

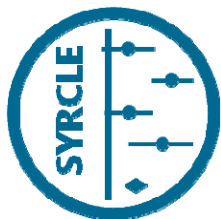
Improving animal research using a science driven approach:

Systematic reviews of animal studies

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EUSAAT, August 2016

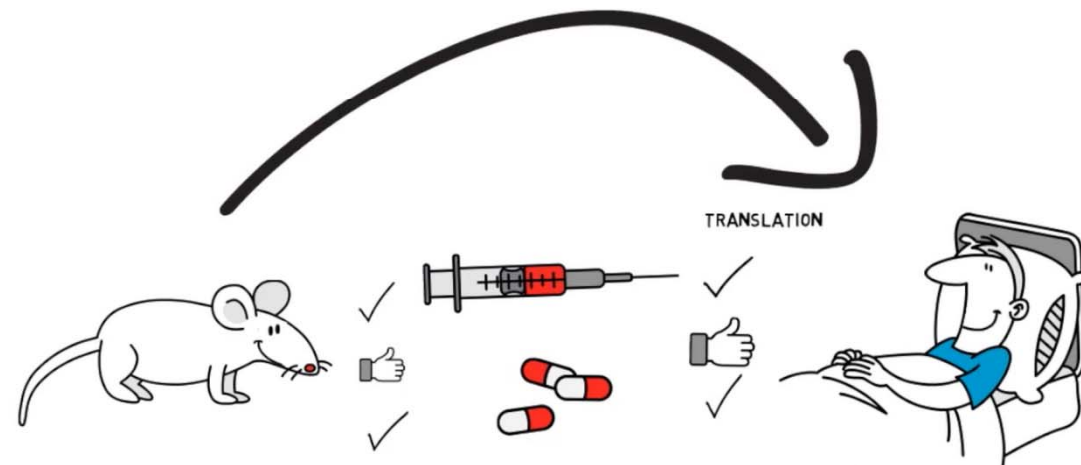
Linz, Austria



Radboudumc

Why evidence-based animal research

- **Decrease:** waste and unnecessary study duplication
- **Increase:** scientific quality (including the 3Rs)
- **Promote:** responsible & justifiable animal use

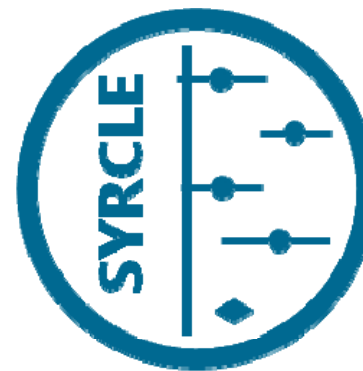


Introduction

Aim: Improving animal-based research



2006 - 2012



2012 - now

SYRCLE
SYstematic
Revue
Centre for
Laboratory animal
Experimentation

Dutch surveys on 3R search

How is the search for the 3Rs performed and how are the 3Rs implemented?

- Questionnaires locally and nationally:
 - Leenaars et al. ATLA 2009 – local researchers
 - Van Luijk et al. ATLA 2011 – national researchers
 - Van Luijk et al. LAJ 2013 – animal welfare officers



Dutch 3R Questionnaires

Main findings:

- Need for different strategy per “R”
- No budget/time for specific 3R search
- Personal communication vs. literature search
- Relevant 3R information not found / not used

Follow-up: 3R workshop

Participants: *Researchers*
 Animal Welfare Officers
 Animal Ethics Committee Members

Main outcome: Separate the 3Rs in daily practice
 “Replacement” & “Best Practice”

Ways to improve:

- Transparency & collaboration
- Sharing of data (negative results)
- Experimental design (education)

Are Systematic Reviews the way to go?



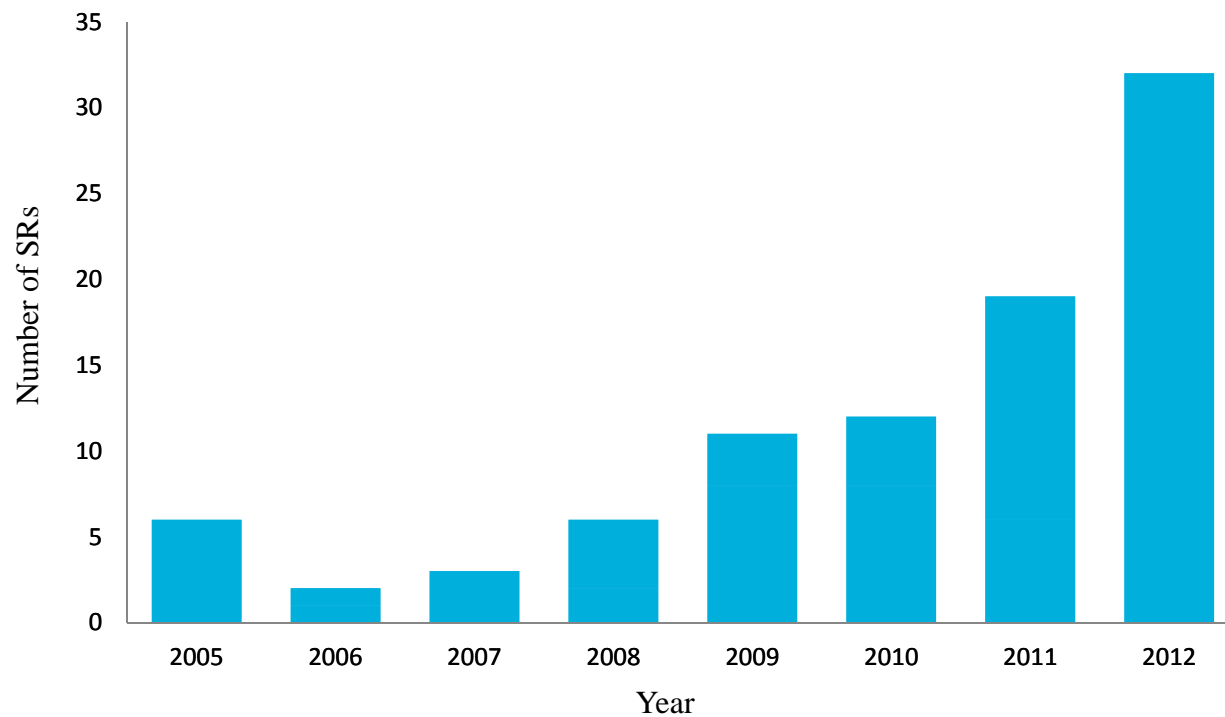
Definitions

- **Systematic Review:**
 - The process of systematically locating, appraising and synthesizing evidence from scientific studies in order to obtain a reliable overview.
- **Meta-analysis:**
 - Combination of results of individual studies in an overall statistical analysis



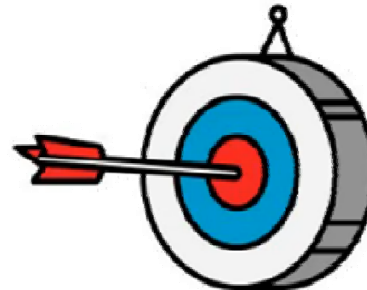
Systematic reviews of animal studies

**Increase of systematic reviews on animal studies
(Medical intervention studies, n=91)**



Added value of Systematic Reviews:

- Provide an overview of available evidence
- Identify knowledge gaps
- Critical appraisal of study quality
- Identify factors influencing treatment efficacy
- Inform experimental design of new studies



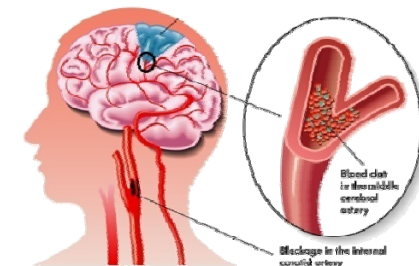
Overviews of available evidence

Table 2. Design characteristics of included studies

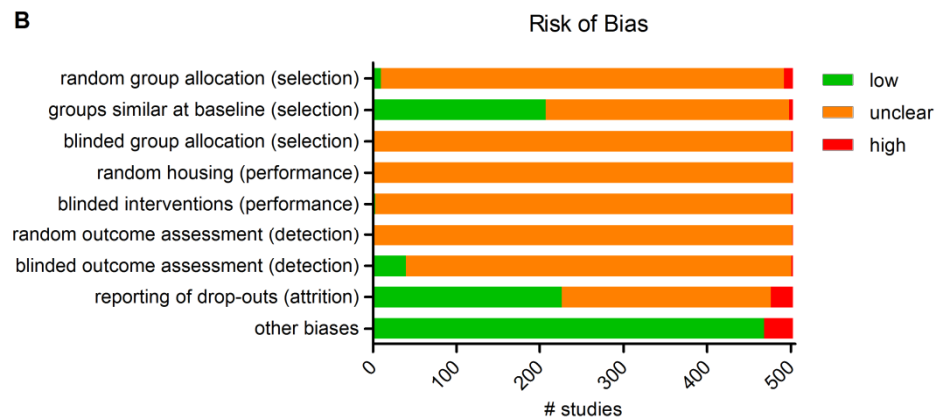
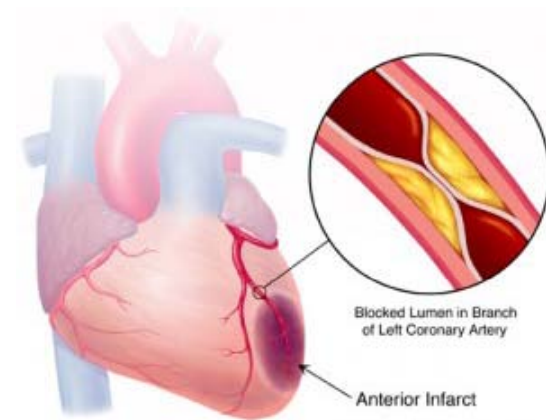
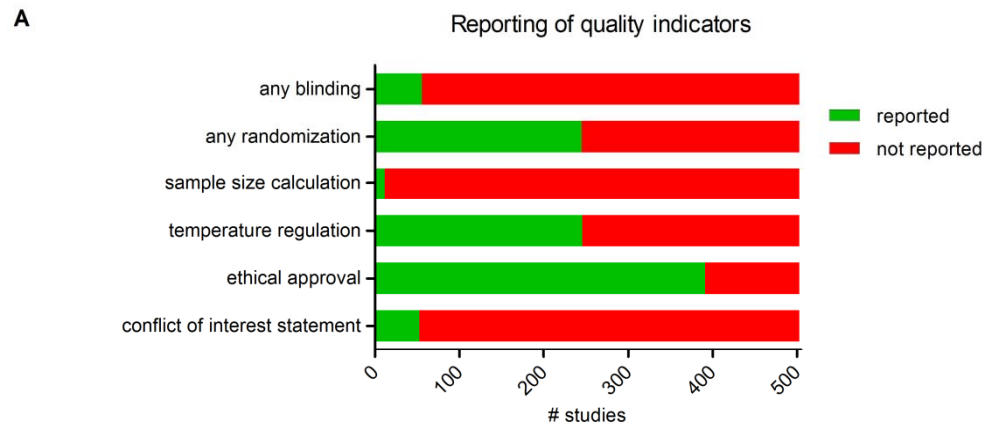
Publication	Gender	n (C)	n (Rx)	Dose range (mg/kg)	Doses in first 24 hr	Time to treatment	Anaesthetic	Permanent or focal ischaemia	Route of drug delivery	Outcome measure
Joo (1998)	Male	6	6	2.5	4	-15 min	Chloral hydrate	Temporary	i.p.	Inf. vol.
Kilic (1999)	Nk	8	6	4	2	0 min	Ketamine	Temporary	Intravenous	Comb
Ling (1999)	Male	9	31	2.5-10	3	-15 min	Chloral hydrate	Temporary	Subcutaneous	Inf. vol.
Peker (2000)	Nk	2	6	2.5	4	-20 min	Not known	Permanent	i.p.	Comb
Borlongan (2000)	Male	11	11	23.2	1	0 min	Halothane	Temporary	Oral	Comb
Sinha (2001)	Male	7	8	20	4	0 min	Chloral hydrate	Temporary	i.p.	Comb
Pei (2002a)	Male	14	61	1.5-50	1	-30 min	Pentobarbital	Temporary	i.p.	Inf. vol.
Gupta (2002)	Male	12	12	20	4	0 min	Chloral hydrate	Temporary	i.p.	Comb
Pei (2002b)	Male	21	23	5-50	1	-30 min	Pentobarbital	Permanent	i.p.	Inf. vol.
Sun (2002)	Male	6	18	2.5-10	3	-15 min	Chloral hydrate	Temporary	i.p.	Inf. vol.
Pei (2003)	Male	44	57	5-15	1-3	0-120 min	Pentobarbital	Temporary	i.p.	Inf. vol.
Torii (2004)	Male	11	10	5	1	0 min	Halothane	Temporary	Oral	Inf. vol.
Lee (2004)	Male	16	16	5	1	90 min	Halothane	Temporary	Intravenous	Comb

Number of animals in control group [n (C)]; number of animals in experimental group [n (Rx)]; dose range; number of doses given in first 24 hr; interval from onset of ischaemia to start of treatment; anaesthetic used; and outcome measure used; Nk, not known; i.p., intra-peritoneal.

Melatonin in Stroke



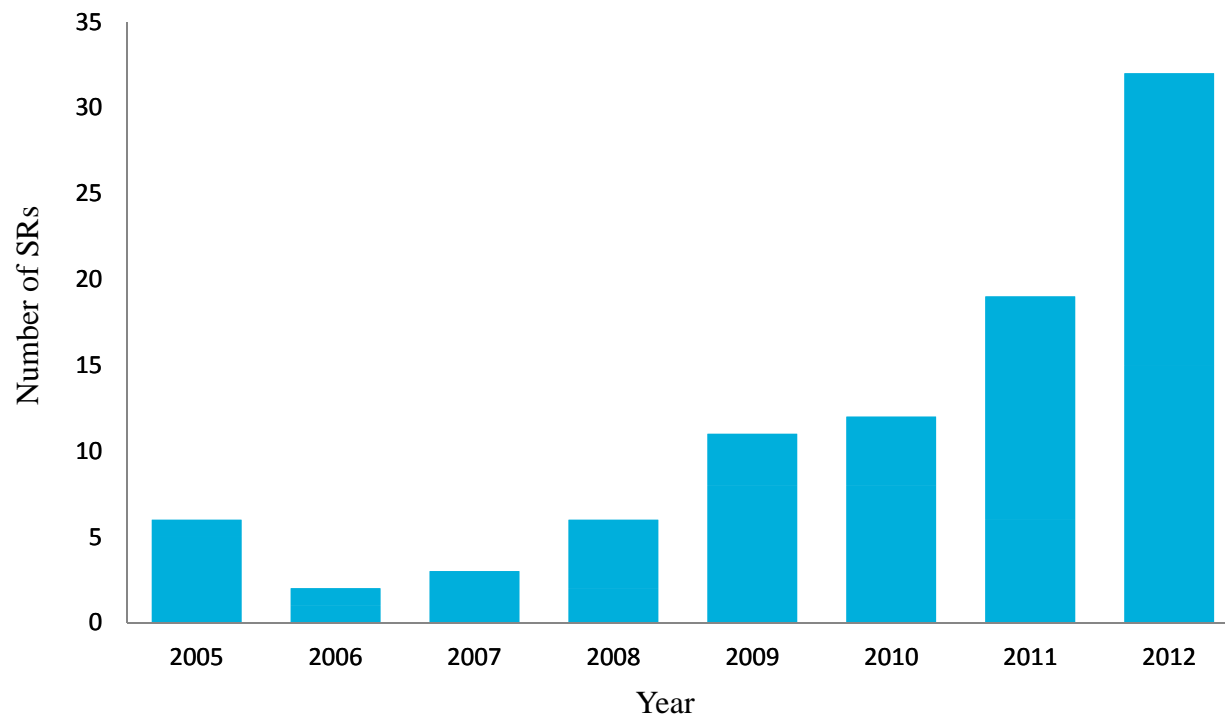
Critical appraisal of study quality



Reporting *and*
Methodological quality

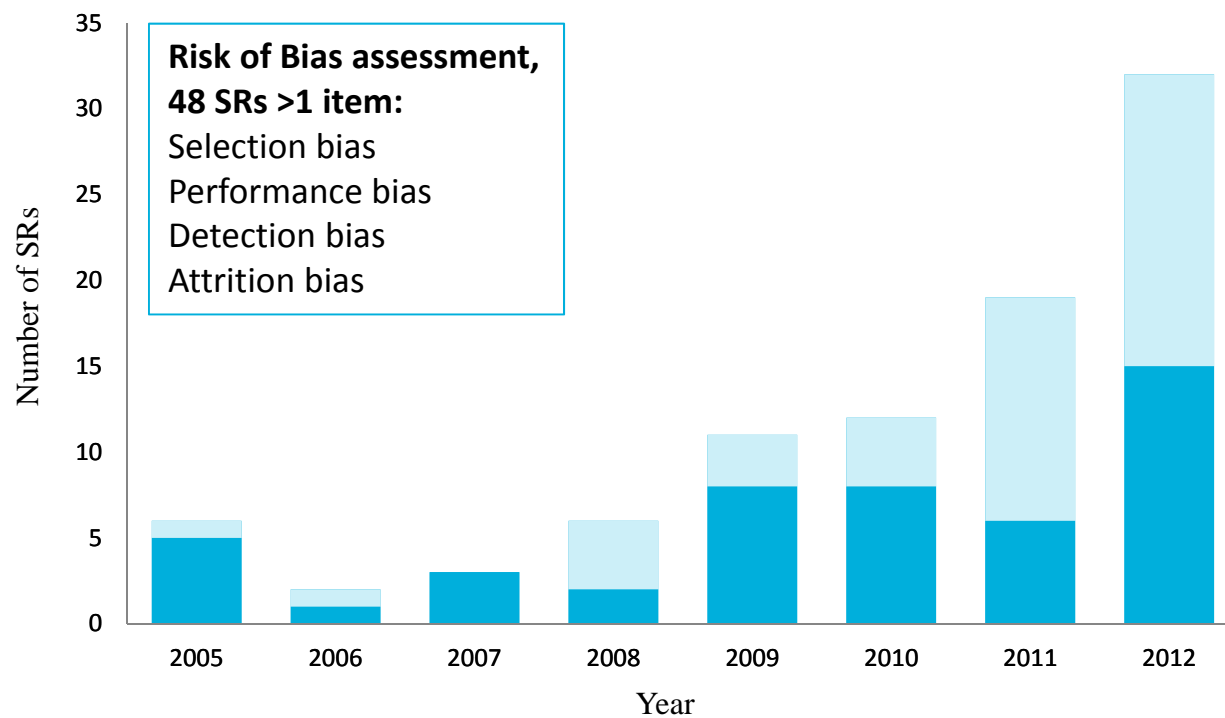
Systematic reviews of animal studies

**Increase of systematic reviews on animal studies
(Intervention studies, n=91)**



Systematic reviews of animal studies

Increase of systematic reviews on animal studies (Intervention studies, n=91)



Take home message

Systematic reviews can be a powerful new strategy to:

- Exposes scientific strengths and weaknesses
(transparency in study validity)
- Provide evidence-based input for future research
(incl. 3R information)

However, interpret outcome with caution!

- Low (reporting) quality of animal studies
- Systematic review methodology under development!



Guideline development & training

