



Better health through  
best evidence

# The Value of Clinical Trials: A *clinician's perspective*

**Prof John Zalcborg OAM**  
ACTA Chair

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

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## ACTA's Vision

*Better health through best evidence*

### **Purpose**

*Our purpose is to promote effective and efficient healthcare in Australia through investigator-initiated clinical trials and clinical quality registries that generate evidence to support decisions made by health practitioners, policymakers, and consumers.*



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## Who is ACTA?

National peak body supporting and representing investigator-initiated clinical trials sector, including:

Clinical Trial Networks (CTNs)

Clinical trial Coordinating Centres (CCs)

Clinical Quality Registries (CQRs)

***That's more than 10,000 clinician-researchers***



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Articles

## Comparison of two standard chemotherapy regimens for good-prognosis germ-cell tumours: a randomised trial

G C Toner, M R Stockler, M J Boyer, M Jones, D B Thomson, V J Harvey, I N Olver, H Dhillon, A McMullen, V J GebSKI, J A Levi, R J Simes, for the Australian and New Zealand Germ Cell Trial Group\*

THE LANCET • Vol 357 • March 10, 2001



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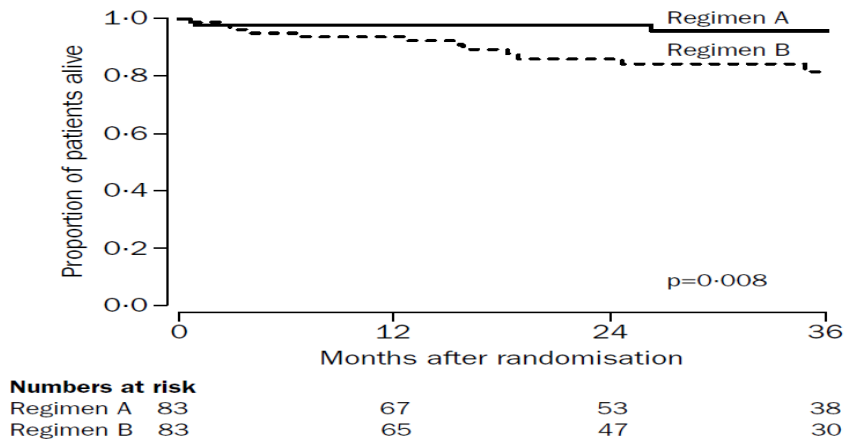


Figure 2: Overall survival (all patients)



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## Unmet need for better evidence

### Original EBM Research



CrossMark

## How good is the evidence to support primary care practice?

Mark H Ebell,<sup>1</sup> Randi Sokol,<sup>2</sup> Aaron Lee,<sup>1</sup> Christopher Simons,<sup>3</sup>  
Jessica Early<sup>2</sup>

*Evid Based Med* June 2017 | volume 22 | number 3 |

**Table 1** Strength of Recommendations Taxonomy<sup>20</sup>

Strength of Recommendations	Definition
A	Recommendation based on consistent* and good quality† patient-oriented evidence‡
B	Recommendation based on inconsistent or limited quality patient-oriented evidence
C	Recommendation based on consensus, usual practice, opinion, disease-oriented evidence or case series

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Includes RCT's, systematic reviews

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**Table 3** Overall bottom-line recommendations by organ system/specialty classification, sorted by the percentage of recommendations that are A or B

Category	Topics in category (n)	A	B	C	A or B*	B or Ct	Total
Pregnancy and childbirth	16	26 (36%)	23 (32%)	23 (32%)	49 (68%)	46 (64%)	72
Cardiovascular	49	66 (30%)	85 (38%)	71 (32%)	151 (68%)	156 (70%)	222
Oncology	39	35 (20%)	78 (44%)	65 (37%)	113 (63%)	143 (80%)	178
Psychiatric	20	27 (28%)	33 (35%)	35 (37%)	60 (63%)	68 (72%)	95
Neurological	48	40 (19%)	8	8	8	8	8
Gastrointestinal	58	59 (20%)	112 (39%)	119 (41%)	171 (59%)	231 (80%)	290
Respiratory	36	36 (23%)	53 (34%)	69 (44%)	89 (56%)	122 (77%)	158
Congenital	23	16 (16%)	36 (37%)	46 (47%)	52 (53%)	82 (84%)	98
Gynaecological	29	27 (20%)	44 (32%)	66 (48%)	71 (52%)	110 (80%)	137
Skin disease	56	46 (19%)	82 (33%)	120 (48%)	128 (52%)	202 (81%)	248
Musculoskeletal and rheumatological	61	31 (11%)	102 (37%)	140 (51%)	133 (49%)	242 (89%)	273
Renal	20	13 (14%)	31 (33%)	49 (53%)	44 (47%)	80 (86%)	93
Male genitourinary	18	11 (15%)	24 (32%)	40 (53%)	35 (47%)	64 (85%)	75
Infectious disease	61	41 (15%)	77 (29%)	147 (55%)	118 (45%)	224 (85%)	265
Trauma and injuries	32	21 (15%)	39 (28%)	77 (56%)	60 (44%)	116 (85%)	137
Perinatal and infant	17	10 (12%)	26 (31%)	47 (57%)	36 (43%)	74 (88%)	83
Haematological	20	7 (8%)	31 (35%)	50 (57%)	38 (43%)	81 (92%)	88
Eye diseases	23	19 (18%)	25 (24%)	61 (58%)	44 (42%)	86 (82%)	105
Ear, nose and throat/allergy	36	17 (12%)	38 (28%)	83 (60%)	55 (40%)	121 (88%)	138
Endocrine	41	25 (13%)	47 (25%)	114 (61%)	72 (39%)	161 (87%)	186
Poisoning and toxicity	18	3 (4%)	24 (29%)	56 (67%)	27 (33%)	80 (96%)	83

\*Recommendations based on patient-oriented evidence (improvements in how well or long patients live).  
 †Studies with inconsistent evidence of benefit, low-validity studies, or based on disease-oriented evidence.

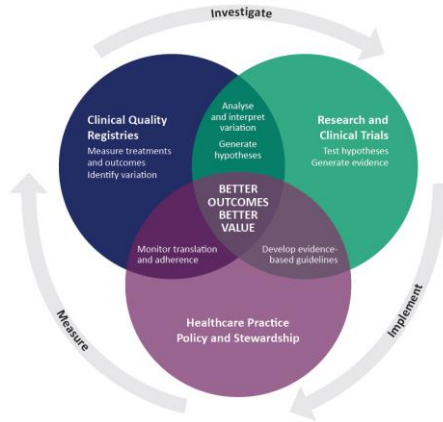
**What are the new findings?**  
 ► In a primary care-oriented medical review, 18% of recommendations were based on consistent, high-quality patient-oriented evidence (Strength of Recommendations Taxonomy (SORT) A), while approximately half were based on expert opinion, usual care or disease-oriented evidence (SORT C).

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## Current Australian Colorectal Cancer Guidelines

Grade of Recommendation	Description	Levels of Evidence
A	Body of evidence can be trusted to guide practice	1
B	Body of evidence can be trusted to guide practice in most situations	1
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application	16
D	Body of evidence is weak and recommendation must be applied with caution	17
Consensus		16

## A Learning Healthcare System



### Fundamental principles

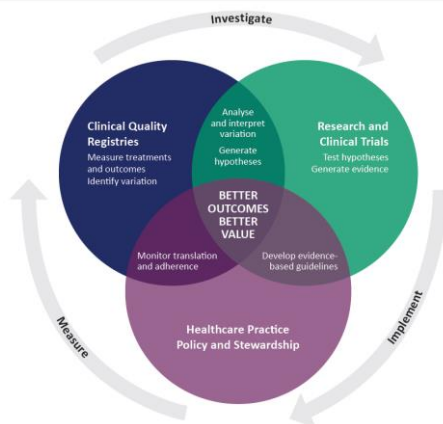
1. High quality healthcare is critical to patients and saves money
2. High quality care (value-based healthcare) is evidence-based
3. Best evidence is derived from randomised clinical trials (RCTs)



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## A Learning Healthcare System



**The role of RCTs is to test interventions to prove/disprove a hypothesis**



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## The research engagement/outcome relationship

### ORIGINAL INVESTIGATION

# Better Outcomes for Patients Treated at Hospitals That Participate in Clinical Trials

Sumit R. Majumdar, MD, MPH; Matthew T. Roe, MD, MHS; Eric D. Peterson, MD, MPH;  
Anita Y. Chen, MS; W. Brian Gibler, MD; Paul W. Armstrong, MD

*Arch Intern Med.* 2008;168(6):657-662

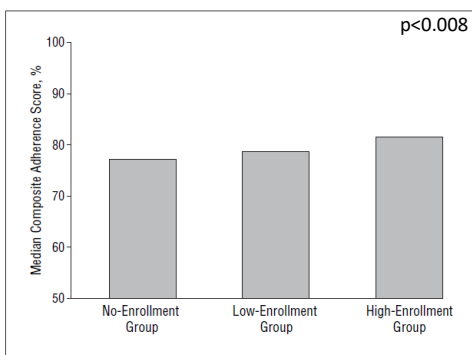
Total inpatient pool – 174,062  
Total trial accrual – 4,590 (3%)  
in 145 hospitals



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## Adherence to evidence-based guideline recommendations



At 494 CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) hospitals.

*Arch Intern Med.* 2008;168(6):657-662

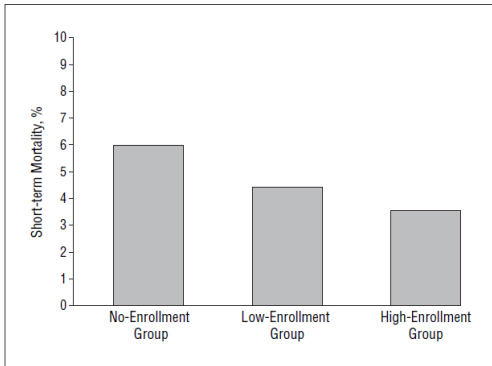
Hospitals that participated in trials had higher adjusted guideline adherence than non-participating hospitals



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## Short-term Mortality



In 174,062 patients with acute coronary syndrome treated at 494 CRUSADE hospitals.

*Arch Intern Med.* 2008;168(6):657-662

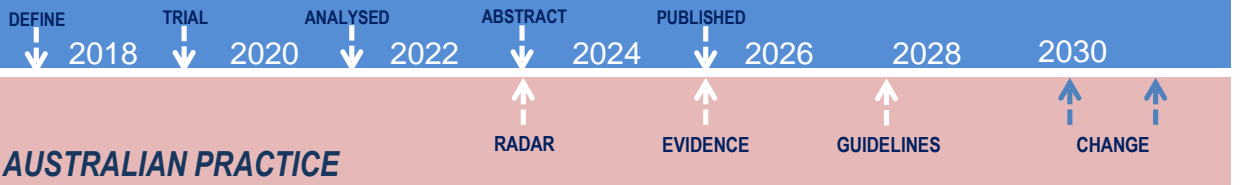
Patients treated at trial participating hospitals had significantly lower mortality than non-participating hospitals



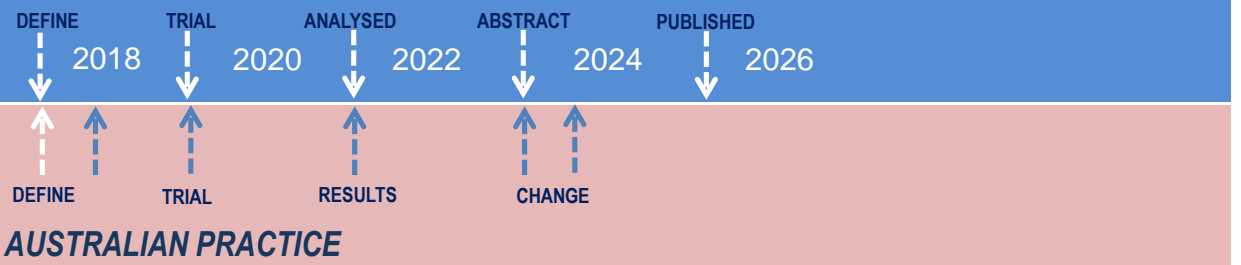
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## Why is it so important to do studies in Australia?

### USA TRIAL



### AUSTRALIAN TRIAL





**TOP GEAR: TRIAL OF PREOPERATIVE THERAPY FOR GASTRIC AND ESOPHAGOGASTRIC JUNCTION ADENOCARCINOMA**

**A randomised phase II/III trial of preoperative chemoradiotherapy versus preoperative chemotherapy for resectable gastric cancer**

Protocol number AG0407GR TROG number 08.08

Version 6, 10 July 2012

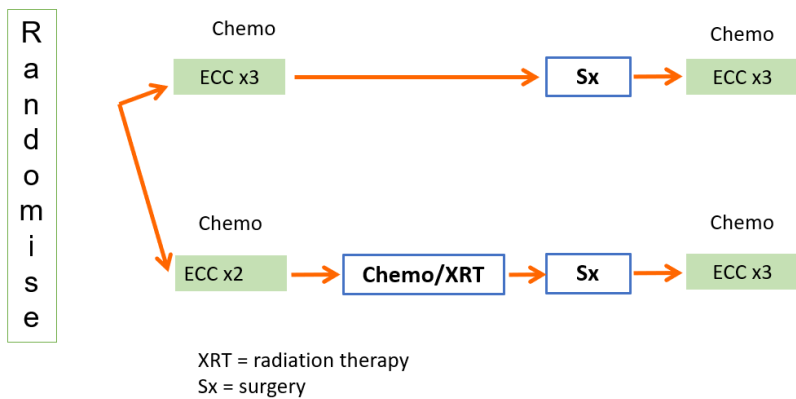
**Study Chair:** Trevor Leong  
 cf. NHMRC Clinical Trials Centre  
 Locked Bag 77  
 Camperdown NSW 1450  
 Telephone: 61-2-9562 5000  
 Fax: 61-2-9562 5092

**Sponsor:** Australasian Gastro-Intestinal Trials Group (AGITG)  
 Locked Bag 77  
 Camperdown NSW 1450  
 Telephone: 61-2-9562-5000  
 Fax: 61-2-9565-5094



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# TOPGEAR Trial



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## Clinical Trials' ROI

- Benefit-to-cost ratio for networks = 5.8:1 = **\$5.80 for every \$1 invested**
- Gross benefit ~ \$2 billion (*measured through better health outcomes and reduced health service costs*)
- Reductions in health service cost = 30% (\$580 million)
- Patient better health outcomes = 70% (\$1,377 million)
- Every dollar awarded in NHMRC grants to the 25 trials returned \$51.10

### How do ROI occur?

- Trials of new treatments – Better outcomes after proof of effectiveness from RCTs
- Comparative effectiveness trials – identification that expensive treatments are not better, so avoided cost



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## ACTA's Key Roles

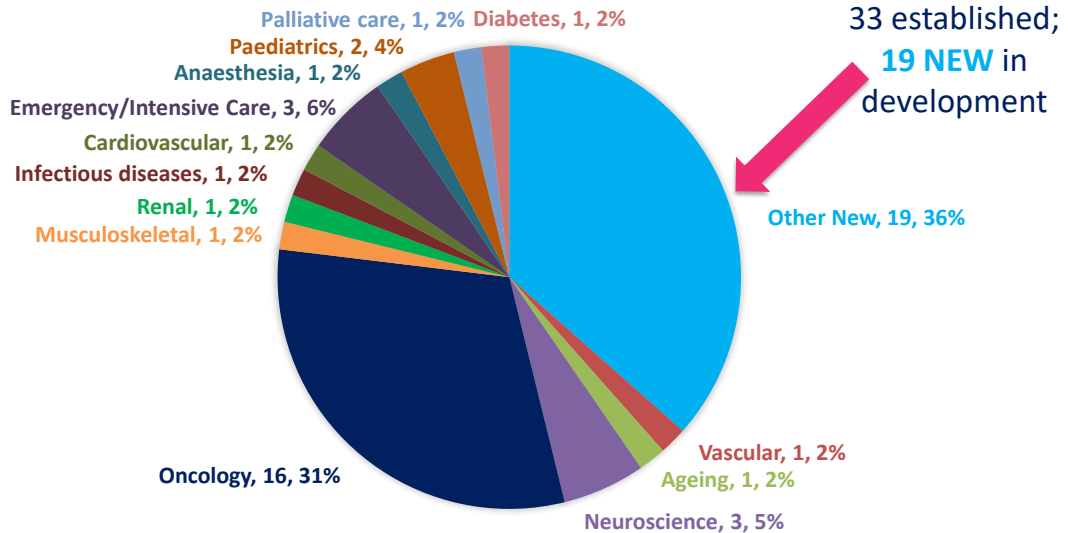
1. Providing Leadership for Collaboration
2. Engaging Stakeholders
3. Building Capacity and Capability
4. Fostering Innovation
5. Translating Research into Healthcare



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## Clinical Trial Networks in Australia



## New CTNs: Actively addressing high priority areas

- Strategic facilitation: Primary care, Indigenous health, regional and rural health
- Developing CTN structure: Child & Youth Mental Health
- New and Upcoming: Adult mental health network

## ACTA-facilitated New CTNs

- > Primary care
- > Surgical disciplines
- > Dementia
- > Nursing
- > Burns
- > Trauma
- > Indigenous health
- > Regional and rural health
- > NECST (Endometriosis)
- > Lifestyle Medicine and Nutraceuticals (mental health)
- > Child & Youth Mental Health
- > Adult mental health network
- > Dermatology
- > Duchenne Network Australia
- > ANZACT (Cardiovascular)
- > DACRIN (substance)
- > Centre for Eye Research Australia
- > Paediatric network
- > Pulmonary fibrosis network (PACT)



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# ***ACTA 2020-2025***



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## Priorities 2020-2025

### Key themes of future work

- **Improve recruitment**
- **Improve equity**
- **Remove barriers**
- **Innovate**

1. New Networks

2. Disinvestment Trials

3. Embedding, Governance, and Digital Data

4. Facilitating Industry-Sponsored Trials

5. Novel Recruitment and Site-Approval Strategies

6. Clinical Quality Registries

7. Consumer Awareness, Involvement and Engagement

8. Representing the Sector

9. Innovative Trial Design



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## Opportunities under development

- **Improve recruitment** – Teletrial model; Facilitating industry-sponsored trials
- **Improve equity** – Consumer engagement; More new networks
- **Remove barriers** – Registry randomised trials; Embedding trials in health system through digital health and AI; Governance Framework
- **Innovate** – Disinvestment trials; Innovative trial designs



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# *Welcome to the ACTA International Trials Conference*

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