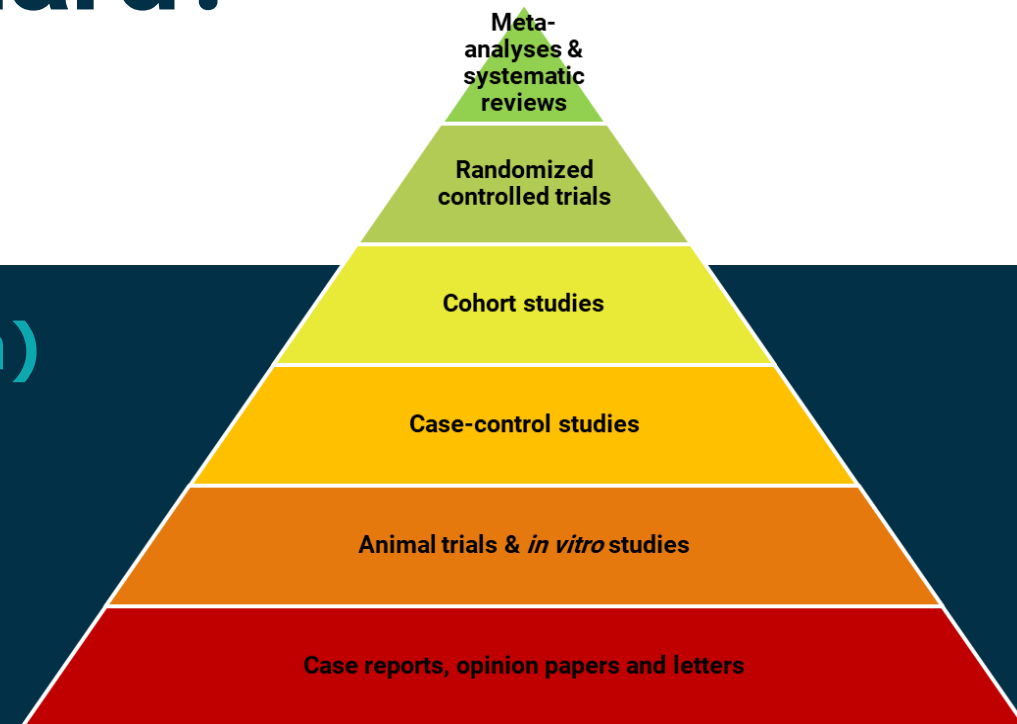


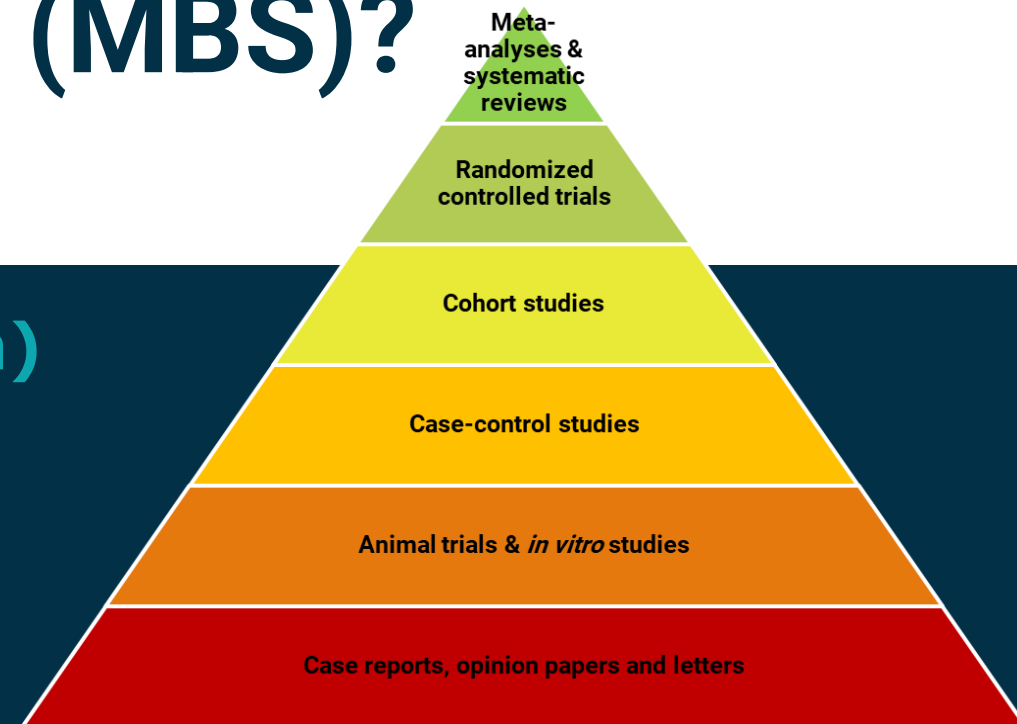
The randomized clinical trial (RCT)- why it is still the gold standard?

Paulina Salminen, MD, PhD, FACS (Hon)
Professor of Surgery
University of Turku
Turku, Finland
IFSO World IH PG-course, Toronto



The randomized clinical trial (RCT)- why it is still the standard in metabolic bariatric surgery (MBS)?

Paulina Salminen, MD, PhD, FACS (Hon)
Professor of Surgery
University of Turku
Turku, Finland
IFSO World IH PG-course, Toronto



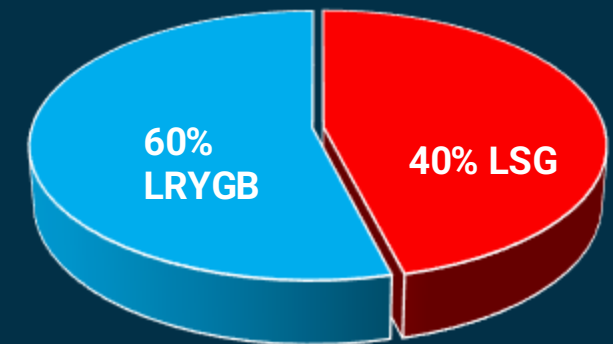


Disclosures

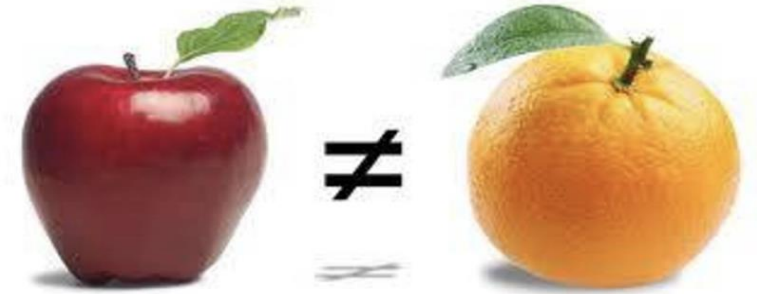


- Lecture fees: Novo Nordisk
- Employment: University of Turku, Turku University Hospital, private practice Terveystalo
- **PI: SLEEVEPASS, APPAC**
- IFSO-EC President elect
- **Editor-in-Chief, Scandinavian Journal of Surgery**
- **Editor, BJS**
- **Editorial Board Member JAMA Surgery and Surgery**
- Data safety monitoring committee: BEST trial, MAGNET-study
- Research grants:
 - European Research Council
 - Academy of Finland
 - Sigrid Jusélius Foundation
 - Mary and Georg C. Ehrnrooth foundation
 - Government research grant foundation (EVO)

Primary procedures



Contents



Why do we need RCTs in MBS?

Personal RCT bias: PI of the SLEEVEPASS and APPAC multicentre RCTs

Conducting RCTs: five stages and challenges

Surgical RCTs 1999 – 2009 - 2019

RCTs in MBS – systematic review and international collaboration



How surgery is sometimes practiced?

Eminence based surgery= *“Making the same mistakes with increasing confidence over an impressive number of years”*

In my hands = *may not work for all surgeons, but works*
IN MY HANDS

Everybody-does-so-I'll do it based medicine
Sounds-like-a-good-idea medicine

How surgery is sometimes practiced?



Eminence based
surgery = *“Making the same mistakes with increasing confidence over an impressive number of years”*

In my hands = *may not work for all surgeons, but works IN MY HANDS*

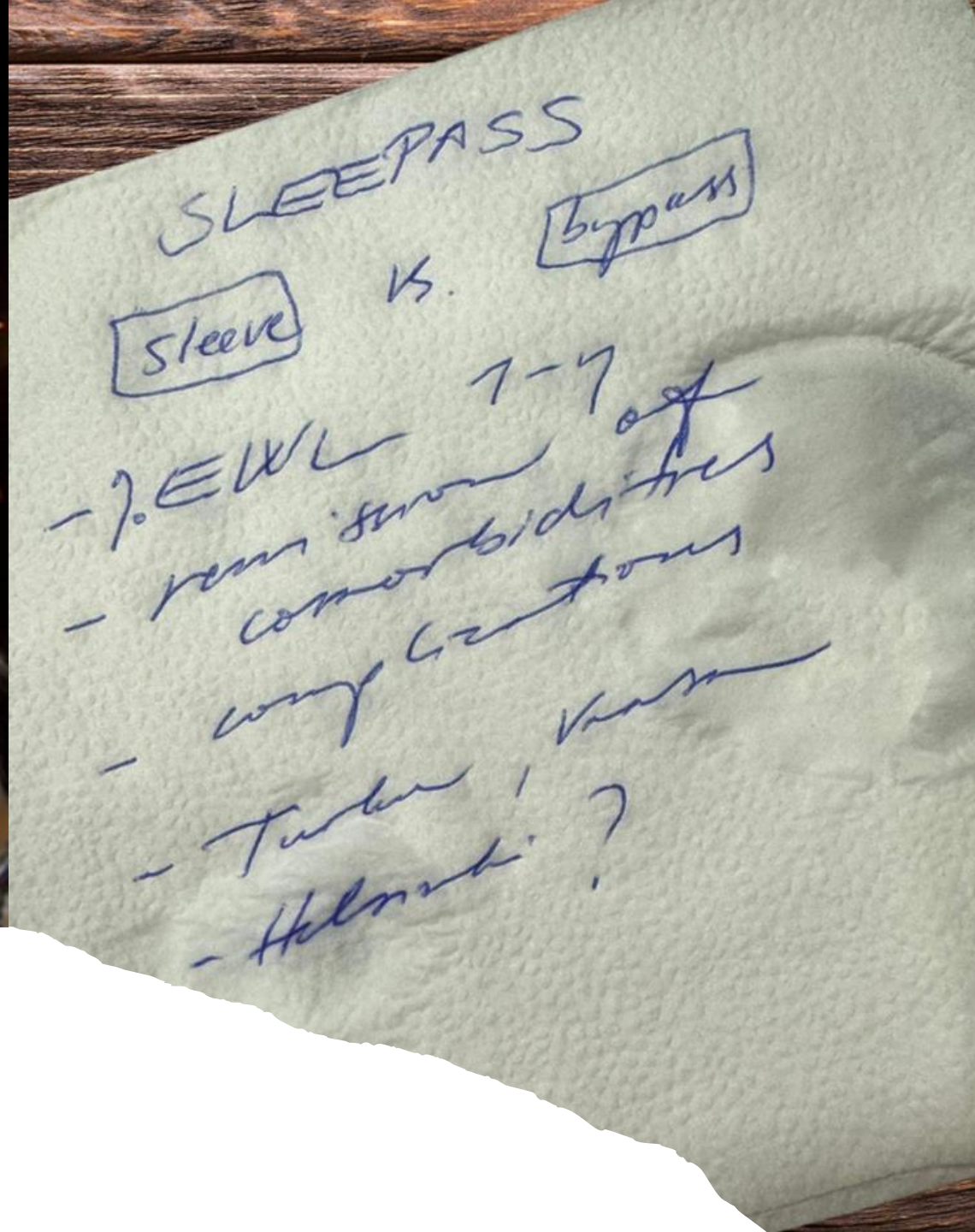
Everybody-does-so-I'll do it
based medicine

Sounds-like-a-good-idea
medicine

Mikael Victorzon
1959-2018



The story of the SLEEVEPASS trial:
It all began....





APPAC IV – Oral antibiotic outpatient therapy vs. placebo

Double-blind randomized clinical multicenter noninferiority trial

- Can antibiotics be omitted for uncomplicated acute appendicitis?
- Can hospitalization be avoided - could patients be treated at home?



III

APPAC III – Double-blind pilot RCT antibiotics vs. placebo

→ Antibiotics not needed?

Publication: *British Journal of Surgery* 2022; 109(6):503-509

II

APPAC II – Oral vs. intravenous followed by oral antibiotics

→ Oral antibiotics are sufficient

Publication: *JAMA* 2021; 325(4):353-362

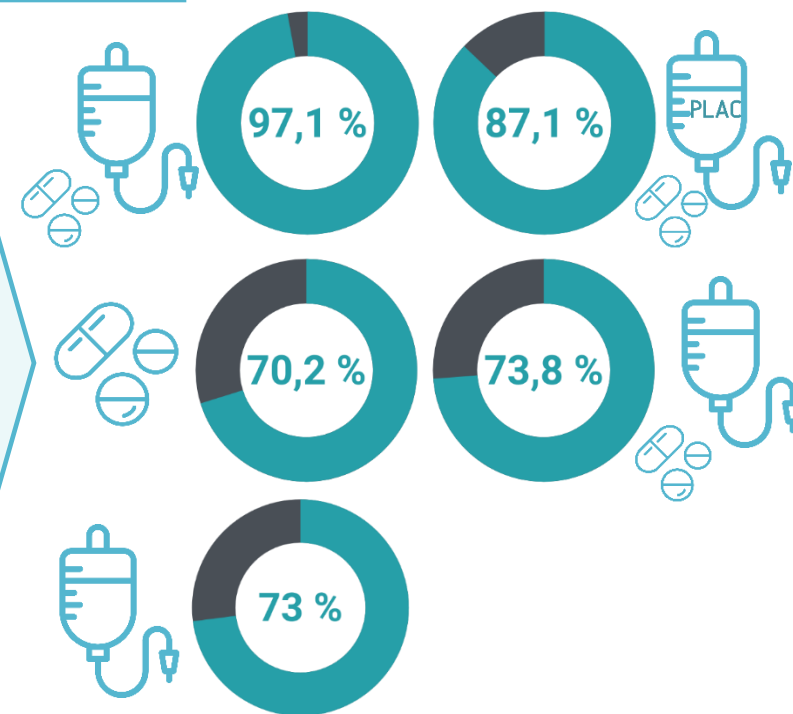
I

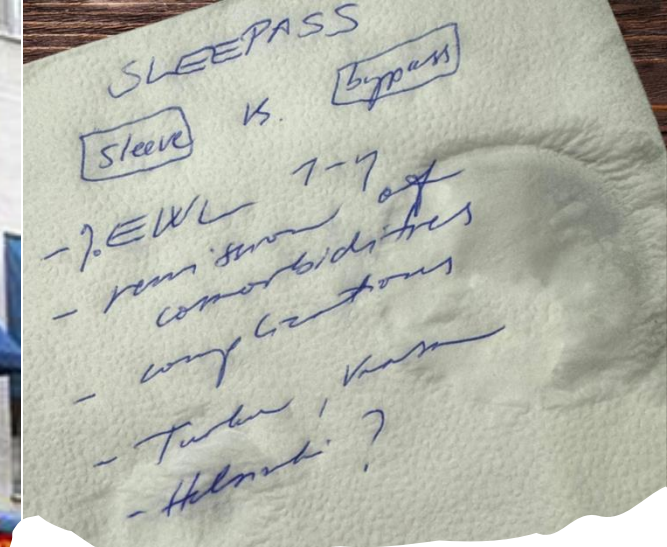
APPAC – Appendectomy vs. antibiotics

→ Surgery not needed for the majority of patients

Publications: *JAMA* 2015; 313(23):2340-2348

5-year results: *JAMA* 2018; 320(12):1259-1265, 7-year quality of life: *JAMA Surgery* 2020; 155(4):283-289





SLEEPASS > SLEEVEPASS
1-year > 5-year follow-up



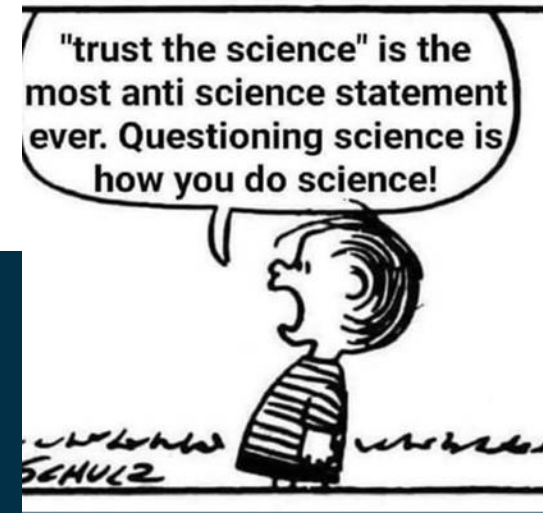
Turku University Central Hospital

Costly damages from Turku hospital fire

The damages from the fire at the Turku University Hospital are expected to run to hundreds of thousands of euros. The blaze broke out early Friday morning in the A-building of the Turku University Hospital, prompting the evacuation of about 180 patients.

How to choose the study type?

Retrospective vs. randomized



Is it possible to randomize?



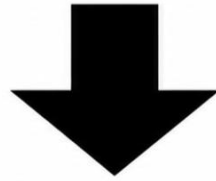
Do a randomized clinical trial!

- FOCUS your energy, time, and funding on one relevant large RCT instead of multiple retrospective studies

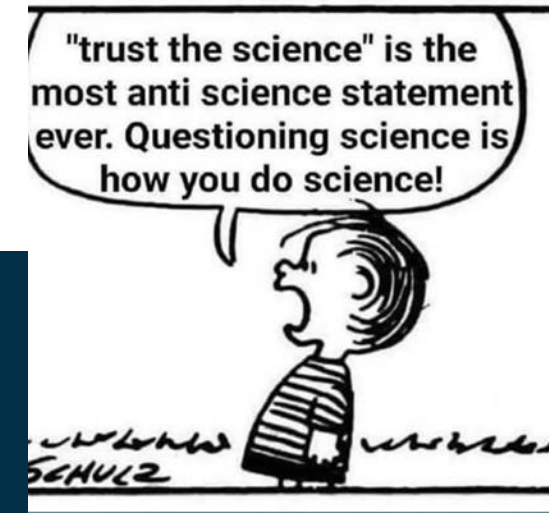
How to choose the study type?

Retrospective vs. randomized

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Do Randomized Clinical Study!



Original article

Practical guide to the Idea, Development and Exploration stages of the IDEAL Framework and Recommendations

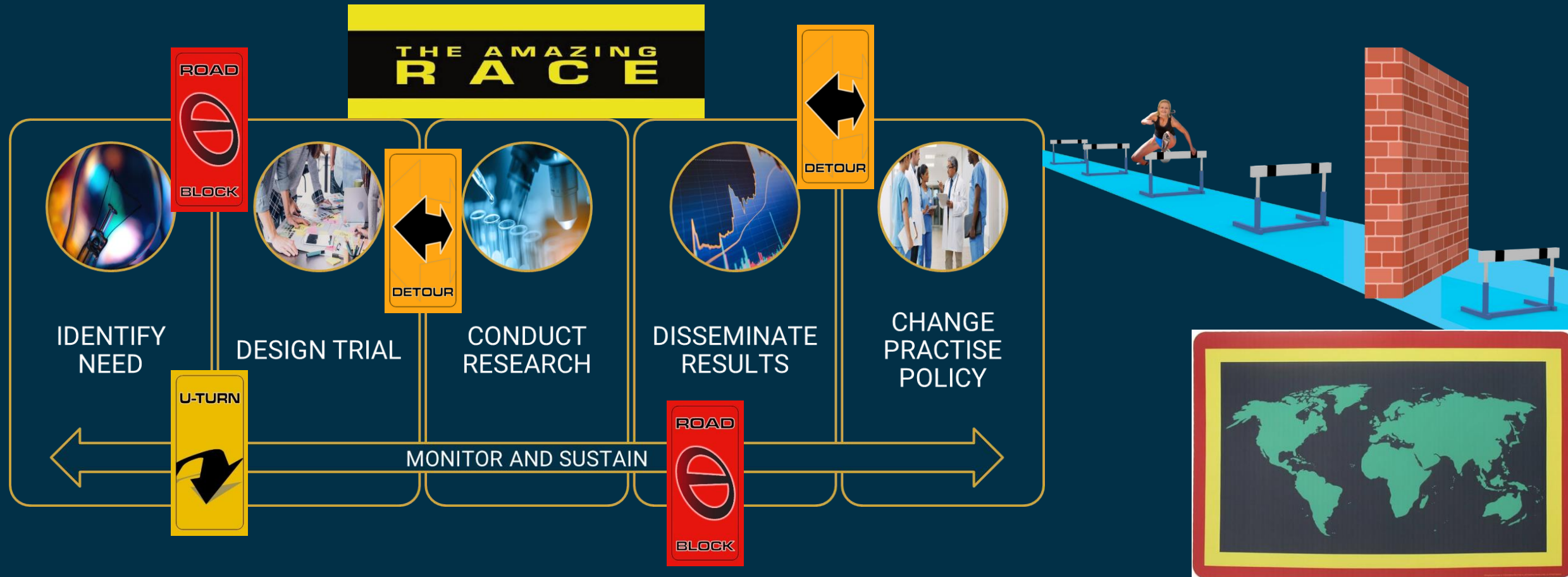
C. P. Pennell¹, A. D. Hirst³, W. B. Campbell⁴, A. Sood², R. A. Agha⁵, J. S. T. Barkun⁶ and P. McCulloch³

Conducting a randomized clinical trial is challenging: Overarching model on improving research relevance and change practice*



*adopted from ANZMUSC

Conducting a randomized clinical trial is challenging



Conducting a randomized clinical trial is challenging: Overarching model on improving research relevance and change practice*



*adopted from ANZMUSC

Conducting a randomized clinical trial is challenging: Overarching model on improving research relevance and change practice*



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Two decades of surgical randomized controlled trials: worldwide trends in volume and methodological quality

Aagje J. M. Pronk^{1,2} , Anne Roelofs^{1,2}, David R. Flum³, H. Jaap Bonjer^{2,4}, Mohammed Abu Hilal⁵, Marcel G. W. Dijkgraaf^{6,7}, Marc G. Besselink^{1,2,*}  and Usama Ahmed Ali^{1,2}

1304 | BJS, 2023, Vol. 110, No. 10

Table 2 Top 10 countries by absolute and relative volume of published surgical randomized trials

Top 10 by absolute volume of surgical RCTs*

Top 10 by relative volume of surgical RCTs per 10 million inhabitants

Rank	1999 (n = 300)	2009 (n = 450)	2019 (n = 438)	Rank	1999 (n = 300)	2009 (n = 450)	2019 (n = 438)
1	USA 65 (21.7)	USA 52 (11.6)	China 81 (18.5)	1	Denmark 23.9	Finland 19.0	Finland 23.5
2	Italy 31 (10.3)	China 40 (8.9)	USA 50 (11.4)	2	Finland 17.1	Netherlands 10.8	Netherlands 15.8
3	UK 30 (10.0)	UK 39 (8.7)	Japan 36 (8.2)	3	Sweden 15.5	Ireland 10.6	Denmark 10.4
4	Japan 24 (8.0)	Italy 37 (8.2)	Netherlands 27 (6.2)	4	Netherlands 8.0	Sweden 9.9	Switzerland 9.3
5	Germany 21 (7.0)	Germany 34 (7.6)	Korea 20 (4.6)	5	Australia 5.8	Switzerland 9.1	Norway 9.3
6	Sweden 14 (4.7)	Japan 26 (5.8)	Egypt 18 (4.1)	6	Switzerland 5.5	Austria 7.3	Sweden 8.0
7	Denmark 13 (4.3)	Turkey 26 (5.8)	Italy 16 (3.7)	7	Italy 5.4	Greece 6.5	Estonia 7.5
8	Netherlands 13 (4.3)	India 19 (4.2)	UK 15 (3.4)	8	UK 5.1	UK 6.2	Lithuania 7.2
9	Australia 11 (3.7)	Netherlands 18 (4.0)	Spain 15 (3.4)	9	Singapore 4.6	Italy 6.0	Bahrain 6.09
10	Finland 9 (3.0)	Egypt 15 (3.3)	Finland 13 (3.0)	10	Greece 4.5	Norway 4.2	Bosnia 6.05

*Values are n (%).

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Table 3 Reported methodological quality of included surgical randomized trials

	1999 (n = 300)	2009 (n = 450)	RR*†	P†^	2019 (n = 438)	RR*	P~
Primary outcome stated explicitly	203 (67.7)	297 (66.0)	0.98 (0.88, 1.08)	0.693	315 (71.9)	0.92 (0.84, 1.00)	0.057
Sample size calculation described	101 (33.7)	218 (48.4)	1.44 (1.20, 1.73)	<0.001	296 (61.4)	0.72 (0.64, 0.80)	<0.001
Baseline present	272 (90.7)	414 (92.0)	1.02 (0.97, 1.06)	0.594	412 (94.1)	0.98 (0.94, 1.01)	0.228
Generation of allocation: reported and adequate	96 (32.0)	213 (47.3)	1.48 (1.22, 1.79)	<0.001	283 (64.6)	1.49 (1.28, 1.74)	<0.001
Computer	52 (17.3)	138 (30.7)			212 (48.4)		
Random table	24 (8.0)	30 (6.7)			41 (9.4)		
Other adequate	20 (6.7)	45 (10.0)			30 (6.8)		
Concealment of allocation: reported and adequate	96 (32.0)	224 (50.0)	1.56 (1.29, 1.88)	<0.001	287 (65.5)	0.76 (0.68, 0.85)	<0.001
Central/pharmacy	32 (10.7)	60 (13.3)			88 (20.1)		
Envelopes	57 (19.0)	145 (32.2)			140 (32.0)		
Other adequate	7 (2.3)	19 (4.2)			59 (13.5)		
Blinding: any type of blinding	103 (34.3)	138 (30.7)	0.89 (0.73, 1.10)	0.300	181 (41.3)	0.74 (0.62, 0.89)	0.001
Double blinding stated	72 (24.0)	90 (20.0)	0.83 (0.63, 1.10)	0.205	71 (16.2)	0.81 (0.61, 1.07)	0.143
Type of analyses							
Intention to treat	60 (20.0)	149 (33.1)	1.66 (1.27, 2.15)	<0.001	156 (35.6)	1.08 (0.90, 1.29)	0.432
Per protocol	9 (3.0)	16 (3.6)			14 (3.2)		
Not stated	231 (77.0)	285 (63.3)			268 (61.2)		
Handling of drop-outs adequate	253 (84.3)	373 (82.9)	1.01 (0.95, 1.07)	0.836	282 (64.4)	0.78 (0.72, 0.84)	<0.001
Low risk of bias	17 (5.7)	66 (14.7)	2.59 (1.55, 4.32)	<0.001	97 (22.1)	1.51 (1.14, 2.01)	0.004

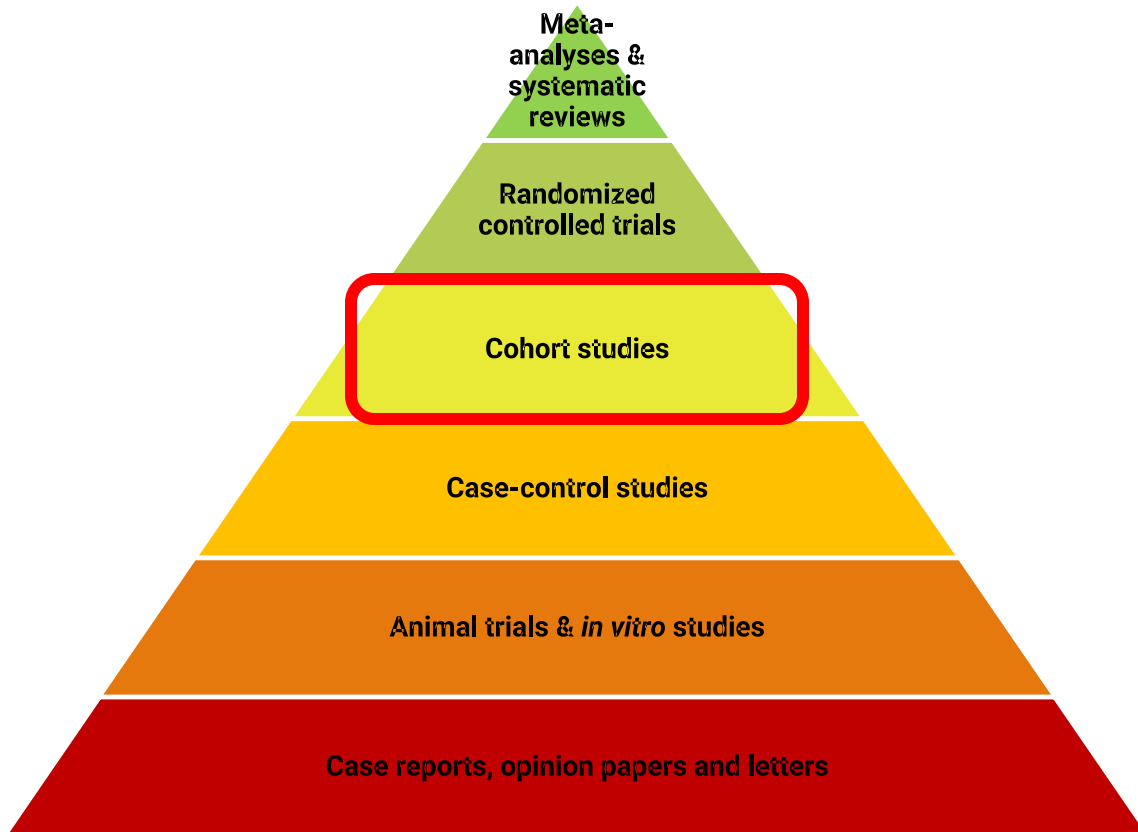
Values are n (%) unless indicated otherwise; *values in parentheses are 95% confidence intervals. †This comparison was performed in the authors' previous study⁸. ^Comparing 1999 and 2009 using Fisher's exact, χ^2 , and Mann–Whitney U tests. ~Comparing 2009 and 2019 using Fisher's exact, χ^2 , and Mann–Whitney U tests. RR, relative rate.

High volume centers:

Prospective observational cohort studies

High quality validated large registries:

Prospective big data



- RCTs = specialized centers, selected patient populations
- Large high-quality registries = real world data
- Validation of the RCT results in large prospective patient cohorts

Clinical Surgical Science



Clinical Surgical Science in MBS: National and international collaboration



RCTs in MBS

International collaboration: Individual Patient Data Meta-Analysis (IPDMA) on T2DM remission

- **GLOBAL IPDMA** for T2DM remission
 - 700-800 patients with T2DM for 10-percentage point's difference
- All RCTs with LRYGB vs. LSG groups and 5-year follow-up

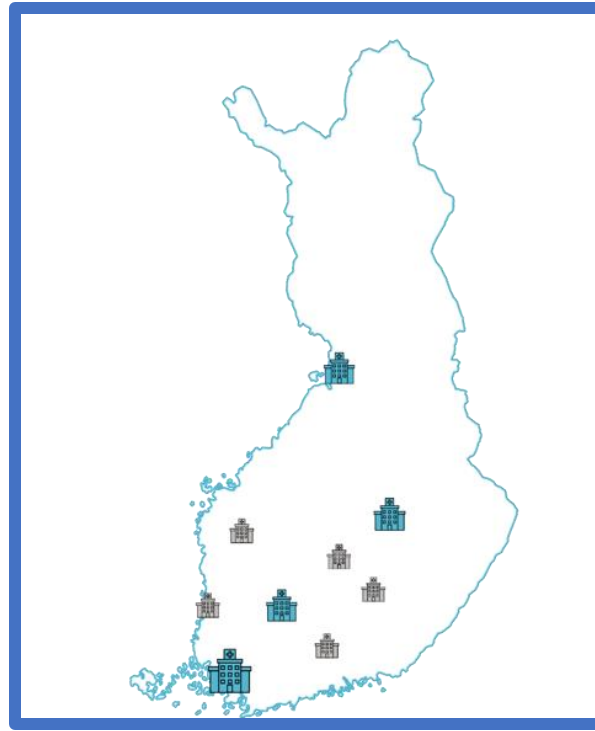


N= 3100, patients with T2D 800

A SYSTEMATIC
REVIEW ON RCTs
within MBS 2000 –
2010 – 2020

Numbers and
quality assessment

Thank you!
APPAC Study group



University hospitals:

Turku

Oulu

Tampere

Kuopio

Helsinki

Central hospitals:

Mikkeli

Seinäjoki

Pori

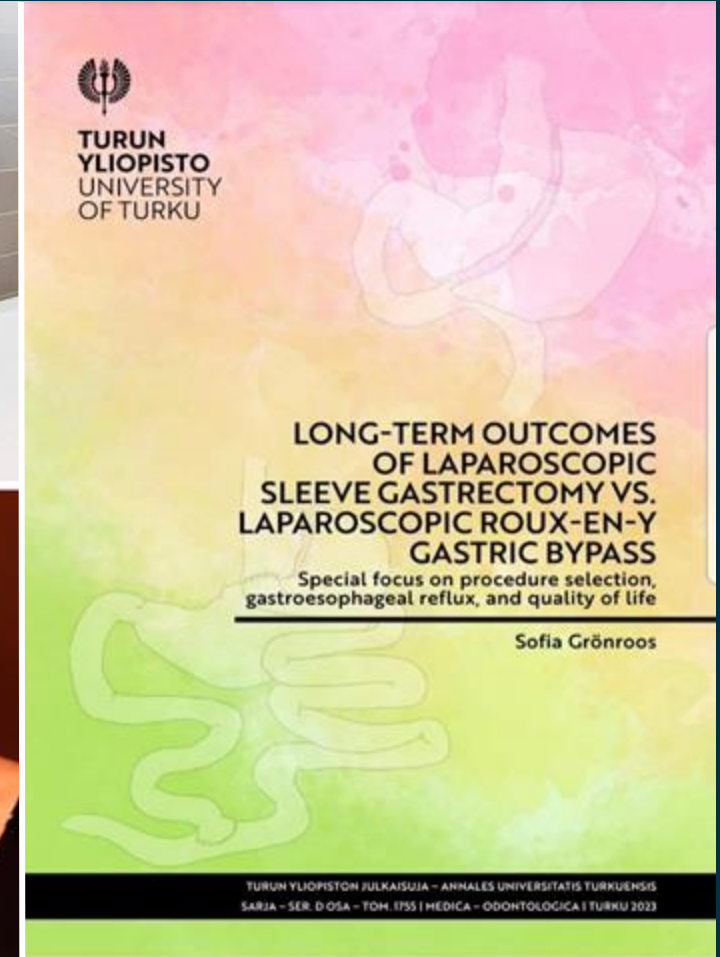
Rovaniemi

Jyväskylä

Lahti



SLEEVEPASS Study Group



Thank you!

