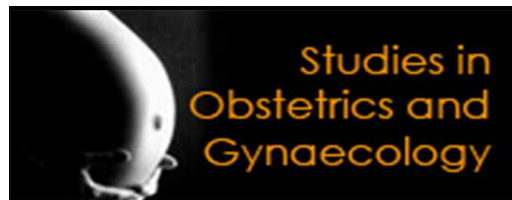

Challenges facing international collaborations in obs/gyn research

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Early Pregnancy Unit



Today

- Background
 - similarities & differences between countries
- Experiences with (inter) national research
 - dutch Consortium Obs/Gyn
 - multicenter research networks
 - facilitators/ barriers
- Conclusions

What we share....

- The need for large trials
- Difficulties recruiting sufficiently per country
less than 1/3 of trials recruited their original target within the time originally specified¹
- Prolonged medical ethical approval rounds
- Difficulties with fundraising
- Insufficient communication at an early stage

¹Campbell 2007

Lasagna's Law



“when trial recruitment starts, the supply of eligible patients becomes a fraction of what it was assumed to be before the trial began” *Lasagna 1979*

What we do not share.....

- Definitions

Recurrent Miscarriage

ESHRE 2006:	≥ 3 consecutive miscarriages	< 20 weeks GA
NVOG 2007:	≥ 2 miscarriages	< 20 weeks GA
RCOG 2011:	≥ 3 consecutive miscarriages	
ASRM 2012:	≥ 2 early pregn losses	

- Advices in guidelines
- Governmental / Institutional rules
- Restrictions by Law
- Differences in reimbursement
- Clinical practice – local protocols

The answer



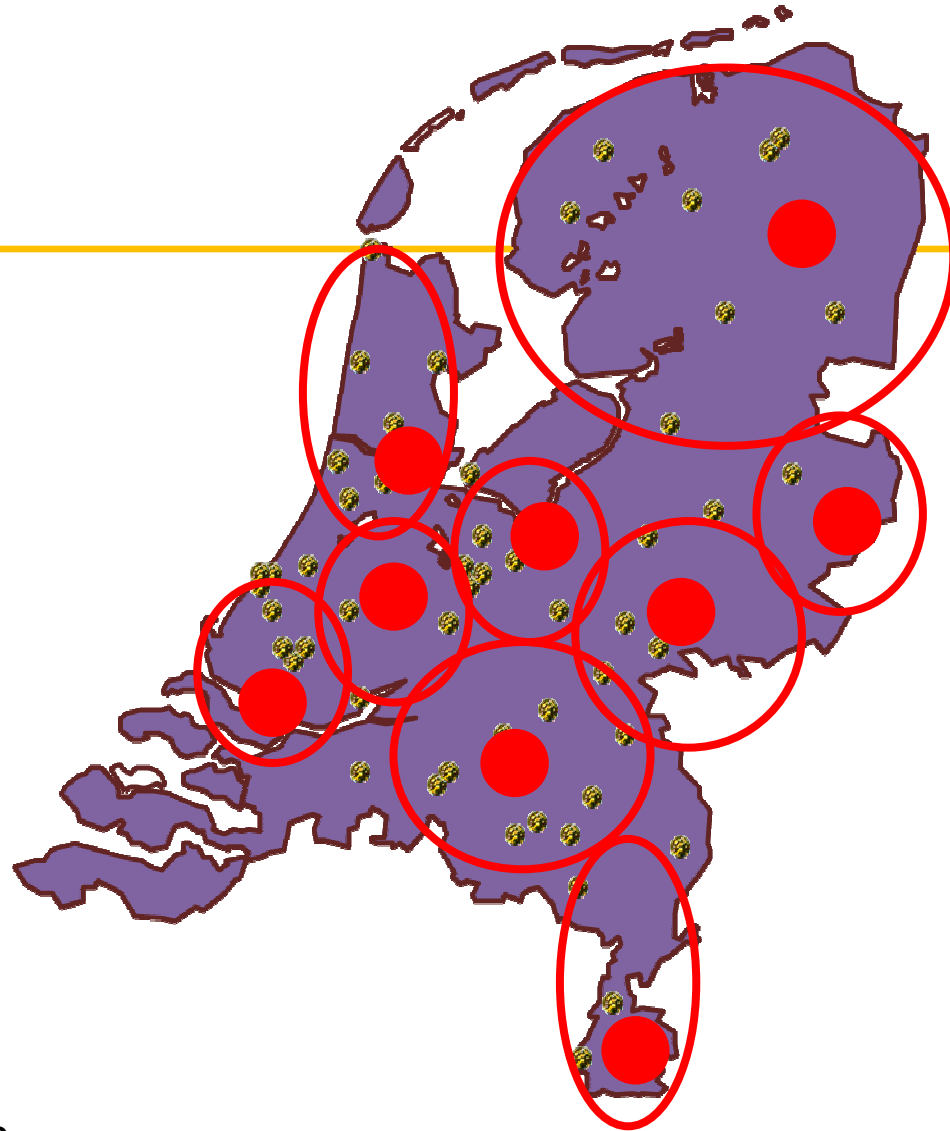
Dutch Consortium in Obstetrics & Gynaecology

- Started with Obstetrical Network in 2003 (BW Mol)
- Now also network for gynaecology and subfertility
- Since 2014 under auspices of NVOG

- Multi centre research:
 - 10 perinatological centers
 - 70 medical centers

- Start up fee: 47.500 euro
17.500 euro annually

- Central management AMC, Amsterdam
 - Database management
 - Secretary (IRB, communication, follow-up)
 - Website



Nine clusters

Dutch Consortium in Obstetrics & Gynaecology

- -Research nurses/ midwives (GCP certified): 1 per hospital
- -9 Clustercoordinators
- -Inclusionfee: 250-300 euro
- -Telephone conferences 1/month
- -Meetings 4/year



Consortium Website: www.studies-obsgyn.nl

The screenshot shows the Consortium website interface. At the top, there is a navigation bar with categories: Obstetrics, Fertility, Neonatology, Fetal medicine, Gynaecological Oncology, and (Uro)gynaecology. Below this is a secondary navigation bar with links: Home, New Trials, Contact, Mission, Results, Documents, Links, and Search. The main content area is titled 'Fertility' and features a sidebar on the left with a 'Fertility' icon and a list of study links: News, Agenda, Documents, Consortium studies (Zon-Mw), FOAM, Freeze-all (progesterone), IMPROVEMENT, IVF 38+, MASTER, M-ovin', SCRATCH, SUPER, and T4-LIFE. The main content area displays 'The Fertility study scheme:' followed by a table with the following data:

AD/ diagnose	Welke patient	Studie	Eindpunten / info
IUI/ICI bij KID	Vrouwen die in aanmerking komen voor KID	AID 6 cycli IUI vs ICI zonder ovariele hyperstimulatie	Live birth P.A.L. Kop: email
Vrouwen met 2 of meer miskramen en erfelijke trombofilie	2 of meer miskramen erfelijke trombofilie	ALIFE2 LMWH vs geen behandeling	Eindpunt: Live birth lj.scheres@amc.uva.nl
IVF of ICSI en hydrosalpinx	Vrouwen met op echo zichtbare hydrosalpingen	DESH Essure vs. Tubectomie	Eindpunt: clinical pregnancy rate email

ALIFE Trial

Target group:	RM unexplained
Method	Aspirin plus Heparin vs Aspirin vs Placebo
No of patients:	364
Main Outcome:	Live Birth Rate
Centers Recruiting:	NL: 8 centers, new network RM clinics
International collaboration	none
Results:	-No difference in LBR between study groups

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Aspirin plus Heparin or Aspirin Alone in Women with Recurrent Miscarriage

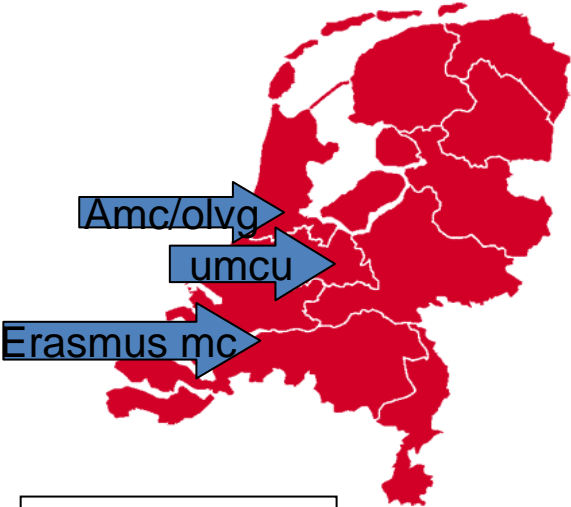
Stef P. Kaandorp, M.D., Mariëtte Goddijn, M.D., Ph.D.,
Joris A.M. van der Post, M.D., Ph.D., Barbara A. Hutten, Ph.D.,
Harold R. Verhoeve, M.D., Karly Hamulyák, M.D., Ph.D.,
Ben Willem Mol, M.D., Ph.D., Nienke Folkeringa, M.D., Ph.D.,
Marleen Nahuis, M.D., Dimitri N.M. Papatsonis, M.D., Ph.D.,
Harry R. Büller, M.D., Ph.D., Fulco van der Veen, M.D., Ph.D.,
and Saskia Middeldorp, M.D., Ph.D.



Early Pregnancy Care influences study logistics



250 x EPU



3 x EPU



unique patient no.

Goals of GONet



Global Obstetric Network forum for collaboration among groups that perform clinical trials and observational studies in maternal fetal medicine and obstetrics.

- To discuss areas of critical importance in obstetrics and identify trials/studies that need to be performed.
- The development of a database of ongoing and planned studies
- To define obstetrical trial/study terms/definitions and create a registry of definitions
- To provide suggested tables/ minimal data to be collected for different clinical problems
- To coordinate study protocols (prospective meta-analyses and retrospective IPD metanalysis)
- To determine if it is feasible to facilitate an international collaboration of funding bodies to support trials
- To enhance international education and training

Launch in 2011/ Society for Maternal
Fetal Medicine



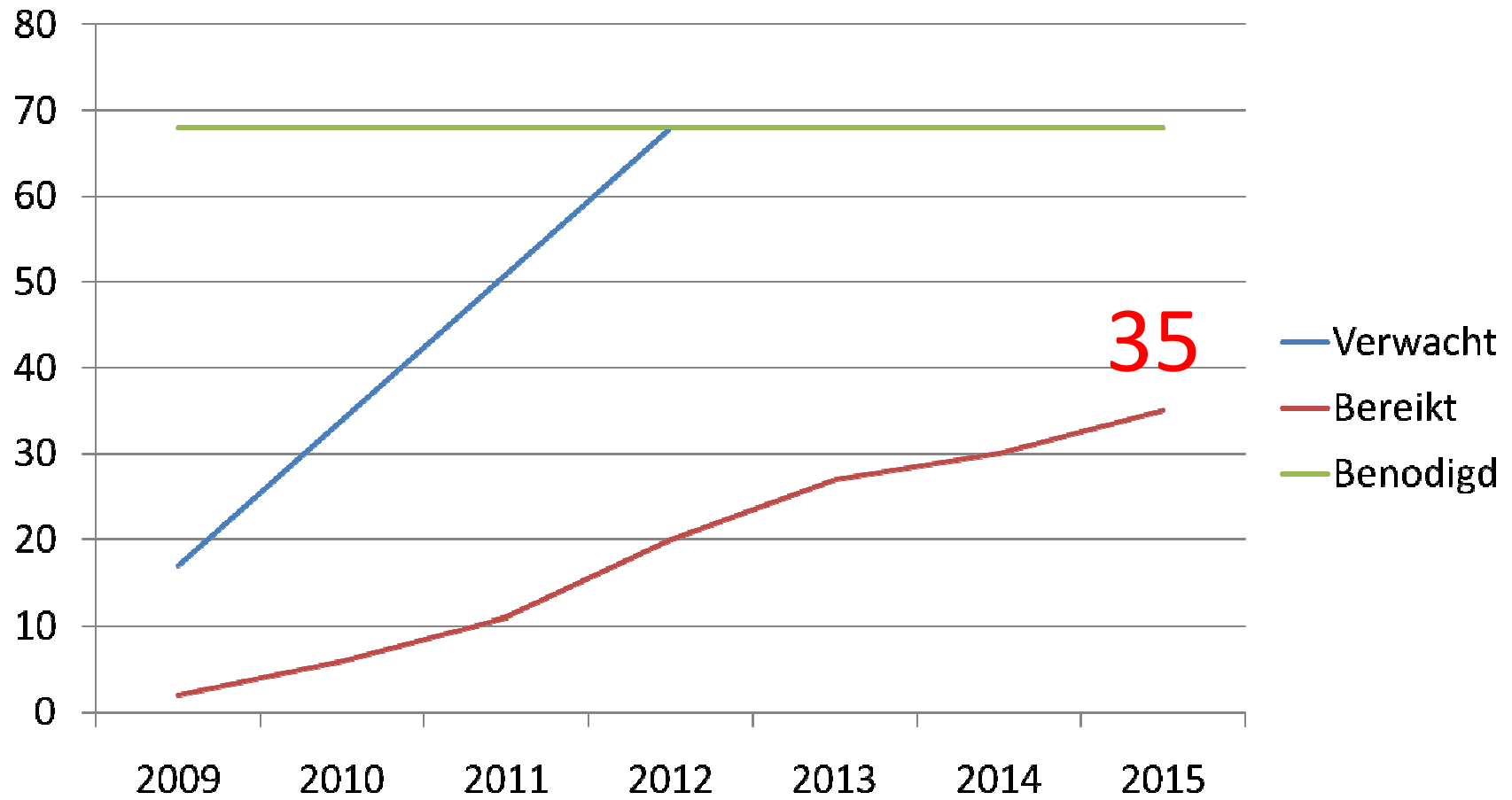
RCTs exemplary for international collaboration



Target group:	RM and a septate uterus
Method :	hysteroscopic metroplasty vs expectant management
No of patients:	68
Main Outcome:	Live Birth Rate
Centers Recruiting:	The Netherlands: 8 UK: 1 Belgium: 1
<i>advantage:</i>	relatively rare clinical problem
<i>disadvantage:</i>	no harmonization of protocols (NL- UK)

www.studies-obsgyn.nl/trust

Inclusions



Promise Trial



Target group:	unexplained RM
Method :	progesterone vs placebo
No of patients:	790
Main Outcome:	Live Birth Rate
Centers recruiting:	UK: 36 NL: 9

international collaboration

<i>advantage:</i>	increase the number of recruited patients
<i>disadvantage:</i>	high workload in non-initiating country

www.medscinet.net/promise

Facilitators for (inter)national collaboration

- A dedicated principal investigator per country
- Investigators who are held in high esteem
- A cancer or drug trial
- Interventions only available inside the trial.
- Clinically important questions
- Results easily applicable to future practice

Campbell 2007

Barriers for (inter)national collaboration

- Variety of definitions
 - guidelines
 - clinical practice
- Overambitious ego's
- The opinion that conclusions of one's own small trial still hold



Future improvements for international collaboration

Study embedded in international networks/ scientific and patient societies

- GoNET
- INREM (internat reprod medicine research networks)
- ESHRE

- coordination of study protocols at an early stage
- one PI per study protocol per country
- Webbased registration of minimum amount of data
- Clear appointments at the start of a trial
 - authorship
 - division of funding/ inclusion fee

Conclusions

- Collaboration is essential to fill in knowledge gaps
- Countries may face comparable problems for research collaboration.
- Country specific problems need to be resolved by national PI
- More adoption in International Research networks is needed

