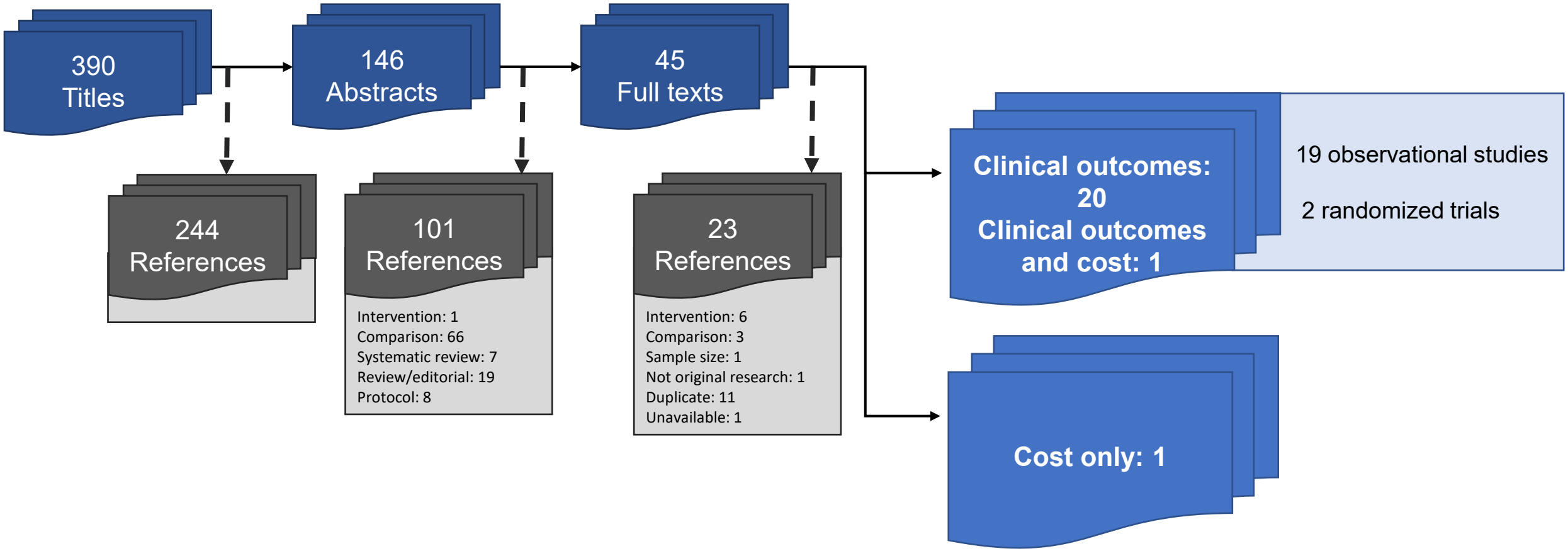

Key questions

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Outcomes of Interest

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Intra-operative

- Operative time
- Estimated blood loss (EBL)
- Lymph node harvest

Short-term

- Anastomotic leak
- Recurrent laryngeal nerve (RLN) palsy
- Pulmonary complications
- Total complications
- Length of stay**
- 90-day mortality

Long-term

- Recurrence
- Cancer-free survival

**U.S. studies only

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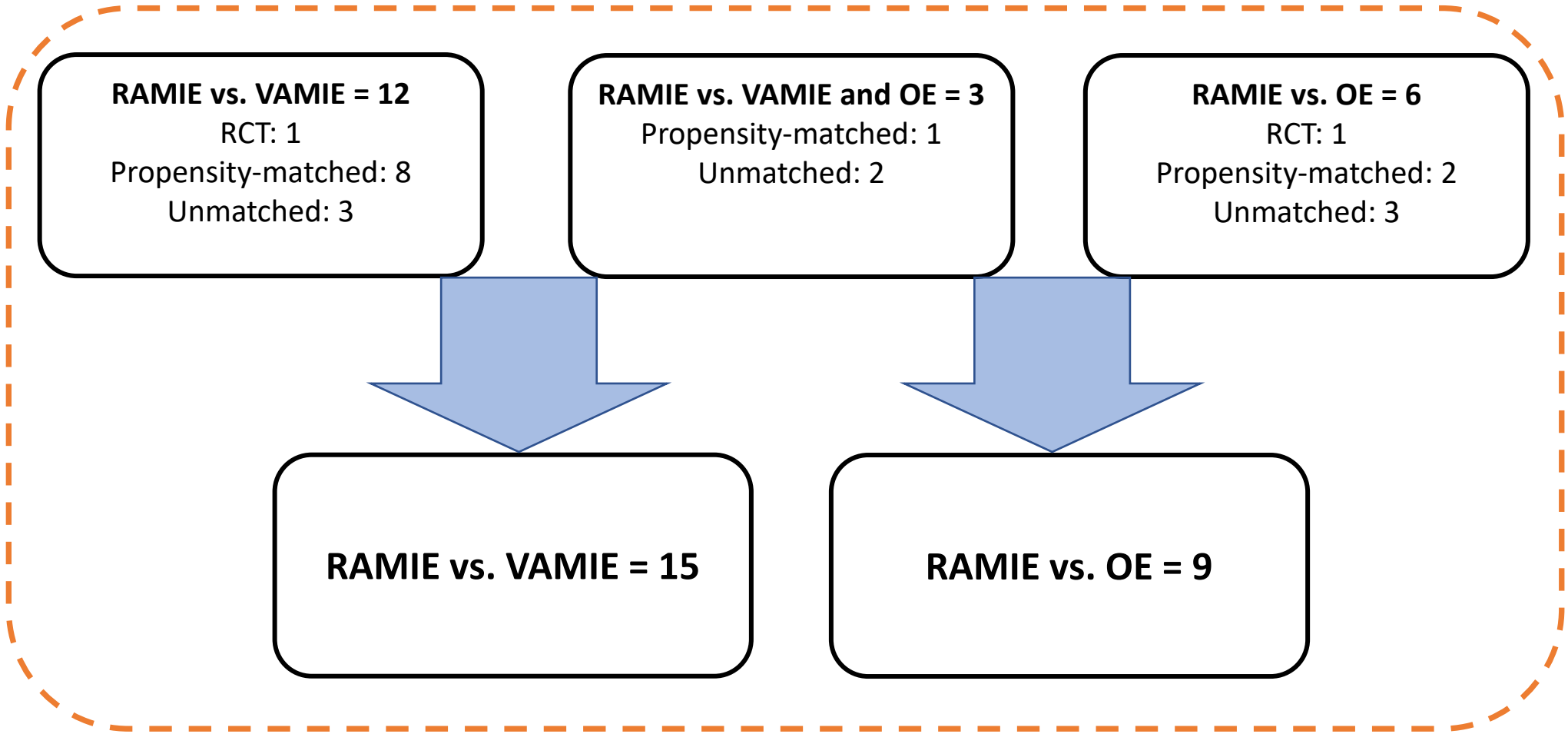
Included Studies



Intraoperative Outcomes – Operative Time

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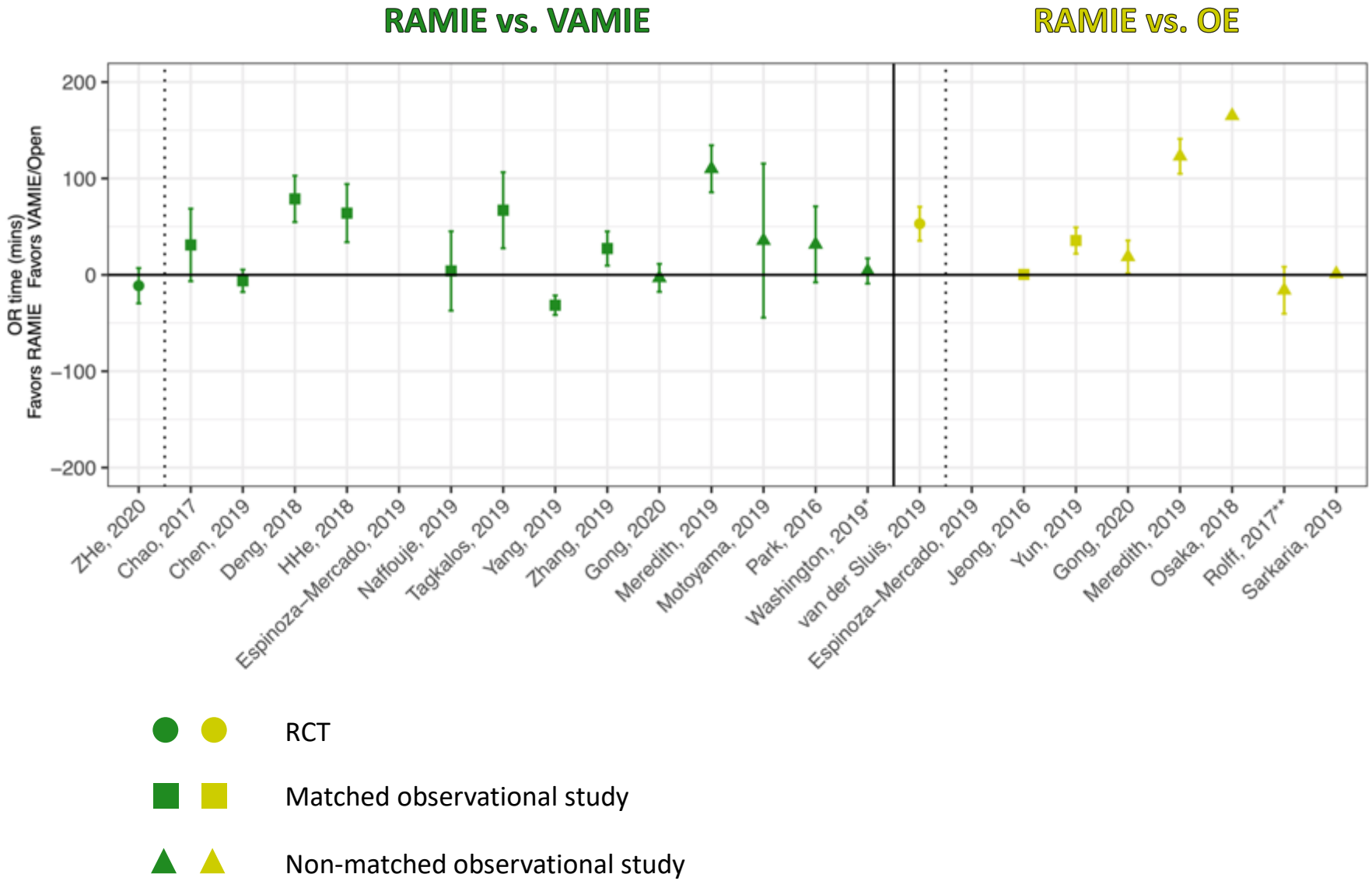

RCT

Matched observational study

Non-matched observational study

RAMIE vs. VAMIE

- RAMIE associated with longer operative time

RAMIE vs. OE

- RAMIE associated with longer operative time

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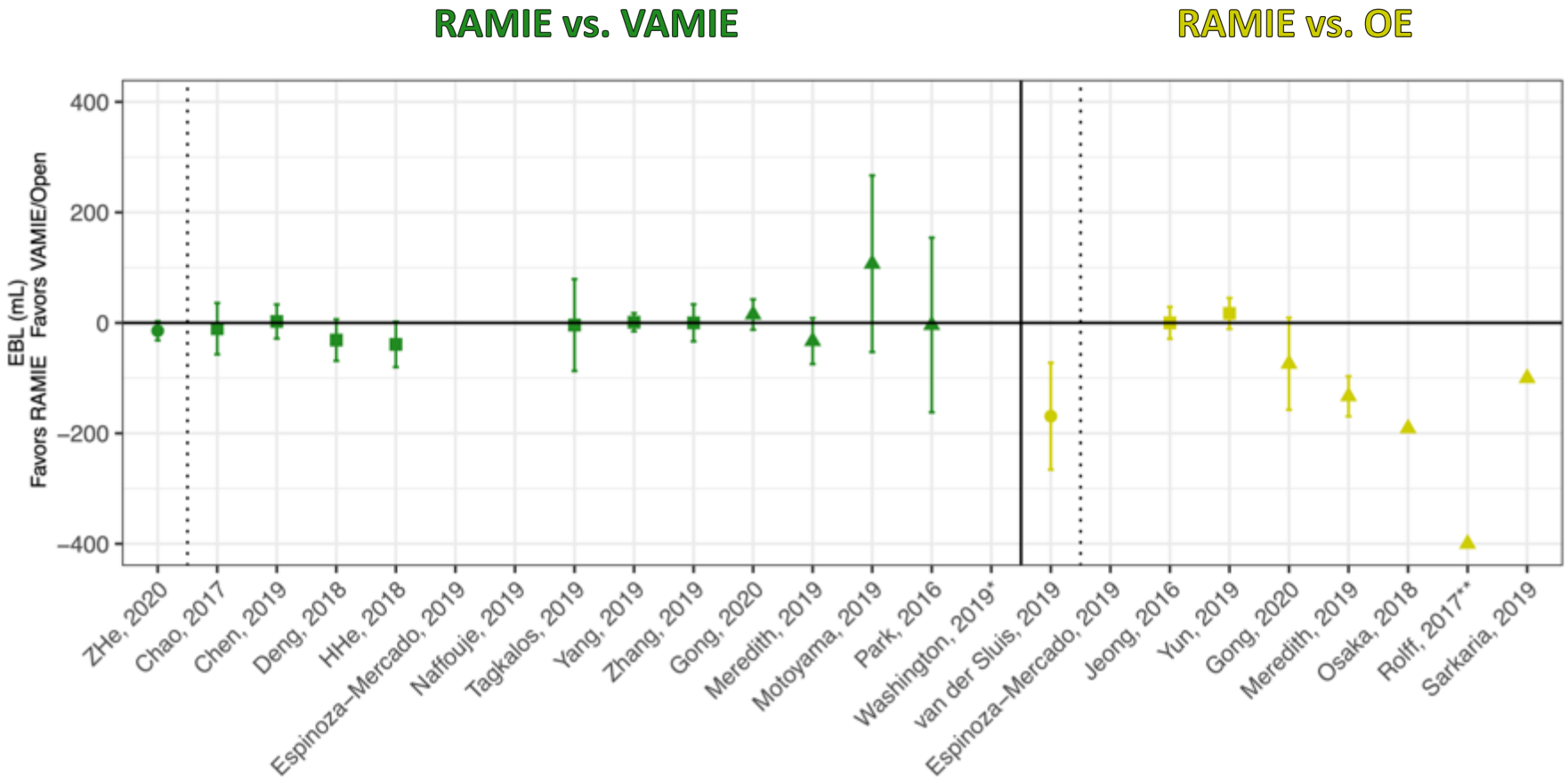
Intraoperative Outcomes – EBL



RCT

Matched observational study

Non-matched observational study

RAMIE vs. VAMIE

- No difference in EBL

RAMIE vs. OE

- RAMIE associated with less EBL

Intraoperative Outcomes – LN Harvest

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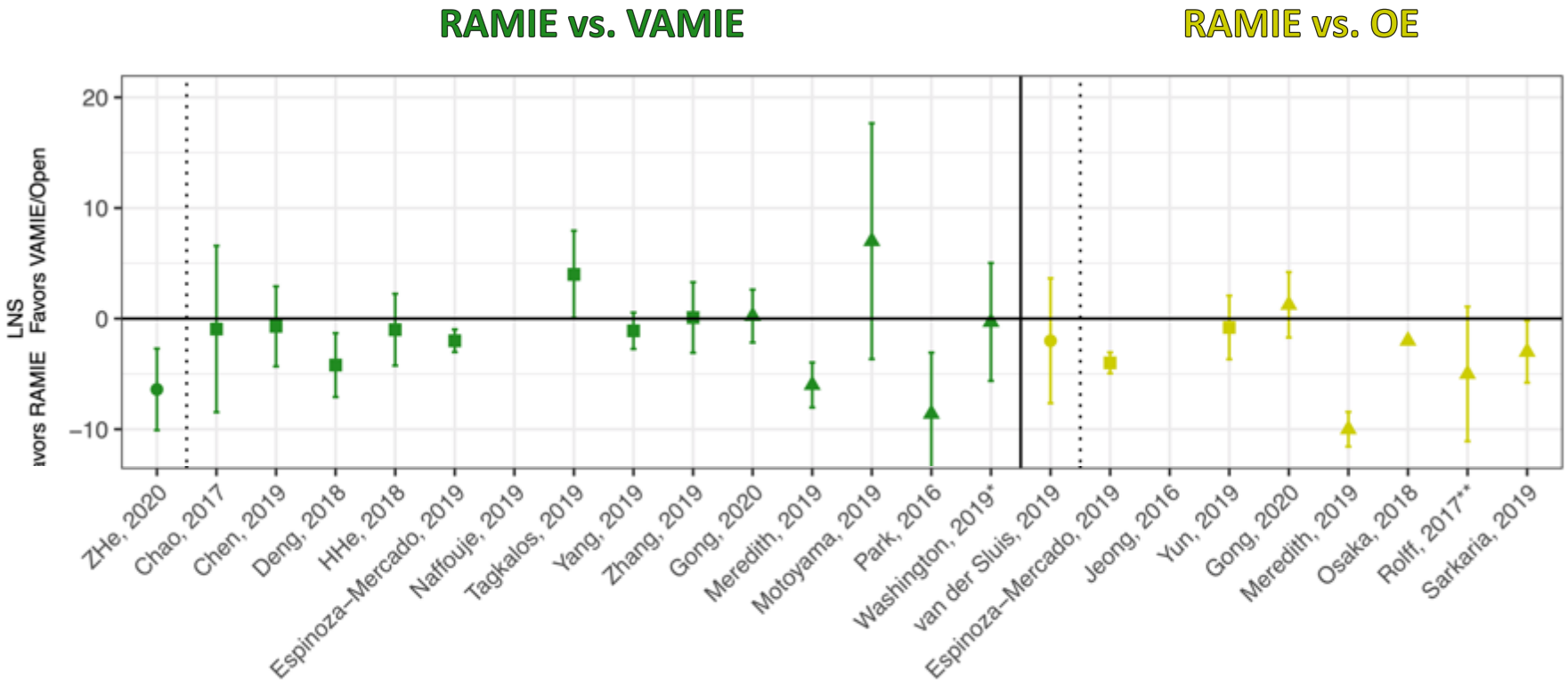

RAMIE vs. VAMIE

- RAMIE associated with larger lymph node harvest

RAMIE vs. OE

- RAMIE associated with larger lymph node harvest

RCT

Matched observational study

Non-matched observational study

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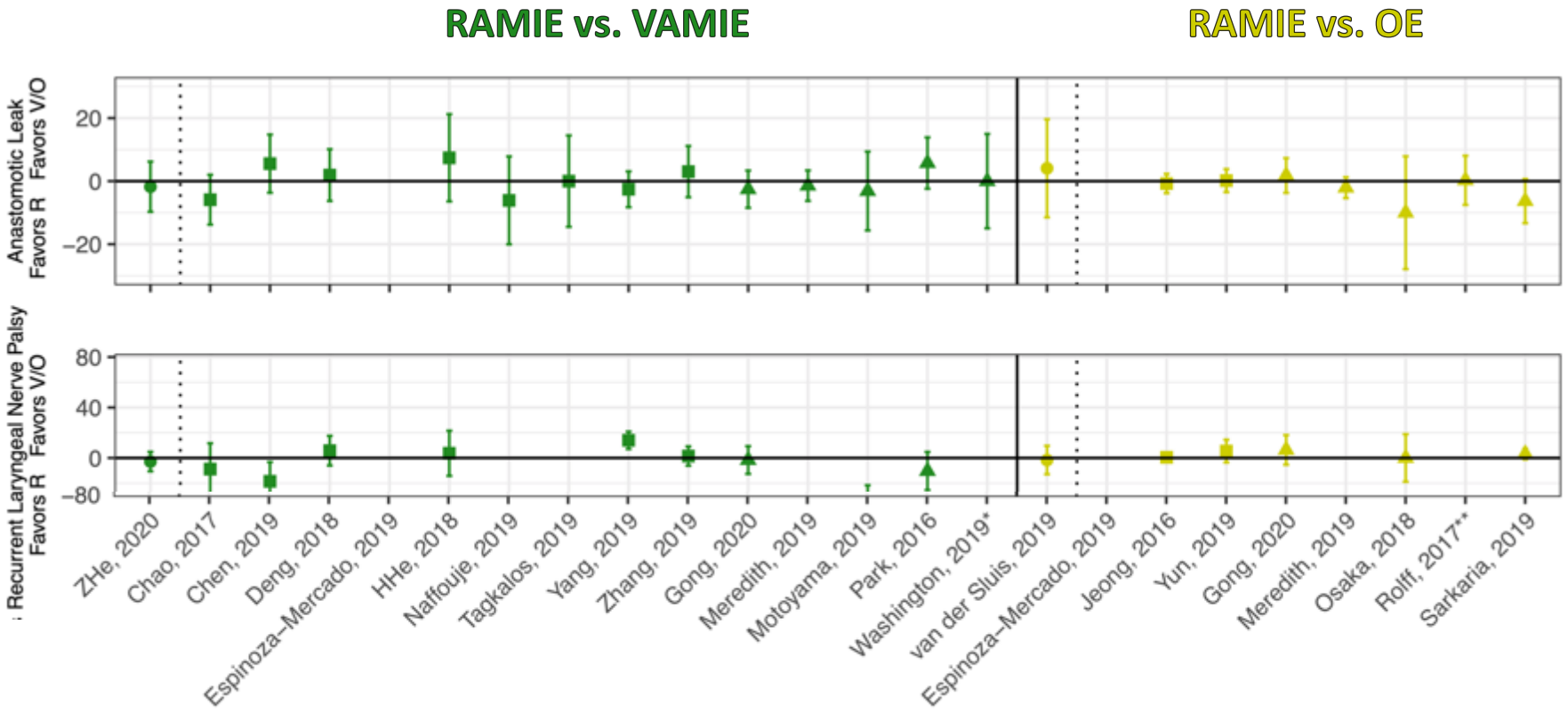
Short-term Outcomes



RCT

Matched observational study

Non-matched observational study

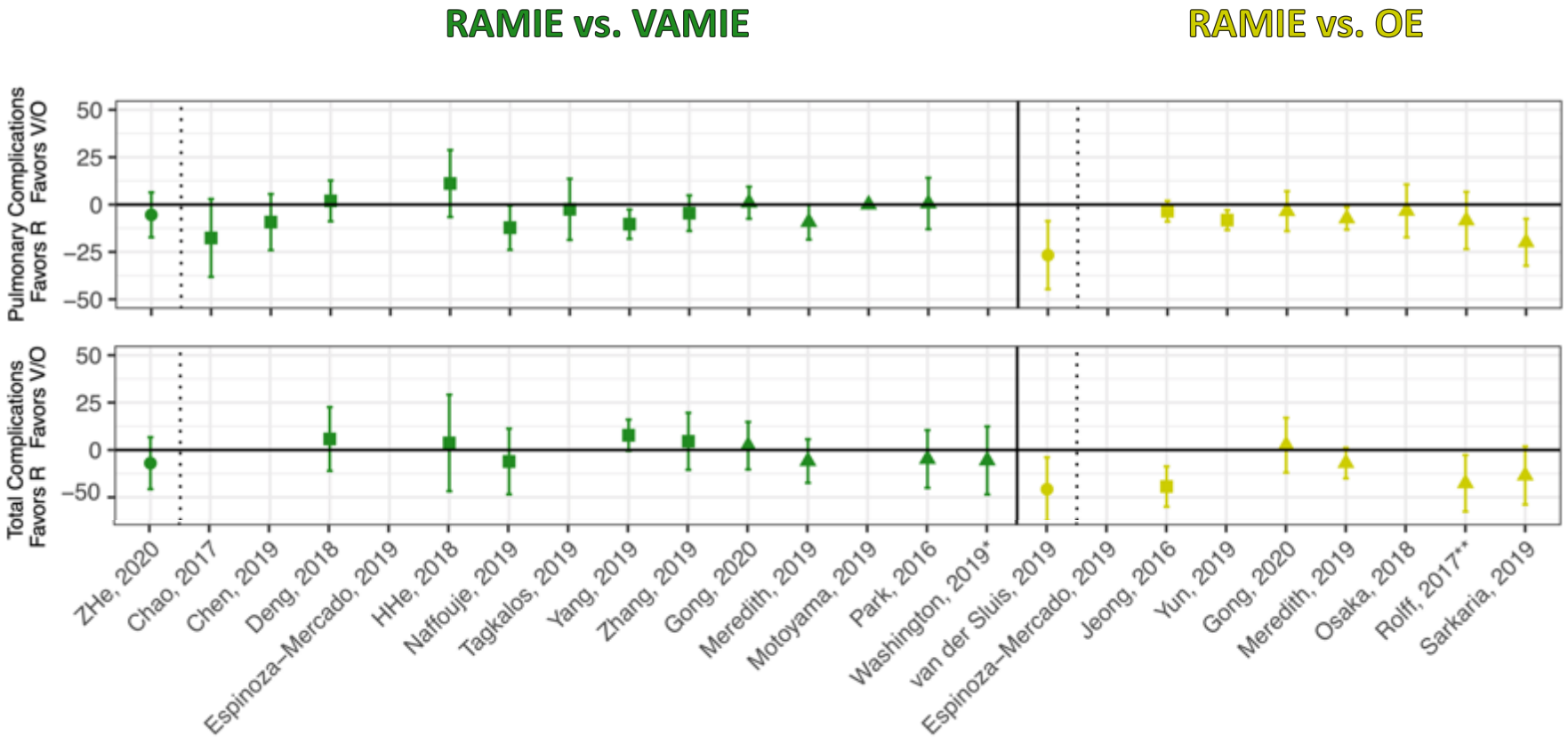
RAMIE vs. VAMIE

- No difference in anastomotic leak or RLN palsy

RAMIE vs. OE

- No difference in anastomotic leak or RLN palsy

Short-term Outcomes cont.



RCT

Matched observational study

Non-matched observational study

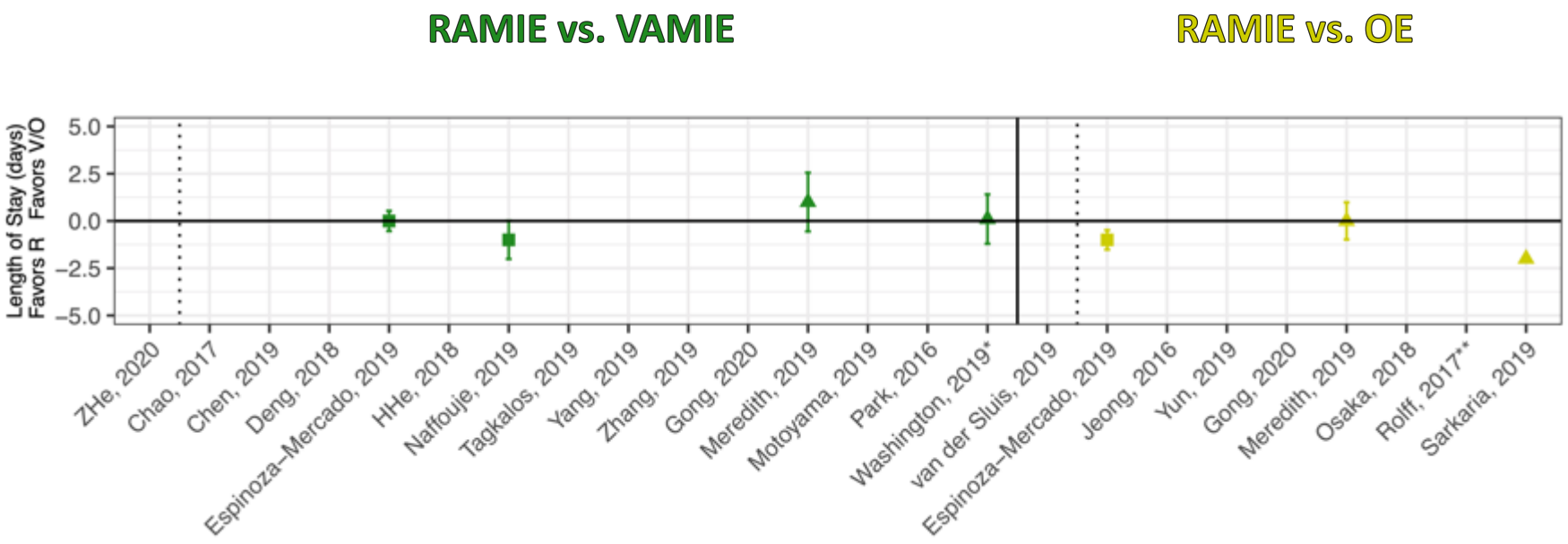
RAMIE vs. VAMIE

- No difference in pulmonary or total complications

RAMIE vs. OE

- RAMIE associated with fewer pulmonary and total complications

Short-term Outcomes cont.



RAMIE vs. VAMIE

- No difference in LOS

RAMIE vs. OE

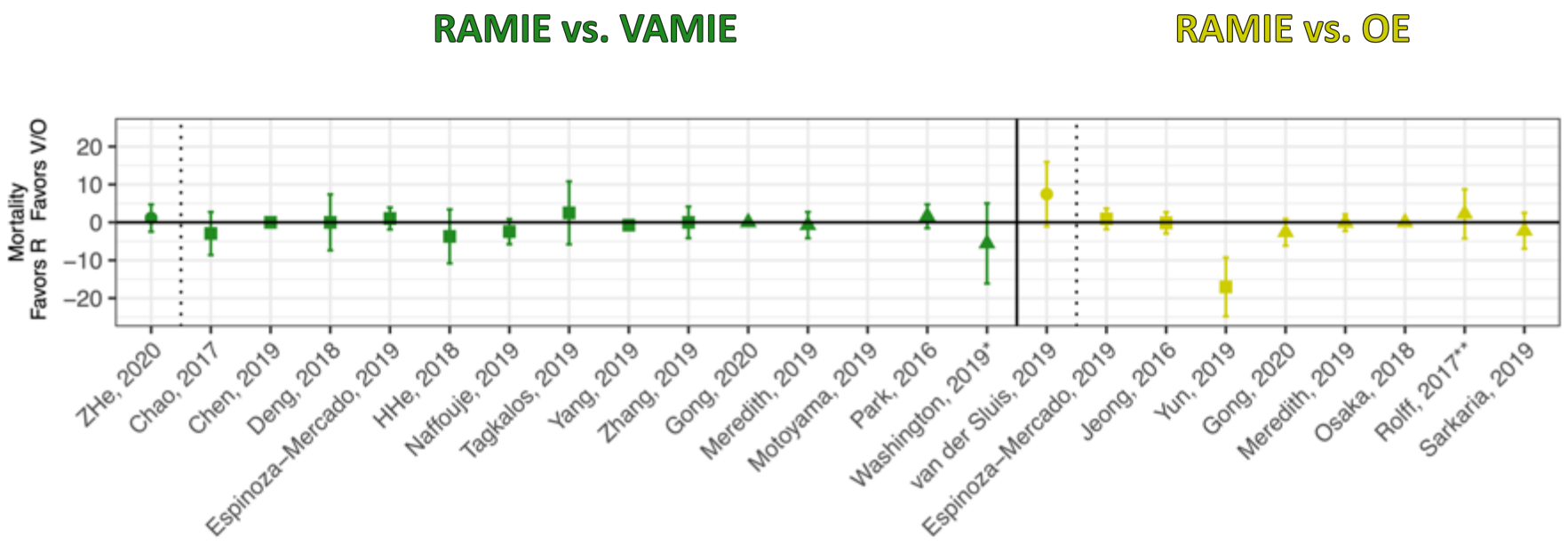
- RAMIE *may* be associated with shorter LOS

RCT

Matched observational study

Non-matched observational study

Short-term Outcomes cont.



RAMIE vs. VAMIE

- No difference in mortality

RAMIE vs. OE

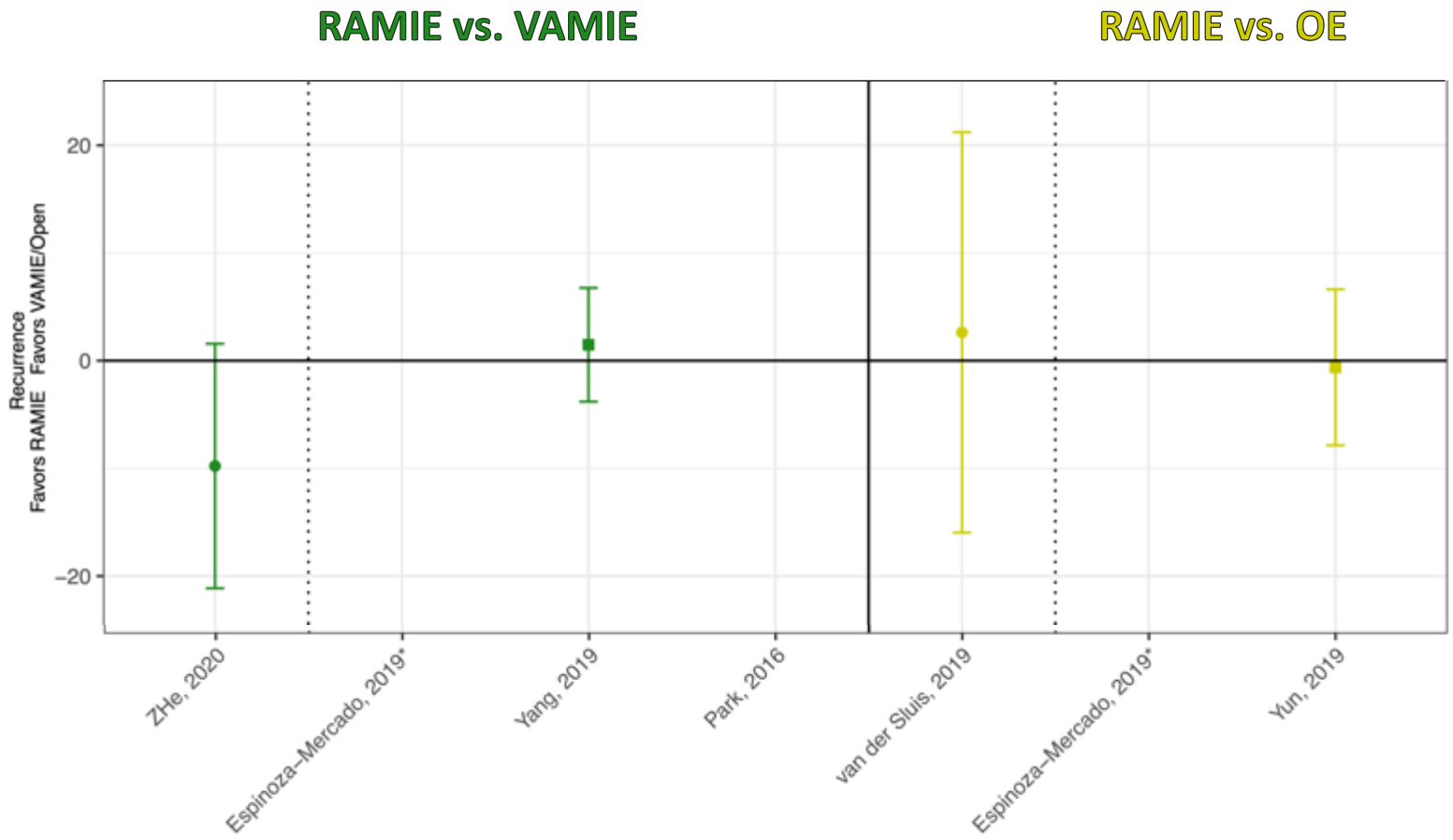
- No difference in mortality

RCT

Matched observational study

Non-matched observational study

Long-term Outcomes - Recurrence



RCT

Matched observational study

Non-matched observational study

RAMIE vs. VAMIE or OE

- No difference in cancer recurrence

Long-term Outcomes – Cancer-free survival

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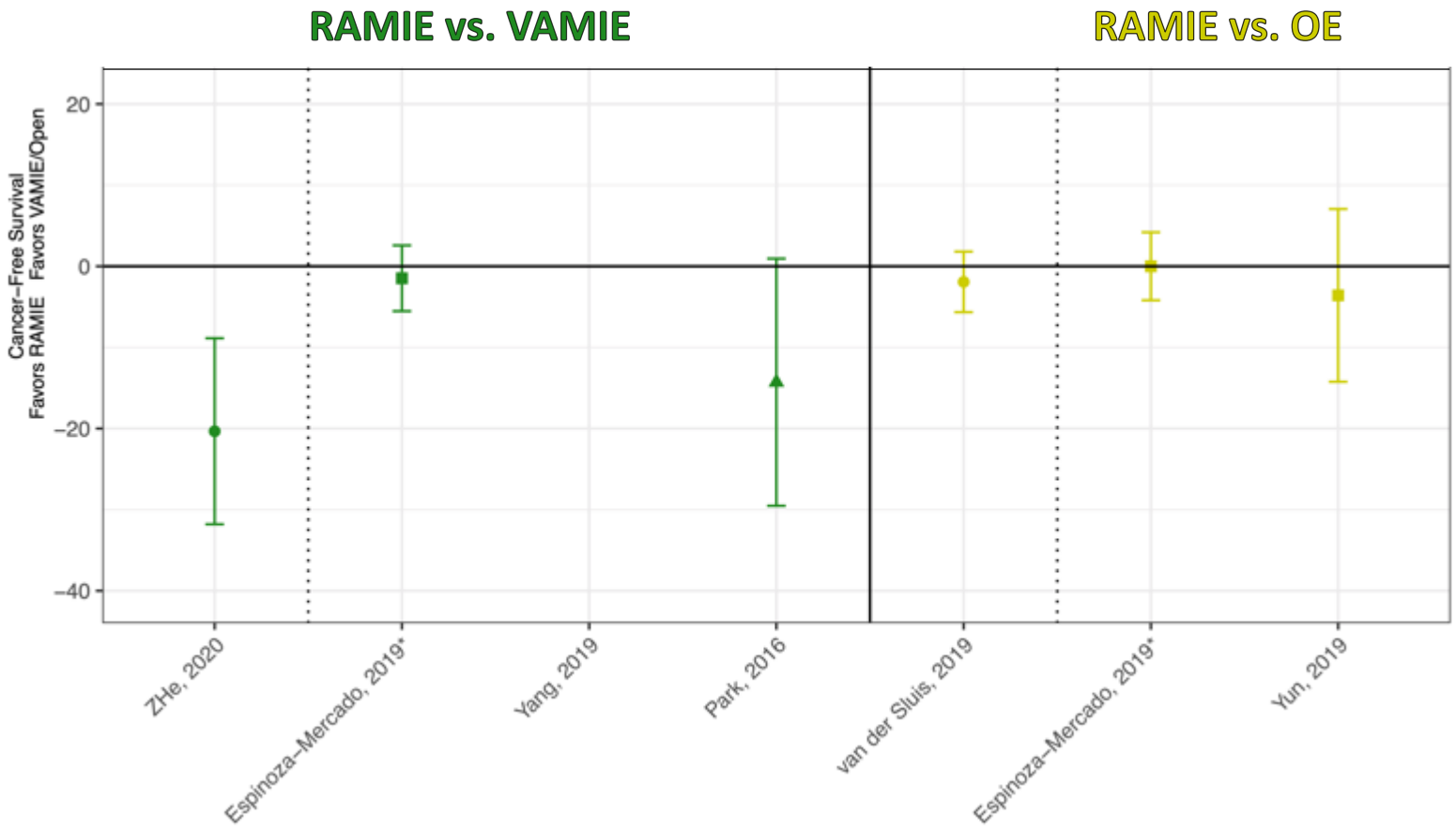

RCT

Matched observational study

Non-matched observational study

RAMIE vs. VAMIE

- RAMIE *may* be associated with longer cancer-free survival

RAMIE vs. OE

- No difference in cancer-free survival

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Summary

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	RAMIE vs. VAMIE	RAMIE vs. Open
Operative Time**	↑	↑
Lymph Node Harvest	↑	↑
EBL	=	↓
Anastomotic Leak	=	=
RLN Palsy	=	=
Pulmonary Complications	=	↓
Total Complications	=	↓
Length of Stay	=	↓
Mortality (90-day)	=	=
Recurrence	=	=
Cancer-free survival	↑(?)	=

**Significant heterogeneity across studies, suggesting differences in the measurement of this outcome

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Key questions

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1) What is the clinical effectiveness of robotic-assisted esophagectomy compared to open or thoracoscopic/laparoscopic esophagectomy for cancer?

2) What is the cost-effectiveness of robotic-assisted esophagectomy compared to open or thoracoscopic/laparoscopic esophagectomy for cancer?

Cost-Effectiveness

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- **No studies evaluated cost-effectiveness**
- **2 studies included some measure of cost**

Source	RAMIE	VAMIE	Open	P-values	Notes
Chen, 2019	**Total Expenses:** $25,300 ± 9,000 (USD) **Expenses/Day:** $1,700 ± 700 (USD)	**Total Expenses:** $20,800 ± 9,000 (USD) **Expenses/Day:** $1,500 ± 400 (USD)		P=0.009 P=0.028	ICU and total length of stay were longer for RAMIE but did not reach significance
Van Der Sluis, 2018	**Mean cost:** €34,892		**Mean cost:** €39,463	P=0.07	RAMIE had a shorter length of stay that did not reach significance

Overview of Findings

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- RAMIE is associated with longer operative times and larger LN harvest compared with VAMIE and open esophagectomy
- Short term outcomes are similar between RAMIE and VAMIE
- RAMIE is associated with less EBL, pulmonary complications, and total complications compared with open esophagectomy
- Insufficient data to make conclusions about long-term outcomes and cost-effectiveness

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Applicability of Findings to the VA Population

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- No studies specific to VA populations.
- Applicability may depend on both similarity of the patients studied to VA and experience of surgical teams using the robot to VA surgical teams.
- Benefits for robotic approach may still be realized despite patient-level differences (VA patients greater burden of comorbidities), which will need to be confirmed in future studies.

Applicability of Findings to the VA Population

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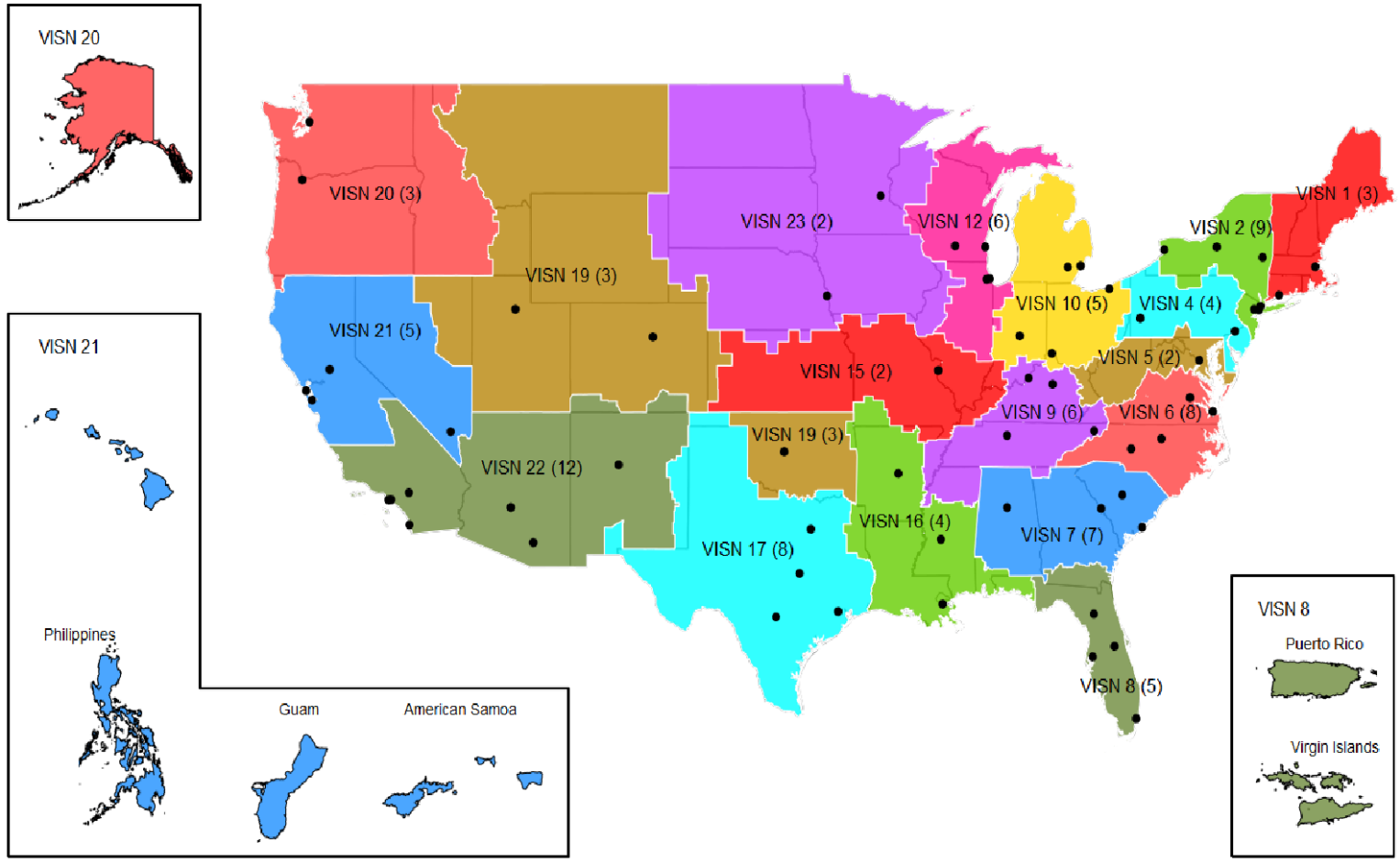
- Robotic systems in the VA increased from **43 to 95** from 2014 to 2019



Applicability of Findings to the VA Population

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- Four-fold increase in robot-assisted thoracic surgery at the VA from 2014-2019

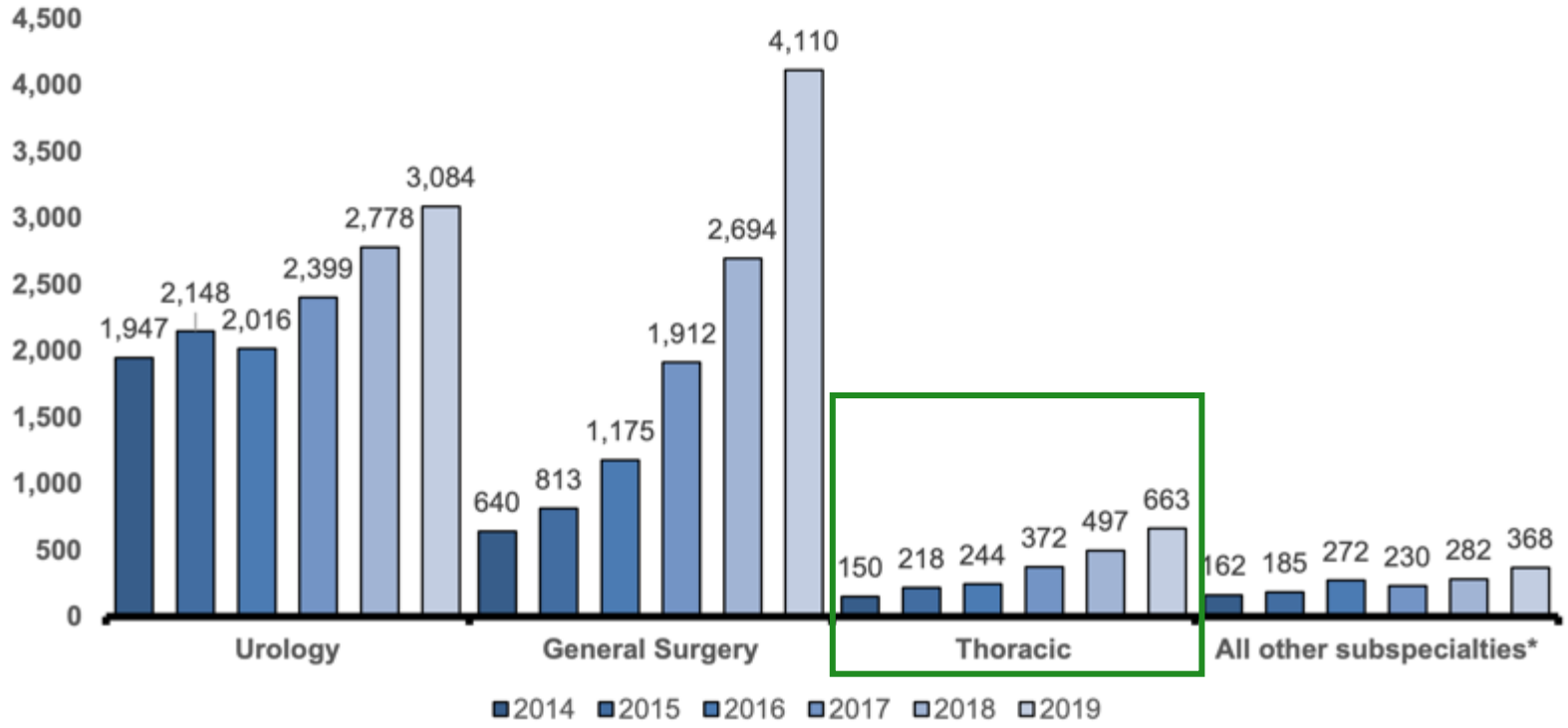

***Figure A.1**. Robotic system utilization for surgical subspecialty procedures by calendar year.*

Research Gaps

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- Need for randomized/well-designed studies evaluating **long-term oncologic outcomes**.
- There are several approaches/techniques to performing an esophagectomy, which is difficult to disentangle (e.g., McKeown, Ivor-Lewis, transhiatal).
- Regional variations in surgical practice, operative volume, and esophageal cancer epidemiology (SCC vs. adenocarcinoma).
- There is a need for high quality cost-effectiveness studies as well as a standardized method to assess cost (i.e., analytics, consistent definitions, accounting for upfront capital, staff training, etc.)

Acknowledgements

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Questions?

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Full-length report and cyberseminar available on ESP website:

http://www.hsrd.research.va.gov/publications/esp/

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Supplemental

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Author, year	Surgical Approach	Technique	Abdomen	Chest	Anastomosis
Chao 2017	RAMIE	McKeown	Laparoscopic	Robotic	Circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled; cervical
Chen 2019	RAMIE	McKeown	NR	Robotic	Circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled; cervical
Deng 2018	RAMIE	McKeown	Robotic	Robotic	Circular stapled or handsewn; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled or handsewn; cervical
Gong 2020	RAMIE	McKeown	Robotic	Robotic	Circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled; cervical
	Open	McKeown	Laparotomy	Thoracotomy	NR

Author, year	Surgical Approach	Technique	Abdomen	Chest	Anastomosis
He 2018	RAMIE	McKeown	Robotic	Robotic	End to side circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	End to side circular stapled; cervical
van der Sluis 2019	RAMIE	McKeown	Laparoscopic	Robotic	End to side handsewn; cervical
	Open	McKeown	Laparotomy	Thoracotomy	End to side handsewn; cervical
Yang 2019	RAMIE	McKeown	Robotic	Robotic	Cervical
	VAMIE	McKeown	Laparoscopic	VATS	Cervical
Meredith 2019	RAMIE	Ivor Lewis	NR	NR	NR
	VAMIE	Ivor Lewis	NR	NR	NR
	Open	Ivor Lewis	NR	NR	NR
Motoyama 2019	RAMIE	Ivor Lewis	NR	Robotic	NR
	VAMIE	Ivor Lewis	NR	VATS	NR

Author, year	Surgical Approach	Technique	Abdomen	Chest	Anastomosis
Naffouje 2019	RAMIE	Ivor Lewis	NR	NR	NR
	VAMIE	Ivor Lewis	NR	NR	NR
Rolff 2017	Hybrid	Ivor Lewis	Robotic	Thoracotomy	NR
	Open	Ivor Lewis	Laparotomy	Thoracotomy	NR
Tagkalos 2019	RAMIE	Ivor Lewis	Robotic	Robotic	Circular stapled; intrathoracic
	VAMIE	Ivor Lewis	Laparoscopic	VATS	Circular stapled; intrathoracic
Zhang 2019	RAMIE	Ivor Lewis	Robotic	Robotic	End to end both circular stapled + handsewn; intrathoracic
	VAMIE	Ivor Lewis	Laparoscopic	VATS	End to end circular stapled; intrathoracic
Washington 2019	RAMIE	Transhiatal	Robotic	NA	Cervical
	VAMIE	Transhiatal	Laparoscopic	NA	Cervical

Author, year	Surgical Approach	Technique	Abdomen	Chest	Anastomosis
Espinoza-Mercado 2019	RAMIE	NR	NR	NR	NR
	VAMIE	NR	NR	NR	NR
	Open	NR	NR	NR	NR
He 2020	RAMIE	McKeown	Robotic	Robotic	
	VAMIE	McKeown	Laparoscopic	VATS	
Jeong 2016	RAMIE	McKeown	Laparotomy	Robotic	Cervical
	Open	Ivor Lewis or McKeown	Laparotomy	Thoracotomy	Cervical or thoracic
Osaka 2018	RAMIE	NR	NR	Robotic	NR
	Open	NR	NR	Thoracotomy	NR
Park 2016	RAMIE	90% McKeown 10% Ivor Lewis	58% robotic 42% open*	Robotic	90% cervical 10% thoracic
	VAMIE	81% McKeown 19% Ivor Lewis	49% laparoscopic 51% open*	Laparoscopic	81% cervical 19% thoracic

Author, year	Surgical Approach	Technique	Abdomen	Chest	Anastomosis
Sarkaria 2019	RAMIE	62/64 Ivor Lewis; 2/64 McKeown	NR	NR	NR
	Open	103/106 open Ivor Lewis; 3/106 thoracoabdominal	NR	NR	NR
Yun 2019	RAMIE	57.1% Ivor Lewis 42.9% McKeown	Robotic or Laparoscopic	Robotic	Circular stapled; cervical
	Open	54.4% Ivor Lewis 45.6% McKeown	Laparotomy	Thoracotomy	Circular stapled; cervical