Logistical management of early pregnancy problems

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The determinants of a successful pregnancy
Dubrovnik September 2010

Universiteit van Amsterdam

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- Background
- Service Organisation
  - Early Pregnancy Units
  - Recurrent Miscarriage Clinics
- Patient Management
- Discussion

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Recommendations

With the appearance of early pregnancy assessment units (EPU), an increasing number of women are being assessed and managed as outpatient attenders.

With an EPU network, a standardized diagnostic classification system is important for accurate and reproducible reporting of ultrasound findings, so that direct comparisons between units can be made (revised nomenclature)

All women with early pregnancy problems should have prompt access to a dedicated EPU that provides efficient management and when necessary adequate counseling and appropriate treatment

www.earlypregnancy.org.uk, www.earlypregnancy.com, Farquharson Hum Reprod 2005, www.rcog.org.uk

Background UK Experience

- Establishment Early Pregnancy Units since 1990 (2007 n = > 250)[1,2]
- most EPU's located at Gynaecology Dept.
- Dedicated accessible care
- Nurse practitioners / Sonographers
- Supervised by Gynaecologists/ Radiologis

Bigrigg 1991, www.earlypregnancy.org.uk

Standards in early pregnancy care

Standard	Core
Patient Information	Designated Reception Area constantly staffed Universal use of clear, understandable terminology
Patient Choice of Management	Education of patient relevant to diagnosis and management Open explanation of expectant, medical and surgical options
Dedicated Quiet Room	Room for breaking bad news away from work area
Availability of Service	5 day opening during office hours
Competence of Scanning	Recognised ultrasound training and RCOG/BMUS preceptor assessment and validation Register of staff competent at scanning

www.earlypregnancy.org.uk; guidelines 2007

Standards in early pregnancy care

Blood HCG level measurement	Laboratory access to blood HCG measurement and same day result
Written information leaflets	Visible open access to written information leaflets in EPU
Acknowledgment of Privacy and Dignity	To provide individualised patient support and acknowledge confidentiality
Bereavement Counselling	All staff trained in emotional aspects of early pregnancy loss To enable access to counselling and provide immediate support
Site of EPU	Geographically separate from all maternity areas

www.earlypregnancy.org.uk; guidelines 2007

Efficiency Service Organisation

EPU

- Reduction hospital admissions[1]
- Decreased workload at night time[1]
- Reduction length of stay[2]
- Savings[3,4]

Remark: EPU's were raised when US equipment was scarce.

RM Clinic

- Less repeat consultations[5]

[1]Sorensen 1999; [2]Brownlea 2005; [3]Bigrigg 1991; [4]Wren 1999; [5]Habayeb 2004

Target groups

Women with (suspicion of):

- Miscarriage — EPU
- Ectopic pregnancy — EPU

- Recurrent Miscarriage — RM clinic

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The Amsterdam experience (AMC)

2005:

- Academic setting
- Many locations
- Many treating physicians
- No uniformal registration

AIM

Establish an EPU with electronic database equipment

Improve quality of care

- collect expertise
- improve accessibility
- dedicated care with improved patient information

Improve efficiency

- ↓ clinical admissions
- ↓ surgical interventions miscarriage
- ↓ repeat consultations recurrent miscarriage
- ↓ no. of parental karyotypes recurrent miscarriage

Additional improvements

Patients

- easy and rapid access
- prevent over/ under care
- waiting time ↓
- interval to start treatment ↓
- informed decisions ↑

Teaching

- care protocol
- ultrasound expertise
- teaching physicians/ midwifes

Logistics

- length of 1st consultation ↓
- repeat consultations ↓
- admissions ↓
- workload non-office hrs ↓

Science

- elektronic registration
- rapid implementation of new evidence
- rapid start new projects
- research nurses

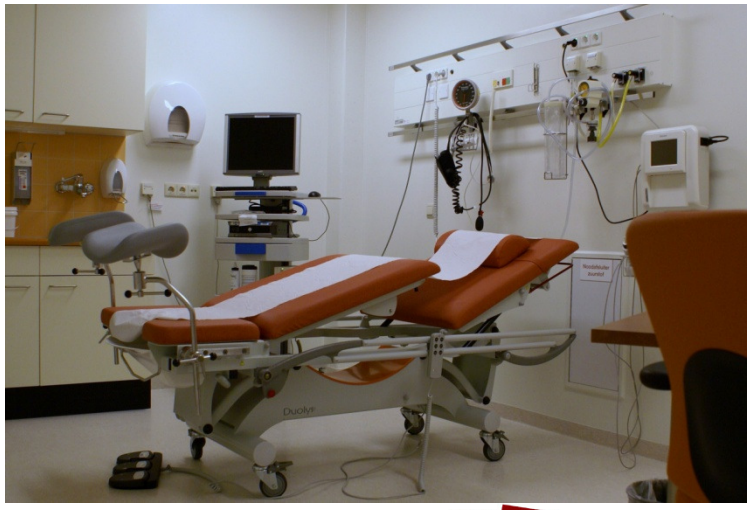
Opening Early Pregnancy Unit may 2008

EPU team

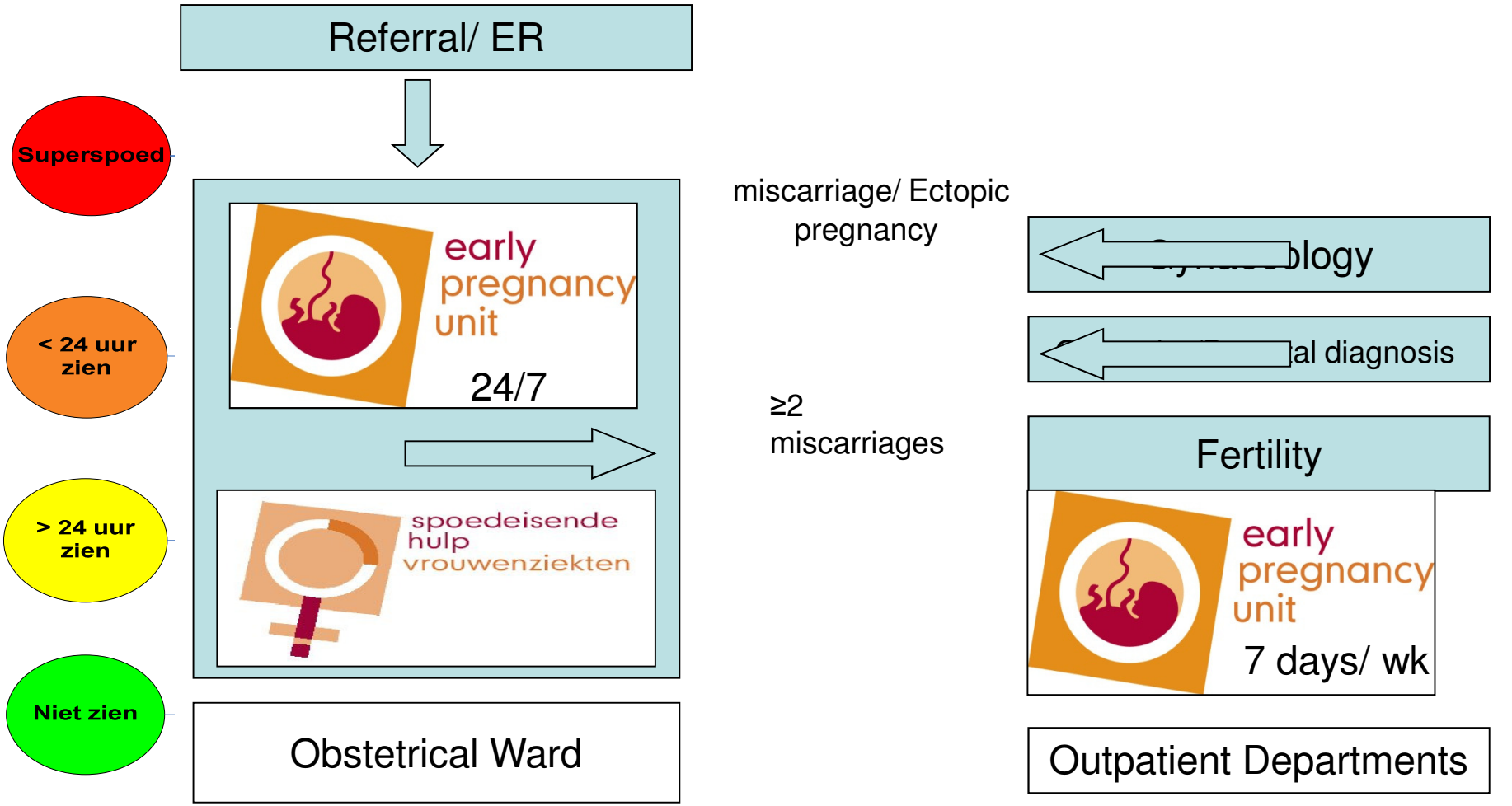
Midwife

Nurse practitioner

Gynaecologist (subspecialization Miscarriage/ EP/ RM)



AMC: since june 2008



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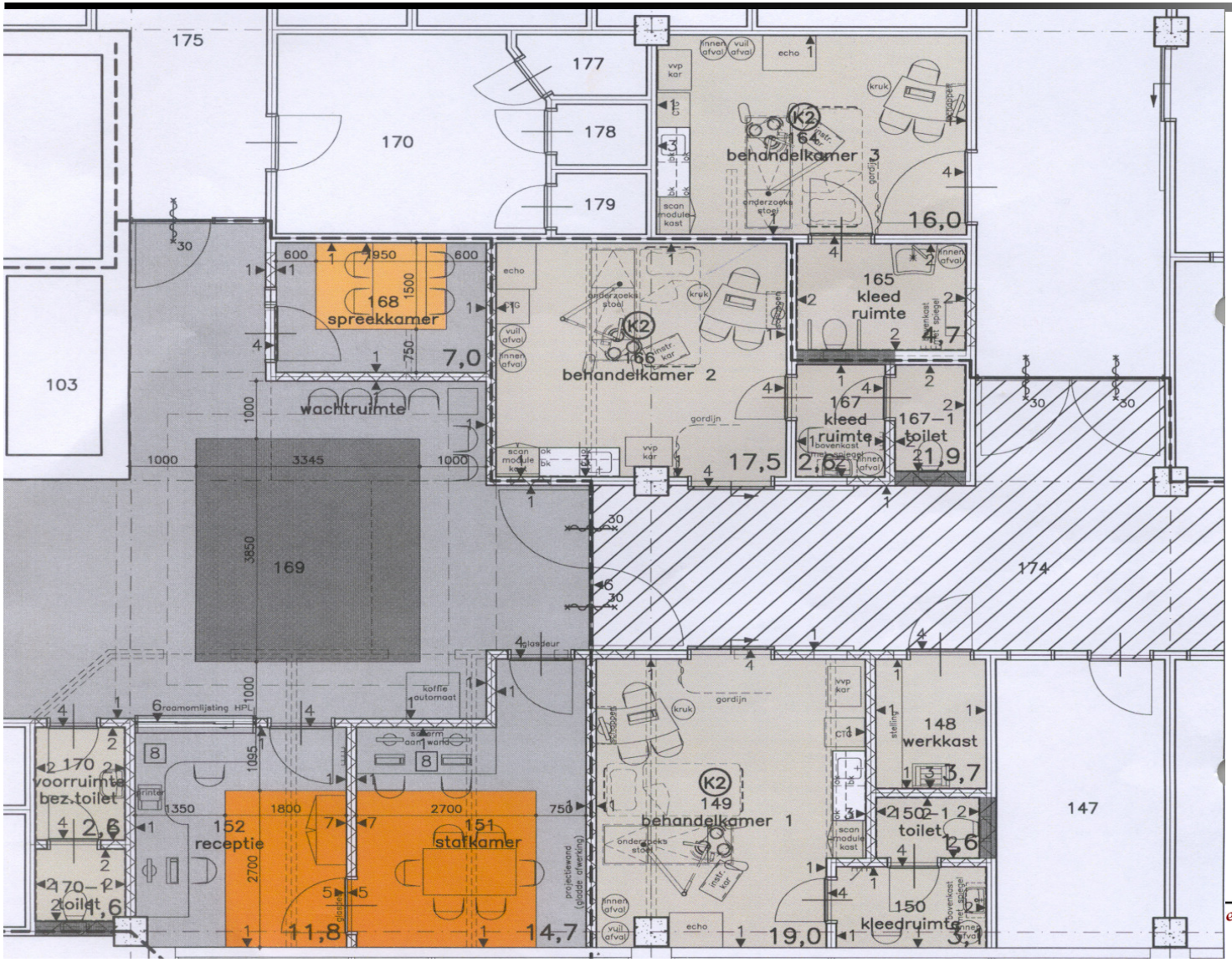
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statkamer
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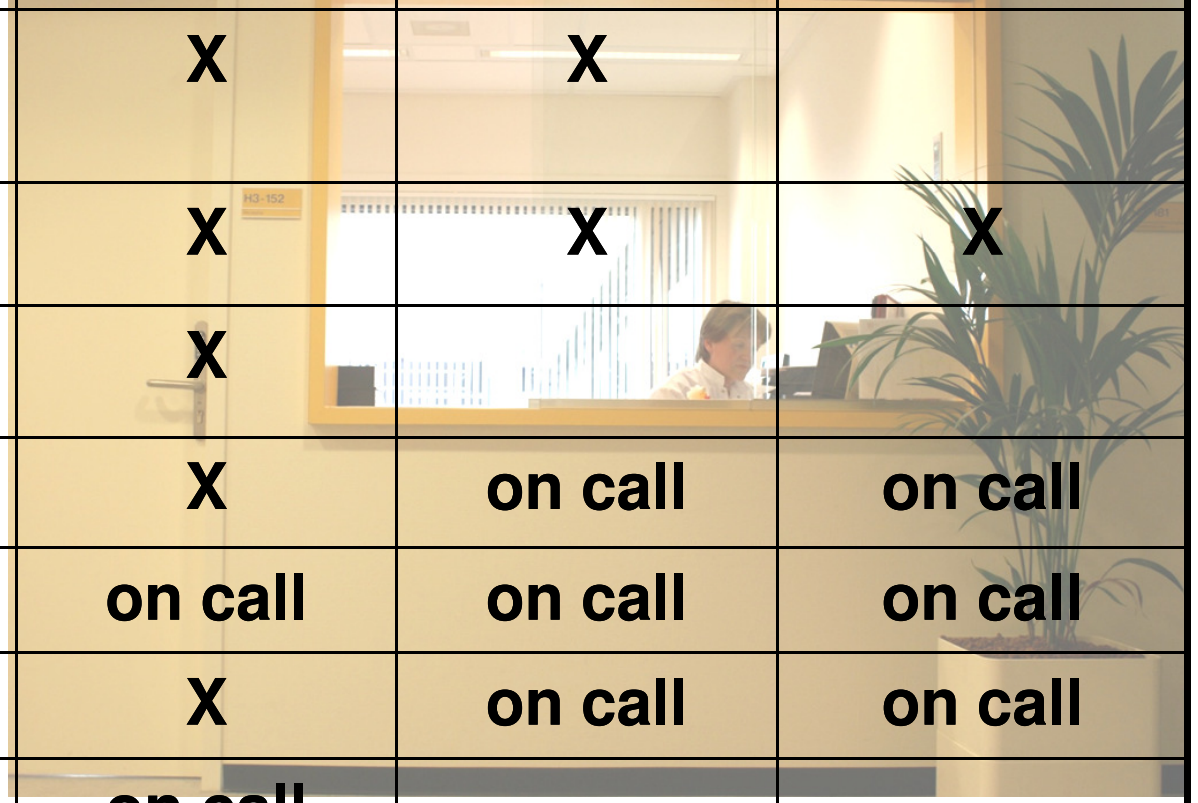
Staff available

	08.00-17.00	17.00-23.00	23.00-08.00
Physician-assistant	**X**	**X**	
Nurse	**X**	**X**	**X**
Research nurse	**X**		
Assistant	**X**	**on call**	**on call**
Midwife	**on call**	**on call**	**on call**
Gynaecologist	**X**	**on call**	**on call**
Social worker	**on call**		



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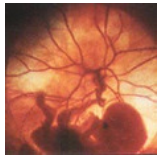
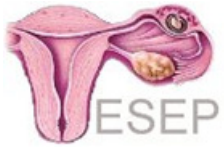
Expertise/ Research

- EP
- Miscarriage
- Recurrent Miscarriage



ALIFE



ALERT

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Evidence Based Protocols

Evidence based Medicine

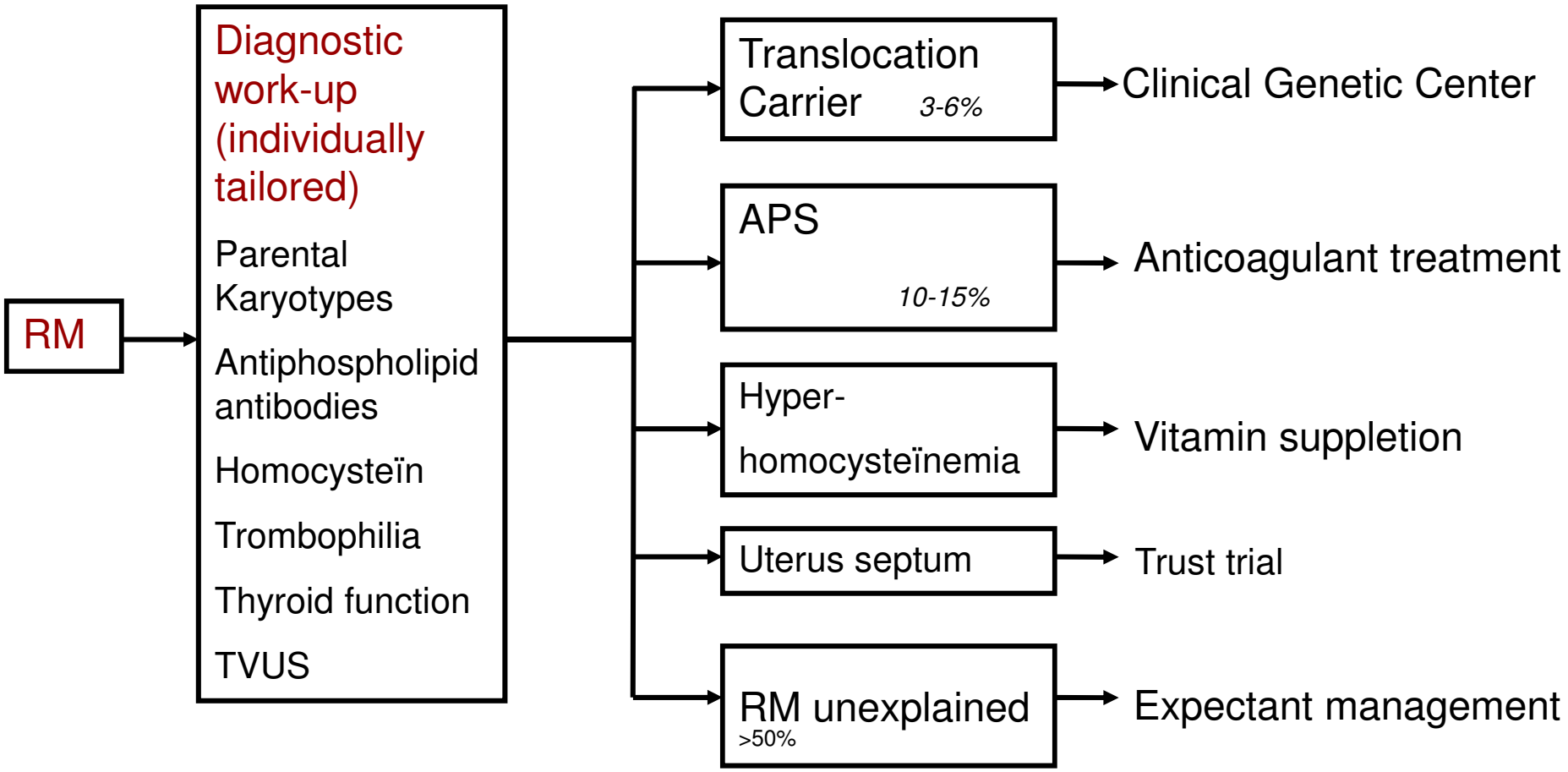
EBM is the integration of best research evidence with clinical expertise and patient values

Sacket 2002

Recurrent Miscarriage Clinic (AMC experience)

- 2005: 5 locations (OPD Obstetrics/ Gyn/ Reprod Med/ PND/ Internal Medicine)
- 2007: 2 locations (OPD Gyn/ Reprod Med)
- 2008: 1 location (Center for Reproductive Medicine)

Work-up Recurrent Miscarriage



All couples: advise on healthy body weight and lifestyle

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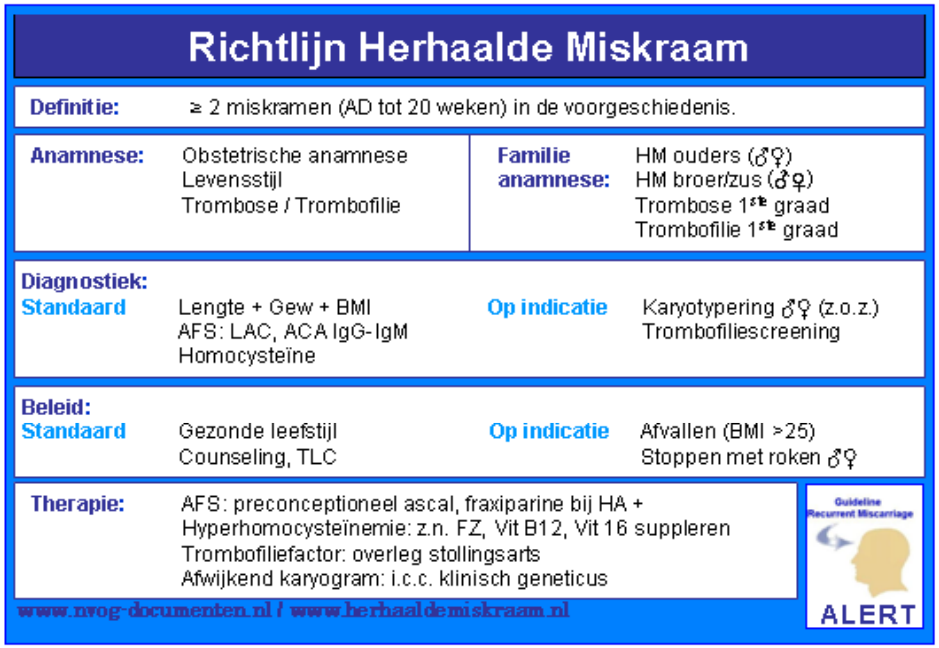
Diagnostic and therapeutic aids



Richtlijn Herhaalde Miskraam

Definitie:	≥ 2 miskramen (AD tot 20 weken) in de voorgeschiedenis.		
Anamnese:	Obstetrische anamnese Levensstijl Trombose / Trombofilie	**Familie anamnese:**	HM ouders (♂♀) HM broer/zus (♂♀) Trombose 1ste graad Trombofilie 1ste graad
Diagnostiek:			
Standaard	Lengte + Gew + BMI AFS: LAC, ACA IgG-IgM Homocysteïne	**Op indicatie**	Karyotypering ♂♀ (z.o.z.) Trombofiliescreening
Beleid:			
Standaard	Gezonde leefstijl Counseling, TLC	**Op indicatie**	Afvallen (BMI >25) Stoppen met roken ♂♀
Therapie:	AFS: preconceptioneel ascal, fraxiparine bij HA + Hyperhomocysteïnemie: z.n. FZ, Vit B12, Vit 16 suppleren Trombofiliefactor: overleg stollingsarts Afwijkend karyogram: i.c.c. klinisch geneticus		

www.nvog-documenten.nl / www.herhaaldemiskraam.nl

Guideline Recurrent Miscarriage

ALERT

Pocket card, RM patient file

Electronic Decision aid

No of obj misc
Maternal age at 2nd misc
Length cm
Weight kg
Smoking (♀)
Passive smoking (♂)
Family History RM
–sibs
-parents
Thrombosis
Family history thrombosis
Family history Thrombophilia

www.freya.nl

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Electronic Decision aid

Advies programma bij herhaalde miskramen.

Relevante vragen	Antwoord	Advies
Rookt uw partner :	Ja	**Stoppen met roken.**
Lengte : Gewicht : BMI :	1.73 95 31.7	**Afvallen**
HM bij ouders van patiënte/partner : HM bij broer/zus van patiënte/partner : Aantal miskramen :	Nee Ja 5	**Risico op gebalanceerde chrom** **Karyotypering patiënte en partn**
Heeft u ooit trombose gehad : Trombose 1ste graads famililid : Trombofilie bij hetzelfde familielid :	Ja Nee Nee	**Trombofiliefactoren bepalen**
Standaard		**Antipfospholipiden antistoffen bepalen** **Homocysteïne bepalen** **Gezonde leefstijl** **Foliumzuur**

Naar uitslagen en beleid

Stop smoking

Loose weight

Risk of carrier status: 7.2%
=> parental karyotyping

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Selective Karyotyping

maternale leeftijd t.t.v. tweede miskraam (jaren)		HM_{ouders} +		HM_{ouders} -	
		≥3 miskr.	2 miskr.	≥3 miskr.	2 miskr.
< 23	HM_{bz} +	**10,2%**	**7,3%**	**7,3%**	**5,2%**
	HM_{bz} -	**5,7%**	**4,0%**	**4,1%**	**2,8%**
23-34	HM_{bz} +	**10,0%**	**7,2%**	**7,2%**	**5,1%**
	HM_{bz} -	**5,7%**	**4,0%**	**4,0%**	**2,8%**
34-37	HM_{bz} +	**5,8%**	**4,1%**	**4,1%**	**2,9%**
	HM_{bz} -	**3,2%**	**2,2%**	**2,2%**	**1,6%**
37-39	HM_{bz} +	**4,0%**	**2,8%**	**2,8%**	**2,0%**
	HM_{bz} -	**2,2%**	**1,5%**	**1,5%**	**1,1%**
≥ 39	HM_{bz} +	**1,8%**	**1,2%**	**1,3%**	**0,9%**
	HM_{bz} -	**1,0%**	**0,7%**	**0,7%**	**0,5%**

Franssen 2005

Refrain from karyotyping at low risk couples

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Consecutive vs non-consecutive

Probability of carrying a structural chromosome abnormality

	Univariable regression analysis		Multivariable regression analysis*	
Covariates	**Odds ratio (95% CI)**	**P-value**	**Odds ratio (95% CI)**	**P-value**
≥2 consecutive miscarriages compared to ≥2 non-consecutive miscarriages	1.4 (0.83-2.39)	0.21	0.90 (0.48-1.7)	0.75
≥3 consecutive miscarriages compared to ≥3 non-consecutive miscarriages	0.99 (0.6-1.6)	0.98	0.71 (0.39-1.3)	0.25

van den Boogaard 2010

Pregnancy outcome RM unexplained

Success rate (≥ 24 weeks)

Number of miscarriages →

Female age ↓

N=222	2	3	4	5
25	89	86	82	79
30	84	80	76	71
35	77	73	68	62
40	69	64	58	52
45	60	54	48	42

Brigham Hum Rep 1999

Overall 75% chance of a successful pregnancy

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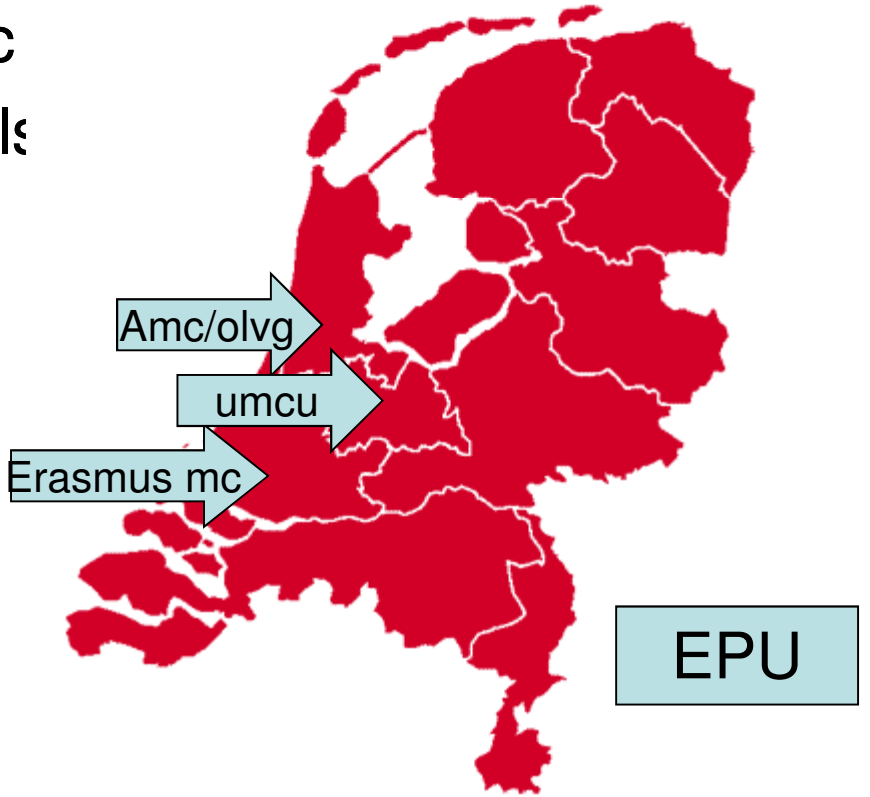
Dutch Early Pregnancy Care

- SIG Early Pregnancy (VEF/NVOG)
- Recurrent miscarriage clinic mainly at academic hospitals
- 3 Early Pregnancy Units in Amsterdam, Utrecht and Rotterdam



Universitair Medisch Centrum Utrecht

amc

Erasmus MC

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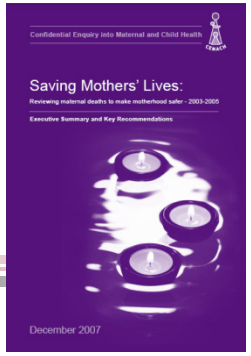
Do we meet (inter) national standards?

Ectopic Pregnancy: MMR



www.cemach.org.uk

Cause of death	1985-87	1988-90	1991-93	1994-96	1997-99	2000-02	2003-05	1985-87	1988-90	1991-93	1994-96	1997-99	2000-02	2003-05
	Numbers							*Rates per 100,000 maternities*						
***Direct* deaths**														
Thrombosis and thromboembolism	32	33	35	48	35	30	**41**	*1.41*	*1.40*	*1.51*	*2.18*	*1.65*	*1.50*	*1.94*
Pre-eclampsia and eclampsia*	27	27	20	20	16	14	**18**	*1.19*	*1.14*	*0.86*	*0.91*	*0.75*	*0.70*	*0.85*
Haemorrhage*	10	22	15	12	7	17	**14**	*0.44*	*0.93*	*0.65*	*0.55*	*0.33*	*0.85*	*0.66*
Amniotic fluid embolism	9	11	10	17	8	5	**17**	*0.40*	*0.47*	*0.43*	*0.77*	*0.38*	*0.25*	*0.80*
Early pregnancy deaths	16	24	17	15	17	15	**14**	*0.71*	*1.02*	*0.73*	*0.68*	*0.80*	*0.75*	*0.66*
Ectopic	11	15	9	12	13	11	**10**	*0.48*	*0.64*	*0.39*	*0.55*	*0.61*	*0.55*	*0.47*
Spontaneous miscarriage	4	6	3	2	2	1	**1**	*0.18*	*0.25*	*0.13*	*0.09*	*0.09*	*0.05*	*0.05*
Legal termination	1	3	5	1	2	3	**2**	*0.04*	*0.13*	*0.22*	*0.05*	*0.09*	*0.15*	*0.09*
Other	0	0	2	0	0	0	**1**	*0.00*	*0.00*	*0.09*	*0.00*	*0.00*	*0.00*	*0.14*
Other causes	15	9	8	0	1	4	**0**	*0.66*	*0.38*	*0.35*	*0.00*	*0.05*	*0.20*	*0.00*
Anaesthetic	6	4	8	1	3	6	**6**	*0.26*	*0.17*	*0.35*	*0.05*	*0.14*	*0.30*	*0.28*
All *Direct*	**139**	**145**	**128**	**134**	**106**	**106**	**132**	***6.13***	***6.14***	***5.53***	***6.10***	***4.99***	***5.31***	***6.24***

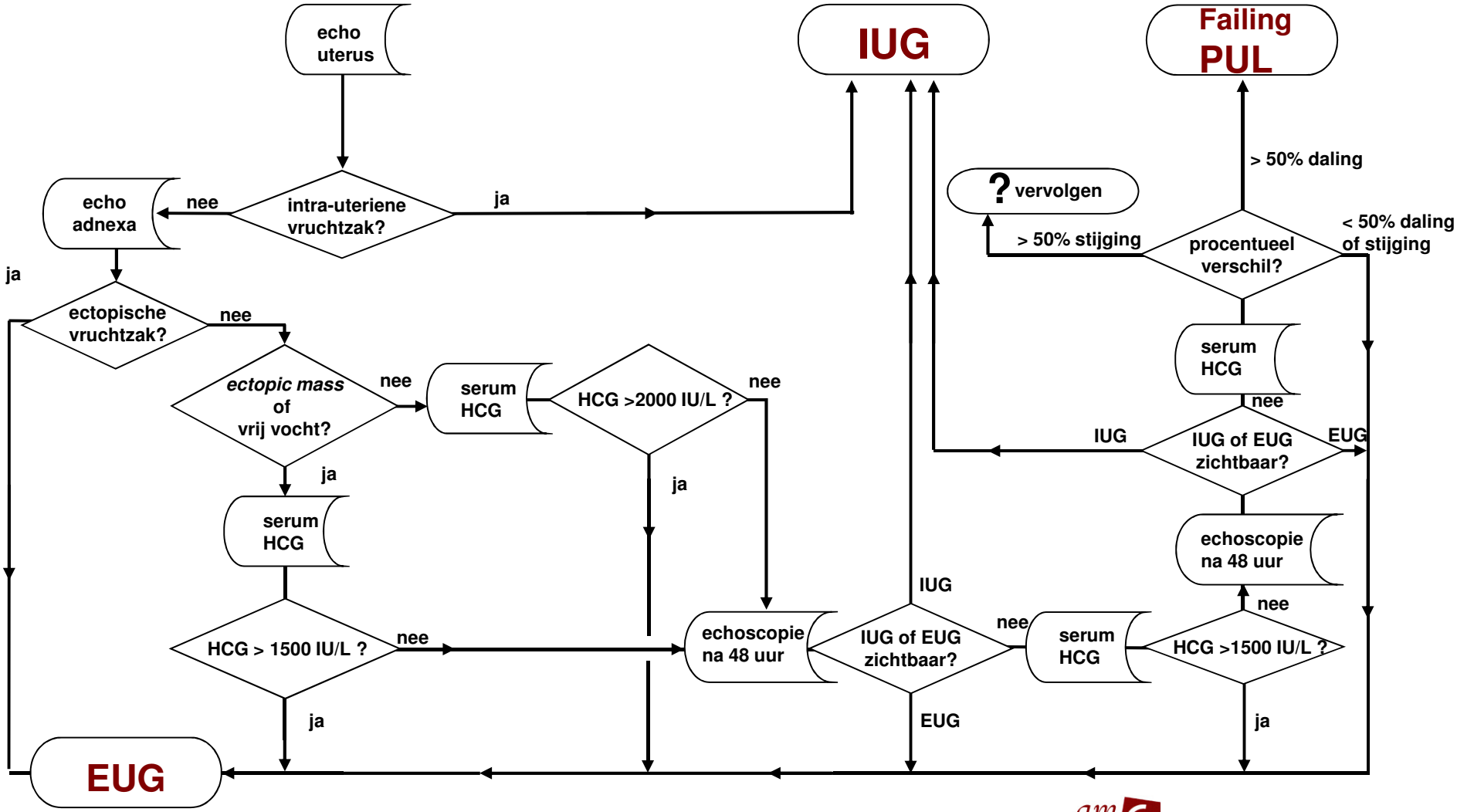
"Guidelines are urgently required for the management of pain and bleeding in early pregnancy"

Ectopic Pregnancy: MMR

	1983-1992		1993-2005		OR (95% CI)
Live births	1,860,807		2,557,208		
	n	MMR	n	MMR	
Total	144	7.3	236	8.8	1.2 (0.99-1.5)
(Pre-)eclampsia	51	2.7	93	3.5	1.3 (0.9-1.9)
EP	**4 (2.8%)**	**0.2**	**5 (2.1%)**	**0.2**	**0.9 (0.3-3.1)**

Schutte *et al*. BJOG 2009

Patient Management: diagnostic algoritm EP



Ankum *et al.* Hum Reprod 1993, BW Mol *et al.* Fertil Steril 1998

Adherence to EP G

numerator / denominator = … %

Process indicators

1. hCG urinary test	n.a.
2. TVUS	98
3. serum hCG measurement	88
4. Surgery if diagnosis 'EP'	75
5. Follow-up if 'EP' suspected (follow up after 48 hrs)	35
6. post-operative serum hCG follow up	78
7. anti-D immunoglobulin	50

Structural indicators

8. 24/7 serum hCG laboratory service	67
9. Surgery office hrs/ vs non office hrs	45

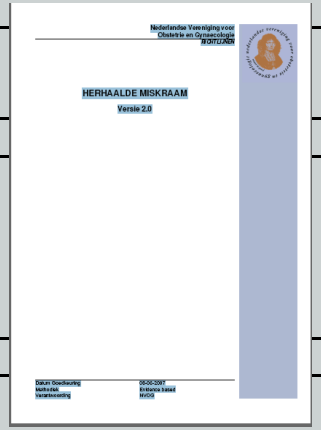
Outcome indicators

10. Successful laparoscopy	89
11. Successful salpingotomy with contralateral tubal pathology	20
12. MTX for persisting trophoblast	90

Low adherence in 1/3 of indicators

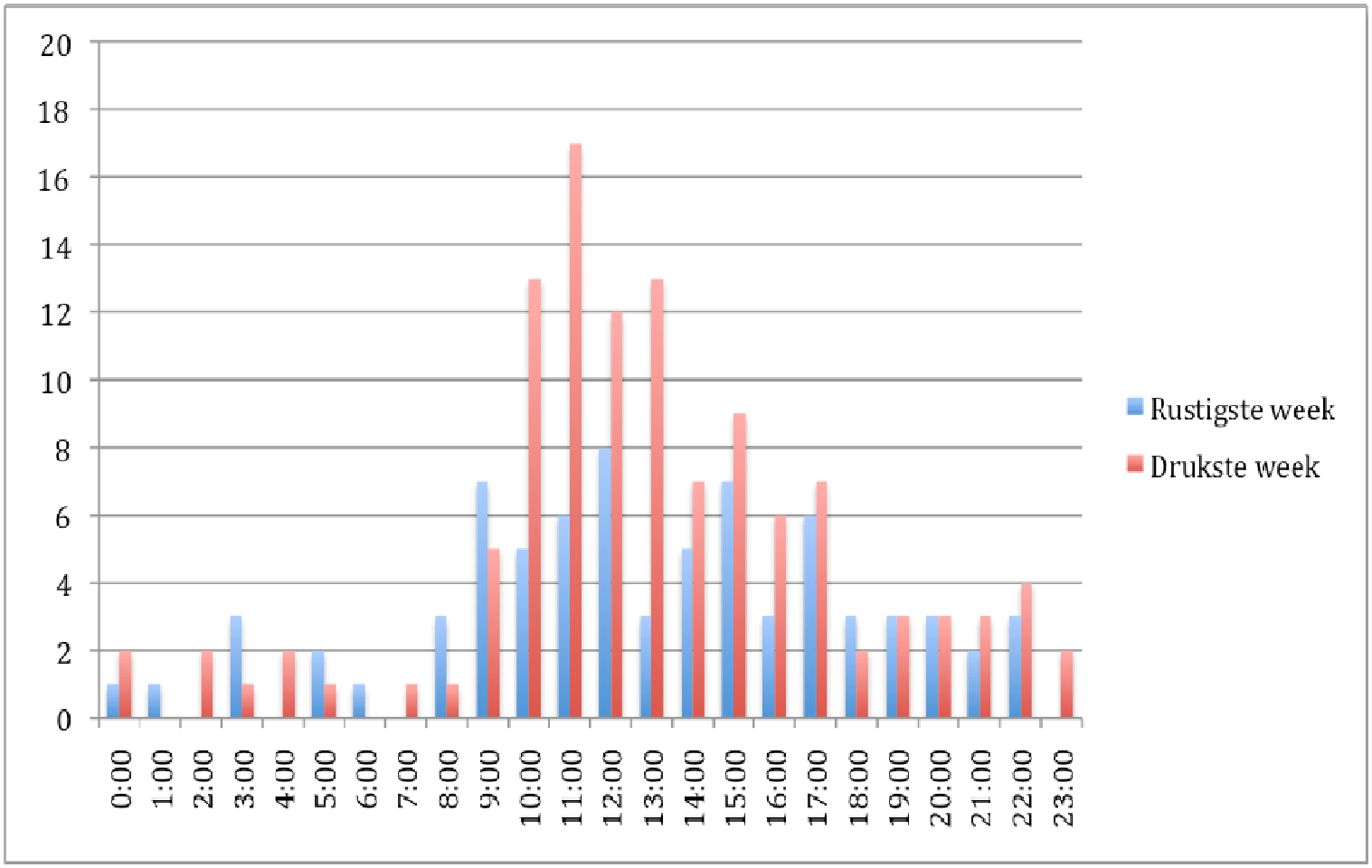
F Mol *et al*. Submitted

KEY RECOMMENDATIONS ELIGIBLE FOR INDICATOR TRANSCRIPTION		Level of evidence
1	Report the number of objectified miscarriages	D
Chromosome abnormalities		
2	Record maternal age at the time of the 2nd miscarriage	B
3	Ask for family history with regard to recurrent miscarriage in parents and brothers/sisters of both partners	B
4	Perform karyotyping selectively	B
5	Refer all couples which were found to be carrier of a balanced structural chromosome abnormality to a clinical geneticist	D
6	Inform all couples which were found to be carrier of a balanced structural chromosome abnormality about their relative high chances of getting a health child in their next pregnancy	B
Anti-phospholipid syndrome		
7	Offer anti-phospholipid antibody screening in all patients (LAC, ACA IgG IgM)	B
8	Start anticoagulant treatment in patients diagnosed with anti-phospholipid syndrome, according to the modified schedule of Rai	B
Trombophilia		
9	Report on history of thrombo-embolisms in all women	B
10	Report on family history of Thrombophilia and thrombo-embolisms	B
11	Perform screening for thrombophilia only in high risk patients	B
Homocystein		
12	Determine random homocystein in all patients	B
13	Supplement vitamins of low vitamin levels are found in hyperhomocysteinemia	C
Lifestyle		
14	Ask for lifestyle, including smoking habits of both patient and partner	B
15	Quit smoking for both patient and partner (in case of smoking)	B
16	Determine length and weight and calculate Body Mass Index (BMI)	B
17	Advise to loose weight,(in case of overweight)	B
General		
18	Prescribe new treatments *only* in the setting of a Randomised Clinical Trial	D
19	Withhold immunotherapy	A
20	Withhold therapy with aspirin in unexplained RM	B
21	Advise preconceptional folic acid (0,4-0,5 mg) to all patients	A
22	Offer Tender Loving Care in unexplained RM	C
23	Determine and discuss individual chances for success in the next pregnancy	B



van den Boogaard RBMonline 2010

Patients /hr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Implementation of evidence

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.

maternale leeftijd t.t.v. tweede miskraam (jaren)		HM_{ouders} +		HM_{ouders} -	
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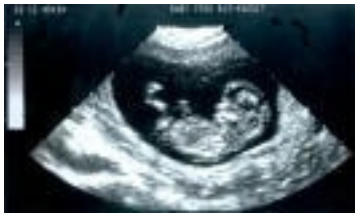
Future improvements

- Electronic registration
- Capacity of Surgery
- Collaboration with other early pregnancy units
- Recruiting for scientific studies
- Adherence to guidelines

Conclusions

- Collaboration of Obstetric, Gynaecology, and Reprod Medicine Departments of utmost importance
- Apply evidence-based care where possible
- In case of absence of evidence, recruit for RCT's
- The real cost-effectiveness of EPU's has yet to be established
- An improvement in quality of care to be expected.



Discussion

- Target group
  - hyperemesis gravidarum
  - Trofoblast diseases
- Who supervises the EPU?
- Interaction peripheral / academic care
  - *Uncomplicated / Complicated cases*
- Open 24/7 vs office hours
- Quality Indicators: measurement of quality of care

Acknowledgments

EPU

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Manja Bunschoten
Marielle Durbridge
Marga van Heemskerk
Fleur de Jager

Alert study group

Emmy van den Boogaard
Rosella Hermens
Jan Kremer
Fulco van der Veen
Nico Leschot

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