

# Improving animal-based research

- About 3Rs and SRs -

*An interactive session*

Judith van Luijk MSc

AUGUST symposium 2017, Aarhus University



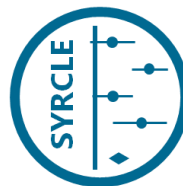
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## My PhD thesis

*Aim: Improving animal based research*



2006 - 2012



**SYRCLE**  
**SY**stematic  
**R**view  
**C**entre for  
**L**aboratory animal  
**E**xperimentation

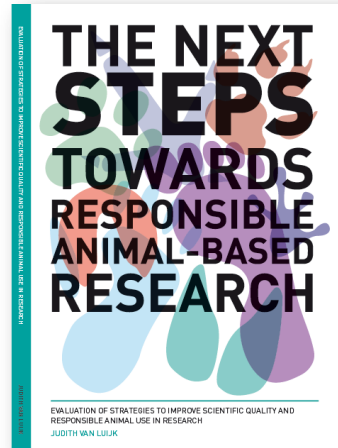
2012 - now

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## Improving animal-based research

### Content:

- Evaluation of 3R search and implementation in the Netherlands
- Identification of future needs (systematic reviews?)
- Methodological evaluations of systematic reviews of animal studies
- Advantages and limitations of SRs in relation to 3Rs



Public defence: 24 May 2017, Nijmegen, the Netherlands

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## About the 3Rs

- 3R principles: Replacement, Reduction and Refinement
- Introduced in 1959 by Russell and Burch
- Gained popularity in the 70's; incorporated in legislation
- **How are the 3Rs addressed in daily practice?**



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## 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



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## Dutch 3R Questionnaires

### **Main findings:**

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

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*Leenaars et al. 2009, van Luijk et al., 2011 & 2013*

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## 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?***

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*Van Luijk et al. 2012*



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## Definitions

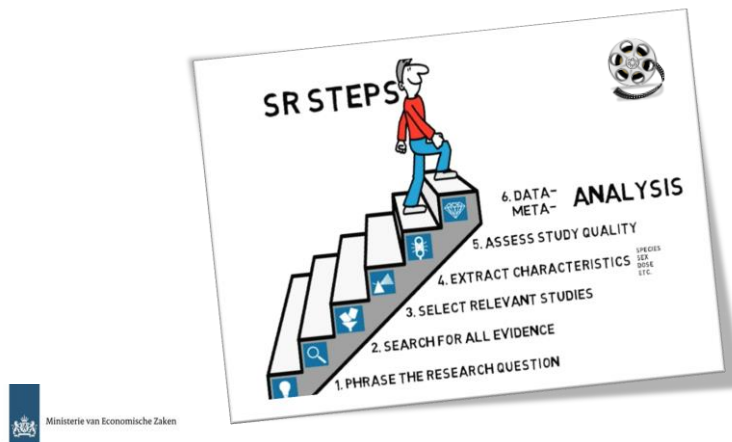
- **Systematic Review:**
  - The process of systematically locating, appraising and synthesizing evidence from scientific studies in order to obtain a reliable overview.
- **Meta-analysis:**
  - Combination of results of individual studies in an overall statistical analysis

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## Videoscribe on systematic reviews

<https://vimeo.com/142124487>



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## Systematic reviews of systematic reviews

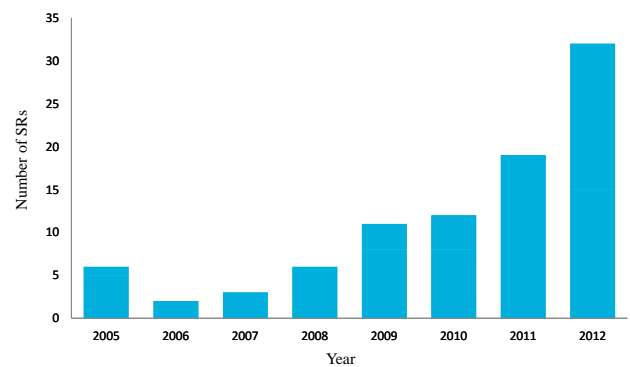


[www.SYRCLE.nl](http://www.SYRCLE.nl)

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# Risk of bias assessment

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

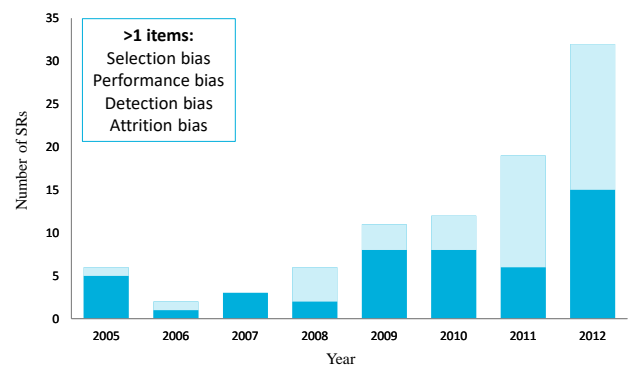


van Luijk et al., 2014

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# Risk of bias assessment

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

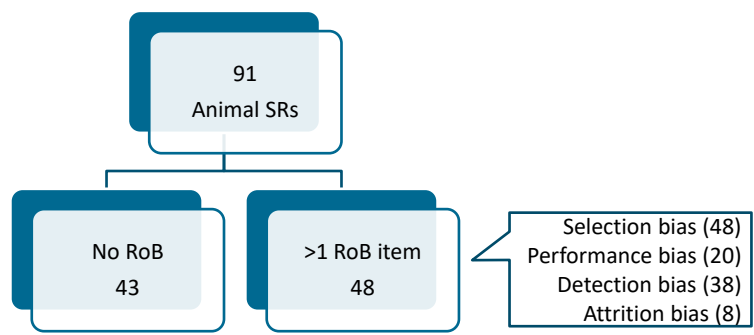


van Luijk et al., 2014

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# Risk of bias assessment

Survey among 91 SRs of animal studies



Van Luijk et al, 2014

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# Systematic reviews of systematic reviews



[www.SYRCLE.nl](http://www.SYRCLE.nl)

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## Decisions in search strategy

Effect of database selection and language restriction

Main outcomes:

- No clear effect of database/language on summary effect in MA
  - Effect research area dependent?
- Large overlap between Pubmed and Embase (66-100%; 2/3 >80%)

Available vs. retrievable (depends on used search strategy)

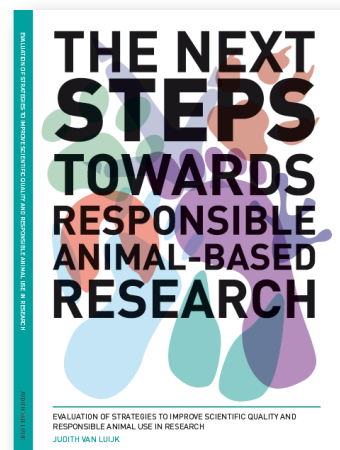
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## Recommendations

- Increase conduct of SRs of animal studies
- Stimulate better reporting
  - *E.g. ARRIVE guideline*
- **Conduct of comprehensive literature searches**
- Training and education



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# A comprehensive literature search

- Is a key element of the systematic review process
- Can also be performed to accumulate relevant information for new animal experiments (including 3R information)

## Available tools:



Step by step search guide  
*Leenaars et al. 2012*



### Animal search filters

- For PubMed  
*Hooijmans et al. 2010*
- For Embase  
*De Vries et al. 2011 (Update: 2014)*

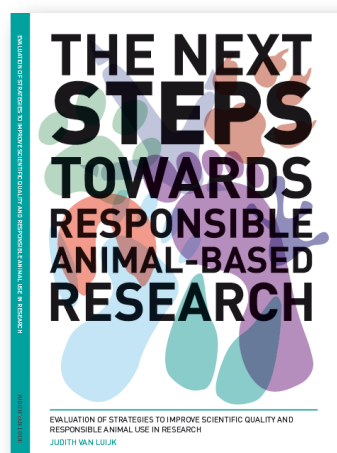
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# PubMed search filter for animals

```
("animal experimentation"[MeSH Terms] OR "models, animal"[MeSH Terms] OR
"invertebrates"[MeSH Terms] OR "Animals"[Mesh:noexp] OR "animal
population groups"[MeSH Terms] OR "chordata"[MeSH Terms:noexp] OR
"chordata, nonvertebrate"[MeSH Terms] OR "vertebrates"[MeSH Terms:noexp]
OR "amphibians"[MeSH Terms] OR "birds"[MeSH Terms] OR "fishes"[MeSH
Terms] OR "reptiles"[MeSH Terms] OR "mammals"[MeSH Terms:noexp] OR
"primates"[MeSH Terms:noexp] OR "artiodactyla"[MeSH Terms] OR
"carnivora"[MeSH Terms] OR "cetacea"[MeSH Terms] OR "chiroptera"[MeSH
Terms] OR "elephants"[MeSH Terms] OR "hyraxes"[MeSH Terms] OR
"insectivora"[MeSH Terms] OR "lagomorpha"[MeSH Terms] OR
"marsupialia"[MeSH Terms] OR "monotremata"[MeSH Terms] OR
"perissodactyla"[MeSH Terms] OR "rodentia"[MeSH Terms] OR
"scandentia"[MeSH Terms] OR "sirenia"[MeSH Terms] OR "xenarthra"[MeSH
Terms] OR "haplorhini"[MeSH Terms:noexp] OR "strepsirrhini"[MeSH Terms] OR
"platyrrhini"[MeSH Terms] OR "tax: ferrets[tiab] OR ferret[tiab] OR polecat[tiab] OR polecats[tiab] OR
Terms:noexp] OR "cercopithecidae"[tiab] OR "mustela putorius"[tiab] OR "guinea pigs"[Tiab] OR "guinea pig"[Tiab] OR
Terms] OR "hominidae"[MeSH Terms]: cavia[tiab] OR callithrix[tiab] OR marmoset[tiab] OR marmosets[tiab] OR
OR "pan paniscus"[MeSH Terms] OR "cebuella[tiab] OR hapale[tiab] OR octodon[tiab] OR chinchilla[tiab] OR
pygmaeus"[MeSH Terms] OR ((animal chinchillae[tiab] OR gerbillinae[tiab] OR gerbil[tiab] OR gerbils[tiab]
OR mus[tiab] OR mouse[tiab] OR mus[tiab] OR jird[tiab] OR jirds[tiab] OR merione[tiab] OR meriones[tiab] OR
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OR monkey[tiab] OR monkeys[tiab] OR anthropoidea[tiab] OR
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leontopithecus[tiab] OR hominidae[tiab] OR ape[tiab] OR apes[tiab] OR
"pan paniscus"[Tiab] OR bonobo[tiab] OR bonobos[tiab] OR "pan
troglodytes"[Tiab] OR gibbon[tiab] OR gibbons[tiab] OR siamang[tiab] OR
siamangs[tiab] OR nomascus[tiab] OR symphalangus[tiab] OR
chimpanzee[tiab] OR chimpanzees[tiab] OR prosimian[tiab] OR.....
```

## Recommendations

- Increase conduct of SRs of animal studies
- Stimulate better reporting
  - *E.g. ARRIVE guideline*
- Conduct of comprehensive literature searches
- **Training and education**



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## Educational programme SYRCLE


- Introductory: lectures and e-learning module
- One-day workshops
  - (Netherlands and abroad)
- Longer courses
  - (including Radboud Summer School & SR trainings for EFSA)
- Coaching of the conduct of SRs




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Systematic Reviews of Animal Studies








START

<https://syrcle.ekphost.nl>  
Registration code: syrcle


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Main menu




This menu allows you to navigate through the course.

 items are mandatory.




1. Introduction






2. Review question






3. Comprehensive search






4. Study selection






5. Study characteristics






6. Quality assessment




7. Meta-analysis



8. Wrap up





Final assessment

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## E-learning module - “fun facts”

- Funded by Ministries of Health and of Economic Affairs
- Launched in October 2015
- Certificate when completed
- After one year: nearly 1000 started, more than 750 completed
- 37 different countries (22% of all users)



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## One-day workshop

### Main topics:

- Comprehensive searching
- Study characteristics and quality (RoB)
- Data extraction and meta analysis

*Theoretical lectures and hands-on practical*



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## One-day workshop

- Goals: thoroughly familiar with concept and steps + basic skills to start own SR (under supervision)
- Maximum of 20 participants – 2 SYRCLE trainers
- Both in the Netherlands and abroad: Belgium, Norway, Denmark, Sweden, Switzerland (tour), Germany, UK, Spain, Italy, Brazil
- Netherlands: Nijmegen funded by Reinier Post Stichting, elsewhere ZonMw
- Evaluations between 8 and 9 (out of 10)

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## Longer courses

### @Radboud University

- Systematic review week (Biomedical sciences)
- Minor Evidence-based Translation (10 weeks; 1 day/week)
- Radboud Summer School course (5 days)

*Additional topics e.g. protocol and reporting quality*



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## EFSA SR trainings (2016-2018)

- 1) Introduction to systematic reviews (4x)
- 2) Data extraction and meta-analysis (2x)
- 3) Critical appraisal of SRs and primary studies (2x)
- 4) Basic and advanced searching techniques (6x)



SYRCLE/Radboudumc in collaboration with:

- Sebastian Hoffmann (seh, EBTC)
- Miranda Langendam (AMC, Cochrane)
- OHAT/NTP (Kristina Thayer, Andrew Rooney)
- RIVM

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## Coaching

- Partly education, partly research
- SR process too complex for participants to be able to conduct SR on their own after workshop/course
- We support and provide feedback on all steps of the SR: from protocol to manuscript
- On average 40-50 hours coaching required
- So far, more than 35 SRs supervised
- Netherlands: Nijmegen funded by RPS, elsewhere ZonMw



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