Systematic review and meta analysis

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Level of evidence

What is a systematic review?

"A process to identify, appraise and synthesize all the research evidence that fits pre specified criteria in order to answer a well specific research question"

Unbiased and rigorous

Value of systematic review

- Address the gap in the knowledge
- Synthesis of multiple studies is compelling than results of single studies
- Give the best estimate of any true effect

World Journal of Clinical Oncology

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SYSTEMATIC REVIEWS

Immune checkpoint inhibitors in head and neck squamous cell carcinoma: A systematic review of phase-3 clinical trials

Jissy Vijo Poulose, Cessal Thommachan Kainickal

Cancer Treatment and Research Communications 32 (2022) 100589

Contents lists available at ScienceDirect

Cancer Treatment and Research Communications

journal homepage: www.sciencedirect.com/journal/cancer-treatment-and-research-communications

Induction chemotherapy in nasopharyngeal carcinoma- A systematic review of phase III clinical trials

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MEDICINE INTERNATIONAL 4: 41, 2024

Anti-epidermal growth factor receptor monoclonal antibody therapy in locally advanced head and neck cancer: A systematic review of phase III clinical trials

LEKHA MADHAVAN NAIR[1], REJNISH RAVIKUMAR[1], MALU RAFI[1], JISSY VIJO POULOSE[2], NIJO JOSE[1], KRISHNAPRIYA PISHARODY[1] and KAINICKAL CESSAL THOMMACHAN[1]

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What motivates the authors ..

- Solve the conflicting evidence
- Explore variations in practice
- To confirm appropriateness of current practice
- Highlight the need for a future research
- For developing practice guidelines

Before starting …

- Clarify your review topic
- Determine whether systematic review is required
- Determine you have necessary time and resources

“Mores specific well thought out questions will result in a better quality product”

Team

Standards

- Cochrane hand book

https://training.cochrane.org/handbook

- Finding What Works in Health Care: Standards for Systematic Review- Institute of medicine(USA)committee

https://pubmed.ncbi.nlm.nih.gov/24983062/

- PRISMA

Preferred reporting items for systematic reviews and meta-analysis

https://www.prisma-statement.org/

Purpose

- Collect the existing research and synthesize the results of several studies
- Same rigor as primary research
- Transparent
- Procedures are explained well in advance
- Replicated
- Studies involved are screened by a team of researchers to avoid bias
- Summarize and understand the evidence

Process of a systematic review

- Clarify your question
- Create a protocol
- Literature search
- Screen the studies
- Extract data
- Appraise the included studies
- Synthesize
- Write the report

Clarify your question

Population

Intervention

Comparison

Outcomes

Study design

Inclusion and exclusion criteria

It should be well defined before the study

Each study should meet all inclusion criteria- Avoid bias

Create a protocol

- It is an important step in review process
- Eligibility criteria, search strategy data extraction
- It helps to reduce the authors bias
- Promotes transparency of methods and process
- Reduces the potential for duplication
- Informs decision making during review process
- Consider registering your protocol

https://www.crd.york.ac.uk/prospero/

Literature search -Where and what?

1st step- Find the data base

Pubmed

Embase

Cochrane central register of clinical trials

2nd step - Search terms

Key words and controlled vocabulary

Keep a record of all search

Additional

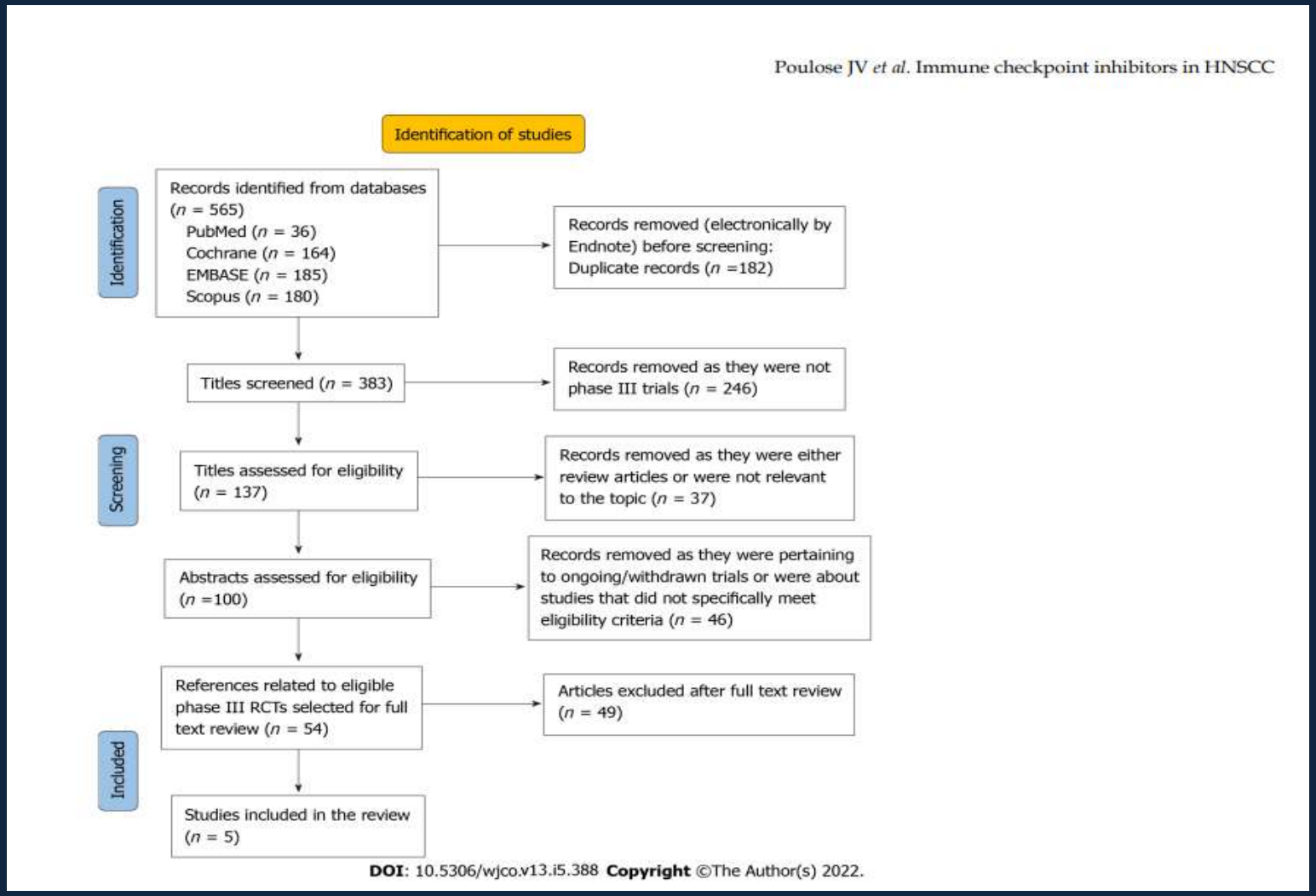
- Abstracts
- Ongoing clinical trials -https://clinicaltrials.gov/
- Proquest dissertation data base- https://about.proquest.com/en/dissertations/

Screen studies

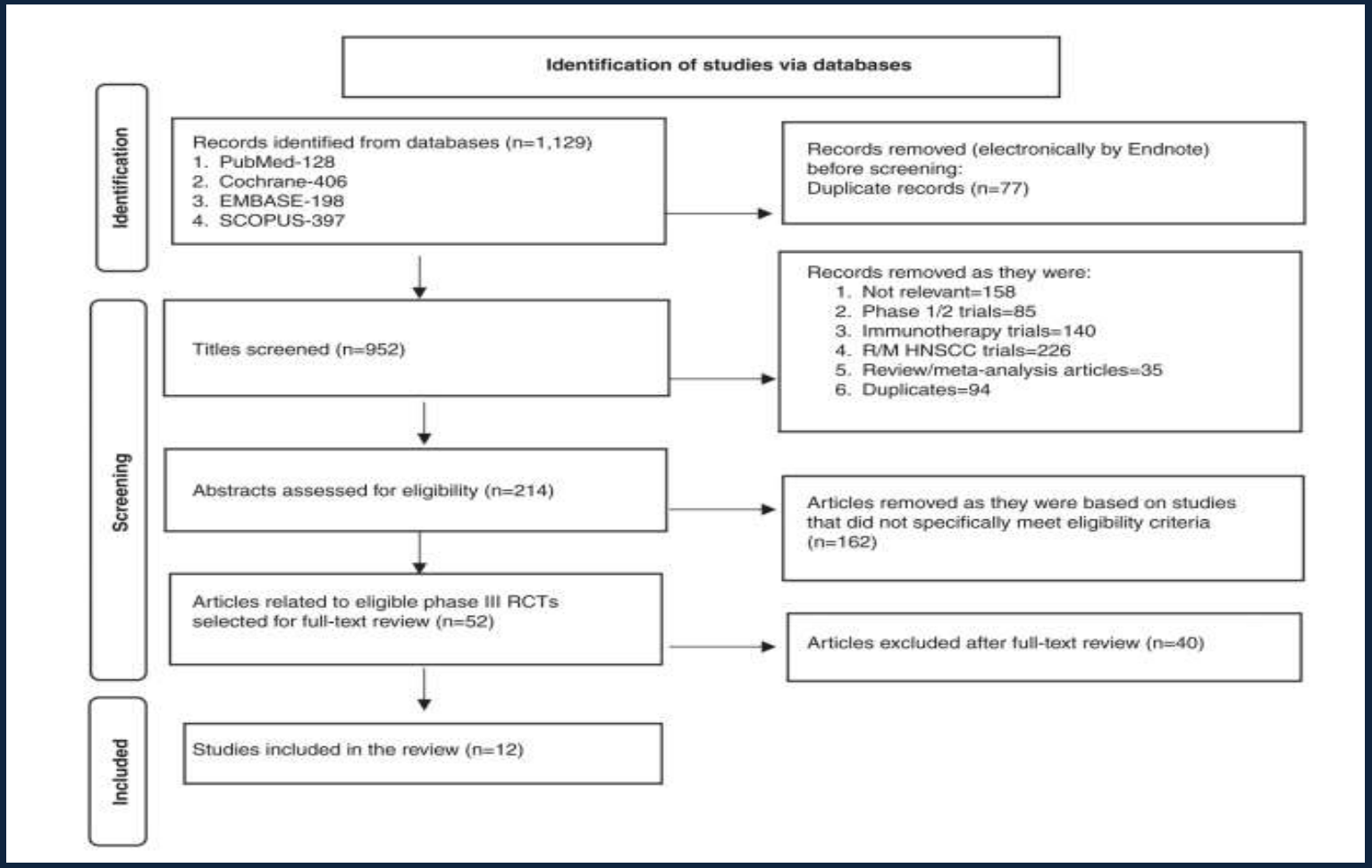
- Remove duplicates
- Examine titles/abstracts
- Retrieve full text of all relevant trials
- Examine the full text to assess the eligibility
- Make final decisions on study inclusion

Minimum 2 members for the process

PRISMA flow chart



PRISMA flow chart



Data extraction

- Create your own- Most common
- Distiller SR
- EPPI-Reviewer
- SRDR- systematic review data repository

https://www.ahrq.gov/cpi/about/otherwebsites/srdr.ahrq.gov/index.html

Appraise the included studies

- Risk of bias
- Appropriateness of study design
- Quality of reporting
- Choice of outcome measure
- Statistical issues
- Generalizability

Synthesis

- Theory of how intervention works
- Summary of findings of studies
- Relationship between the studies
- Over all assessment of the strength of evidence

Value of systematic review

- What was done?
- What was found?
- Clarity of reporting

Challenges for conducting a systematic review

- Lack of funding
- Need for training
- Difficult synthesize data from variety of study designs
- Time consuming

Radiotherapy and Oncology 156 (2021) 281–293

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Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 107 randomized trials and 19,805 patients, on behalf of MACH-NC Group

Benjamin Lacas [a,b], Alexandra Carmel [a], Cécile Landais [a], Stuart J. Wong [c], Lisa Licitra [d], Jeffrey S. Tobias [e], Barbara Burtness [f], Maria Grazia Ghi [g], Ezra E.W. Cohen [h], Cai Grau [i], Gregory Wolf [j], Ricardo Hitt [k], Renzo Corvò [l], Volker Budach [m], Shaleen Kumar [n], Sarbani Ghosh Laskar [o], Jean-Jacques Mazeron [p], Lai-Ping Zhong [q], Werner Dobrowsky [r], Pirus Ghadjar [s], Carlo Fallai [t], Branko Zakotnik [u], Atul Sharma [v], René-Jean Bensadoun [w], Maria Grazia Ruo Redda [x], Séverine Racadot [y], George Fountzilas [z], David Brizel [aa], Paolo Rovea [ab], Athanassios Argiris [ac], Zoltán Takácsi-Nagy [ad], Ju-Whei Lee [ae], Catherine Fortpied [af], Jonathan Harris [ag], Jean Bourhis [b,ah], Anne Aupérin [a,b], Pierre Blanchard [a,b,ai,*], Jean-Pierre Pignon [a,b], on behalf of the MACH-NC Collaborative Group

Clinical and Translational Radiation Oncology 32 (2022) 59–68

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Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology

Original Research Article

Meta-analysis of chemotherapy in nasopharynx carcinoma (MAC-NPC): An update on 26 trials and 7080 patients

Pierre Blanchard [a,b,*], Anne W.M. Lee [c], Alexandra Carmel [b,d], Ng Wai Tong [c], Jun Ma [e], Anthony T.C. Chan [f], Ruey Long Hong [g], Ming-Yuan Chen [h], Lei Chen [h], Wen-Fei Li [h], Pei-Yu Huang [h], Dora L.W. Kwong [i], Sharon S.X. Poh [j], Roger Ngan [c], Hai-Qiang Mai [h], Camille Ollivier [b,d], George Fountzilas [k], Li Zhang [h], Jean Bourhis [l], Anne Aupérin [b,d], Benjamin Lacas [b,d], Jean-Pierre Pignon [b,d], on behalf of the MAC-NPC collaborative Group

Meta- Analysis

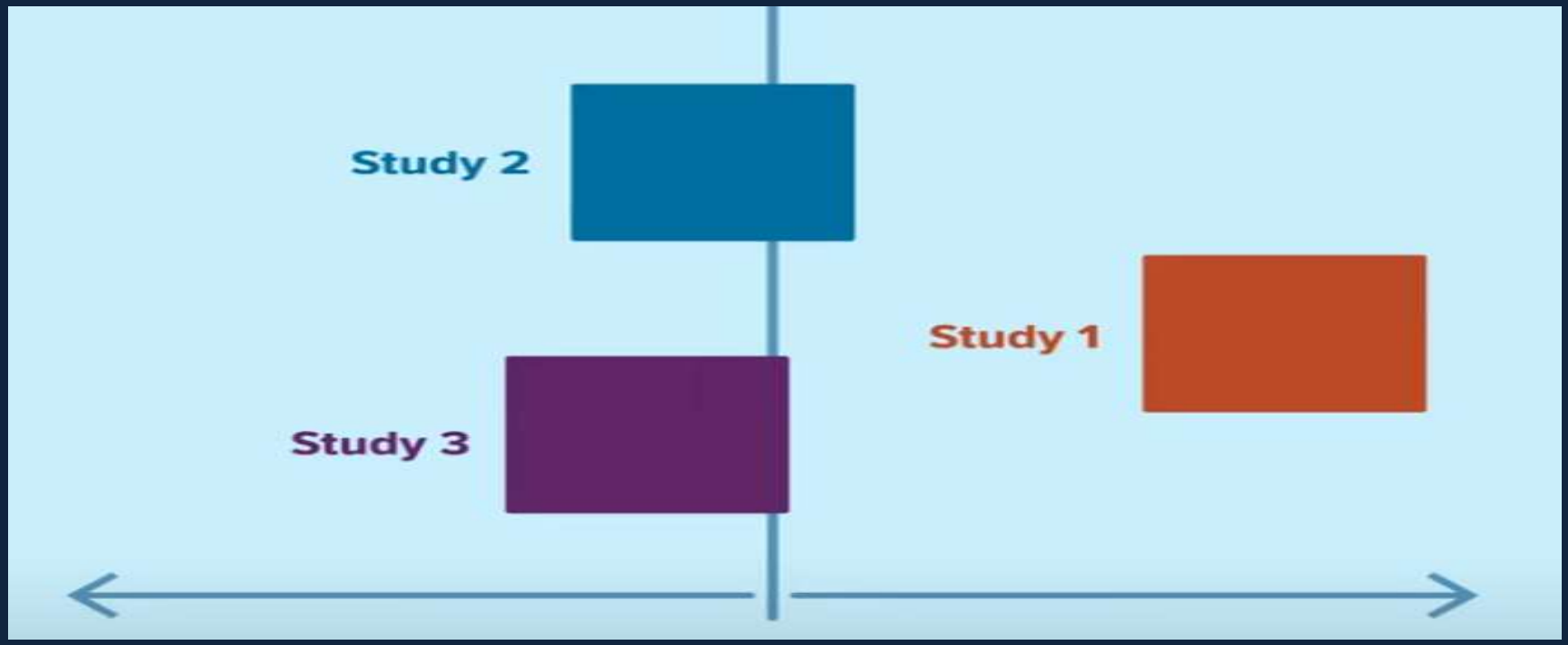
Highest level of evidence

"Research should help practitioners and policy makers choose which treatment and programs to recommend

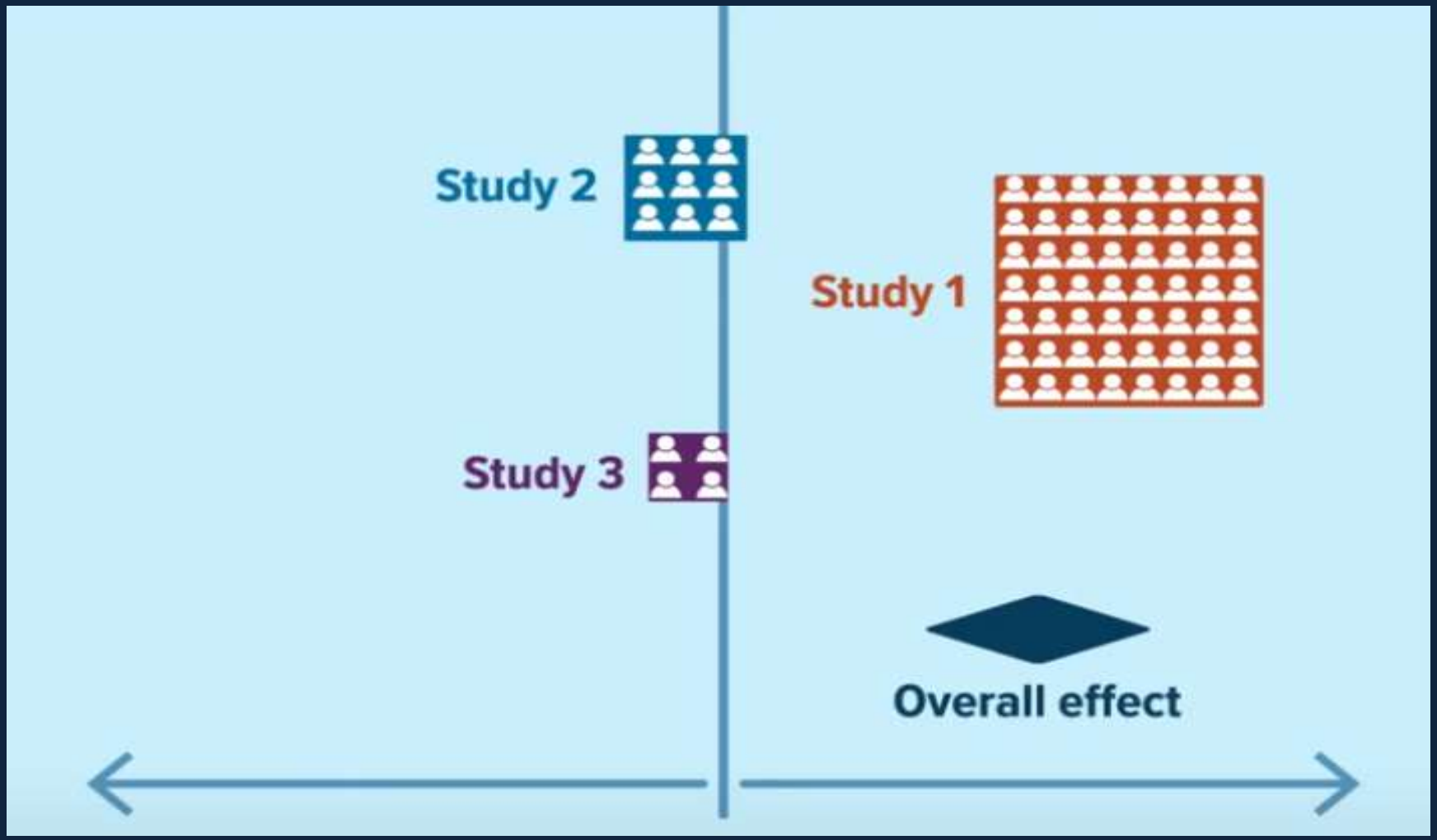
It is the quantitative synthesis of the studies addressing the same question

- New data
- New results
- New conclusions


Study 1
Study 2
Study 3


Study 2
Study 1
Study 3

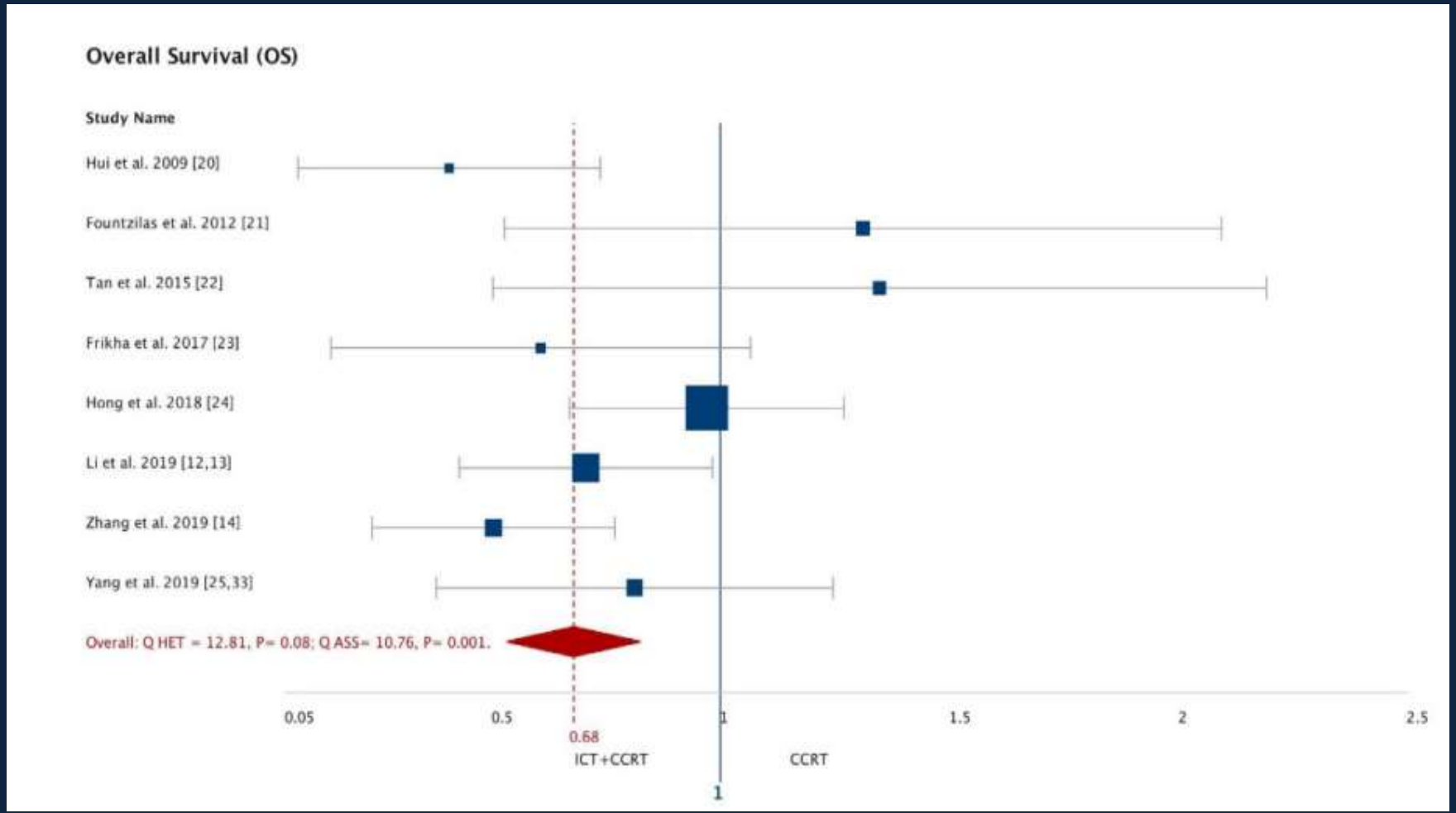
Meta-Analysis



Forest plot

- It is the main figure of any meta -analysis
- It summarizes the results from all studies in one figure
- It also gives the weightage of the study
- Summary of the results
- Vertical line – Line of null effect
- Result of the study is given in box
- Line of each study- confidence interval
- Diamond- represents the combined effect size
- Width of diamond is the confidence interval

Forest plot



The Oncologist 2021;26:e130–e141

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- The primary endpoint was overall survival (OS)
- Event-free survival (EFS)
- Loco-regional failure (LRF)
- 120 day mortality
- Distant failure (DF)
- Cancer and no cancer mortality

Median follow up 6.6 years

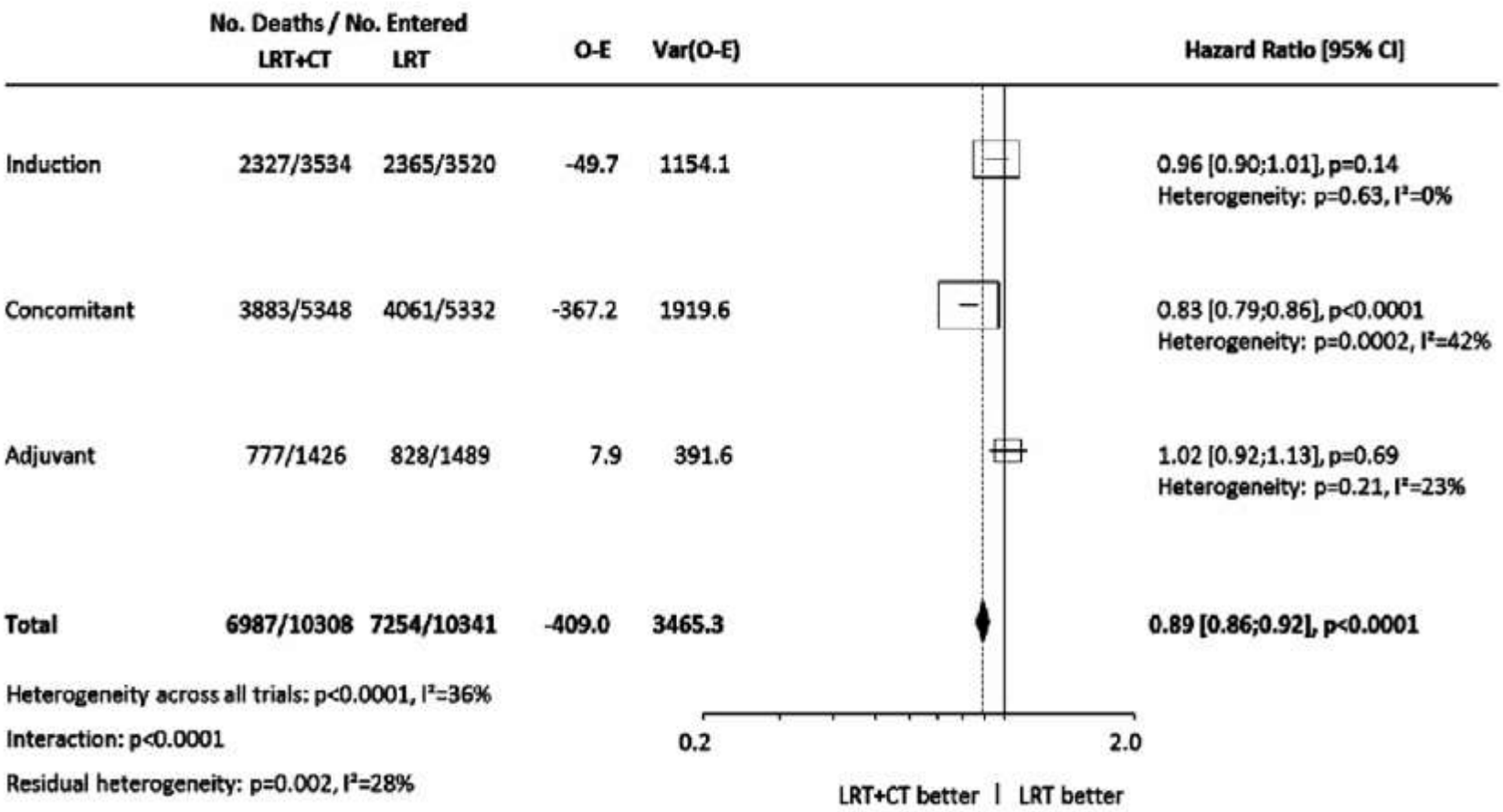
- LRT +/- Chemotherapy
- Concomitant versus Induction chemotherapy

Meta-Analysis

Results of the addition of chemotherapy to loco-regional treatment.

	Overall survival	120-day mortality	Event-free survival	Cancer mortality[§]	Non-cancer mortality[§]	Loco-regional failure*	Distant failure*
Induction							
No. events/No. patients	4692/7054	470/7054	4556/6374	979/2031	320/2031	2574/6342	761/5582
HR of chemotherapy effect [95% CI]; *p*-value	0.96 [0.90; 1.01] *p* = 0.14	1.07 [0.89;1.28] *p* = 0.47	0.96 [0.90;1.02] *p* = 0.14	0.97 [0.86;1.10] *p* = 0.67	0.84 [0.67;1.05] *p* = 0.12	1.07 [0.99;1.15] *p* = 0.09	0.76 [0.66;0.88] *p* = 0.0002
Heterogeneity: *p*-value (I^2)	*p* = 0.63 (0%)	*p* = 0.46 (1%)	*p* = 0.25 (12%)	*p* = 0.24 (19%)	*p* = 0.28 (16%)	*P* < 0.0001 (63%)	*P* < 0.0001 (97%)
Absolute difference at 5 years [95% CI]	+2.2% [−0.2;+4.6]	NA	+1.4% [−0.9;+3.7]	−0.7% [−5.5;+4.1]	−4.8% [−0.4;−9.2]	+3.2% [+0.8;+5.7]	−4.1% [−6.0;−2.2]
Absolute difference at 10 years [95% CI]	+1.3% [−1.9;+4.5]	NA	−0.6% [−3.6;+2.4]	NA	NA	+4.6% [+1.7;+7.5]	−3.5% [−5.7;−1.3]
Concomitant							
No. events/No. patients	7944/10,680	716/10,680	8345/10,457	3730/6483	955/6483	4766/10,076	1034/9022
HR of chemotherapy effect [95% CI]; *p*-value	0.83 [0.79;0.86] *p* < 0.0001	1.07 [0.92;1.24] *p* = 0.37	0.80 [0.77;0.84] *p* < 0.0001	0.79 [0.74;0.84] *p* < 0.0001	1.01 [0.89;1.16] *p* = 0.83	0.71 [0.67;0.75] *p* < 0.0001	1.04 [0.92;1.18] *p* = 0.48
Heterogeneity: *p*-value (I^2)	*p* = 0.0002 (42%)	*p* = 0.01 (30%)	*p* = 0.04 (24%)	*p* = 0.18 (18%)	*p* = 0.80 (0%)	*P* < 0.0001 (85%)	*P* < 0.0001 (96%)
Absolute difference at 5 years [95% CI]	+6.5% [+4.6;+8.4]	NA	+5.8% [+4.1;+7.5]	−9.8% [−12.4;−7.2]	+2.9% [+0.1;+5.7]	−9.3% [−11.3;−7.3]	+0.2% [−1.0;+1.6]
Absolute difference at 10 years [95% CI]	+3.6% [+1.8;+5.4]	NA	+3.1% [+1.5;+4.7]	NA	NA	−9.6% [−11.6;−7.5]	+0.2% [−1.2;+1.6]
Adjuvant							
No. events/No. patients	1605/2915	127/2915	1461/2416	NA	NA	571/2416	324/2224
HR of chemotherapy effect [95% CI]; *p*-value	1.02 [0.92;1.13] *p* = 0.69	1.89 [1.33;2.68] *p* = 0.0003	0.98 [0.88;1.09] *p* = 0.72	NA	NA	0.84 [0.72;1.00] *p* = 0.04	0.77 [0.62;0.96] *p* = 0.02
Heterogeneity: *p*-value (I^2)	*p* = 0.21 (23%)	*p* = 0.10 (34%)	*p* = 0.03 (47%)	NA	NA	*p* = 0.16 (29%)	*P* < 0.0001 (98%)
Absolute difference at 5 years [95% CI]	−0.3% [−4.3;+3.7]	NA	−0.6% [−5.0;+3.8]	NA	NA	−3.7% [−7.2;−0.2]	−3.0% [−6.0;0.0]
Absolute difference at 10 years [95% CI]	+1.2% [−4.1;+6.5]	NA	+3.6% [−2.7;+9.9]	NA	NA	−3.6% [−7.2;0.0]	−3.2% [−6.5;+0.2]
Interaction test (timing × treatment effect)	*p* < 0.0001	0.01	*p* < 0.0001	*P* = 0.003	*P* = 0.15	*p* < 0.0001	*P* = 0.001

Results- OS



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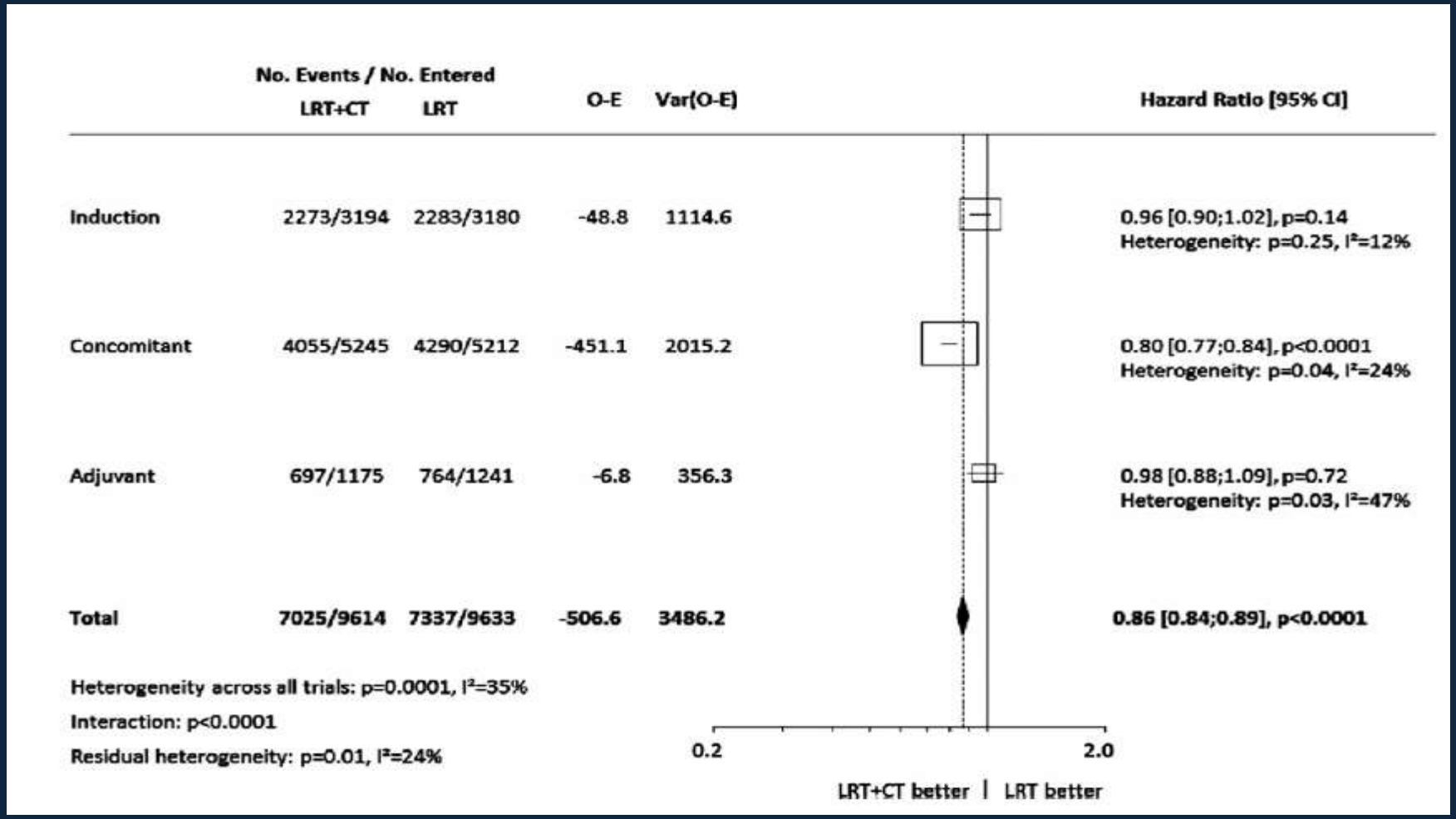
Results- EFS



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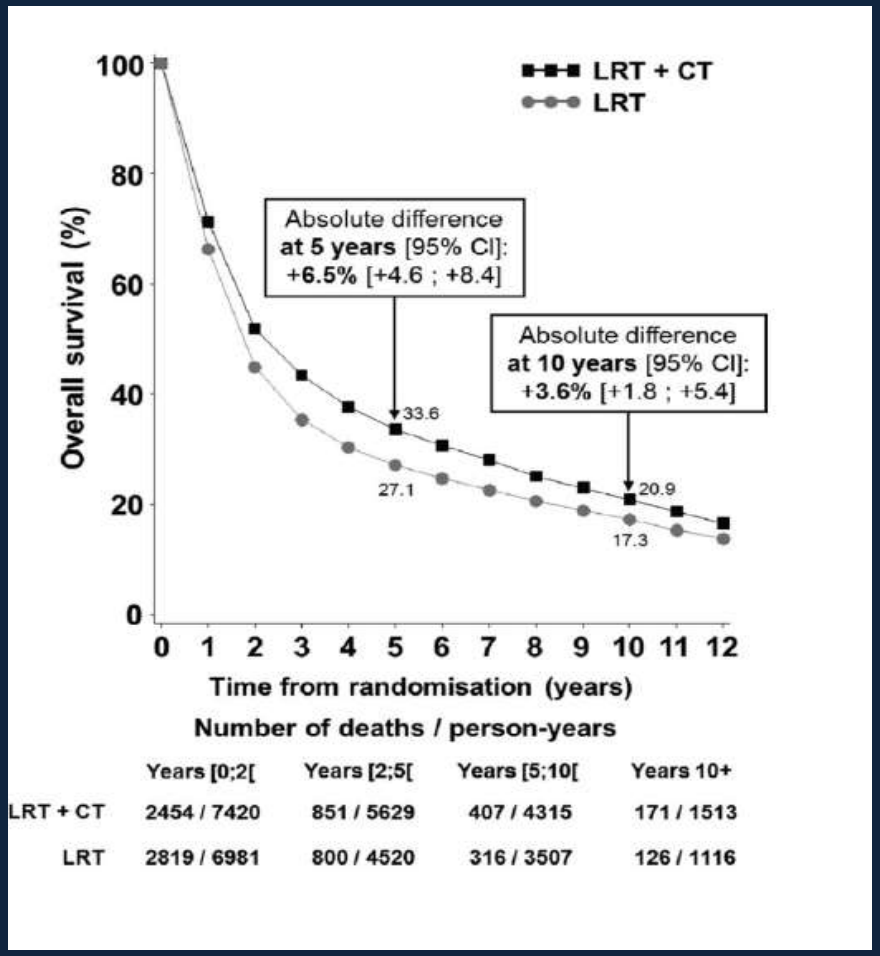
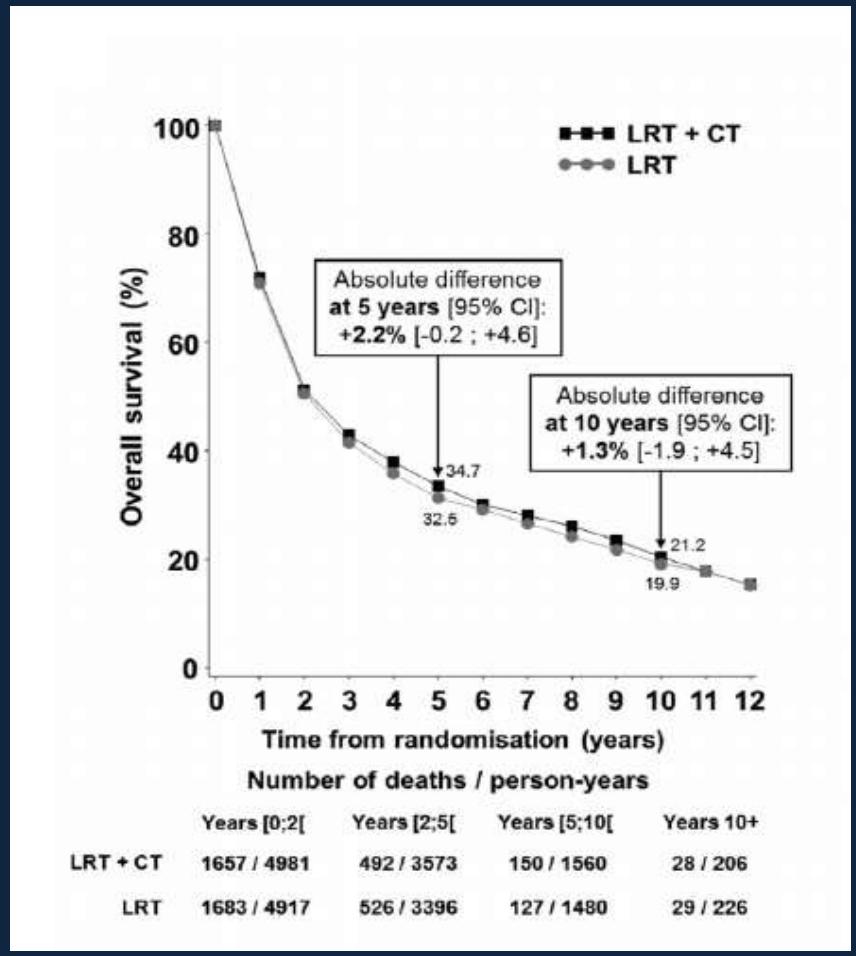
CCRT



	Years [0;2[	Years [2;5[	Years [5;10[	Years 10+
LRT + CT	2454 / 7420	851 / 5629	407 / 4315	171 / 1513
LRT	2819 / 6981	800 / 4520	316 / 3507	126 / 1116

IC



	Years [0;2[	Years [2;5[	Years [5;10[	Years 10+
LRT + CT	1657 / 4981	492 / 3573	150 / 1560	28 / 206
LRT	1683 / 4917	526 / 3396	127 / 1480	29 / 226

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Thank you

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