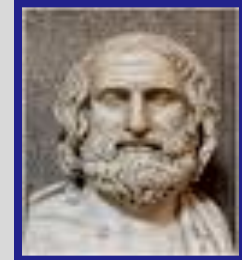


Der Wert des Diaglogs

Hippokrates (Ἱπποκράτης ὁ Κῷος) * 460 BC, † 370 BC)
„Wissenschaftler“ - primum non nocere



Sextus Empiricus (Σέξτος Ἐμπειρικός), 2nd cent.AC
„Empiriker“



David Sackett * 1934, † 2015
Begründer der evidenzbasierten Medizin
“evidence combined with good medical practice”



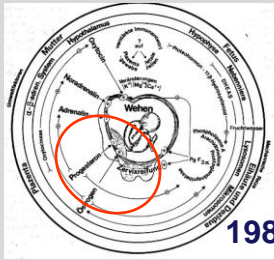
Emile Papiernik * 1936, † 2009
Primäre/ **Sekundäre**/ Tertiäre Prävention



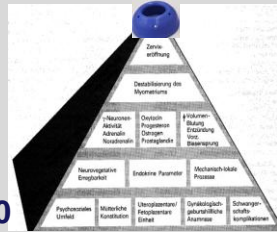
Roberto Romero
Definition Preterm Birth Syndrome



Frühgeburt: Ein Syndrom, viele Ursachen



1980



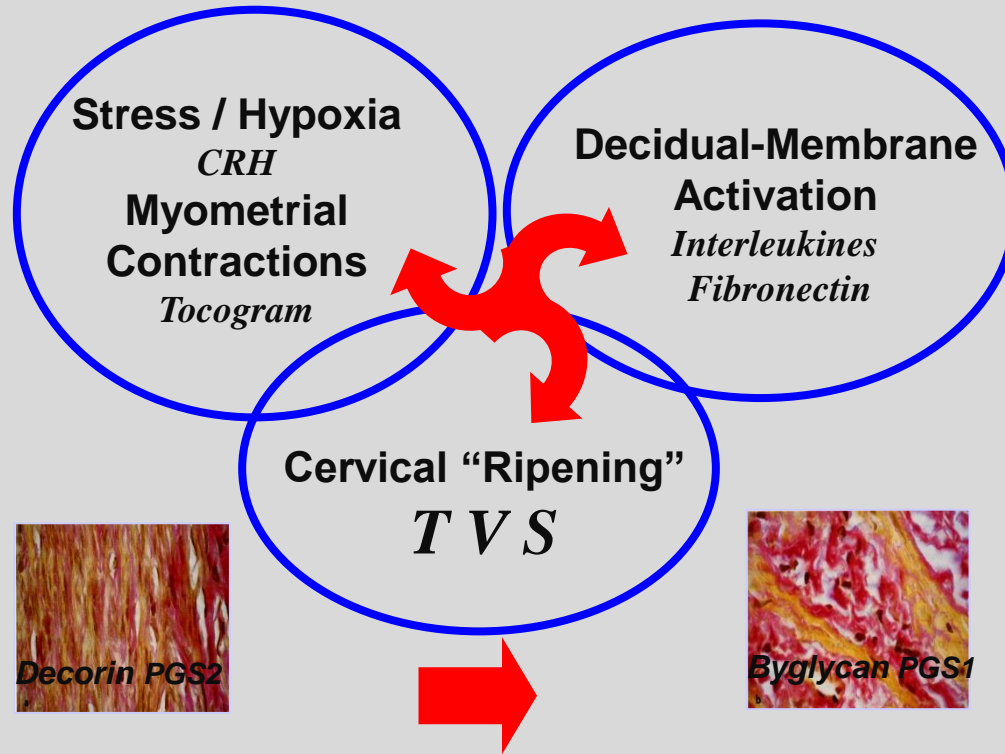
Praxis der Perinatalmedizin

Herausgegeben von Joachim Wolfram Dudenhausen

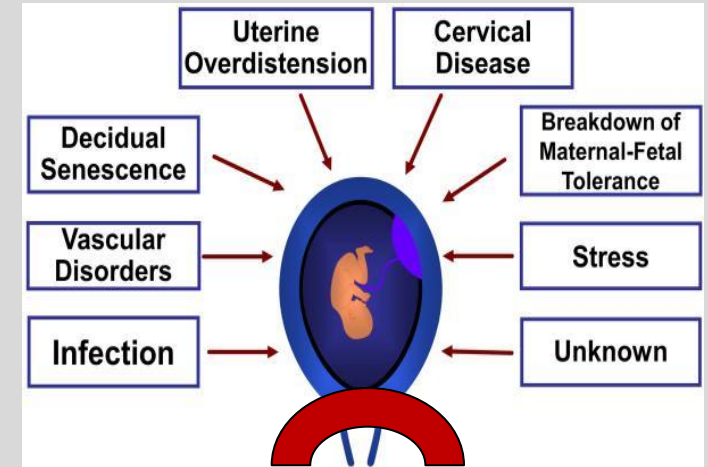


Romero et al. *Ann N Y Acad Sci* 1994; 734: 414-29

Romero et al. *Science* 2014; 345; 6198: 761



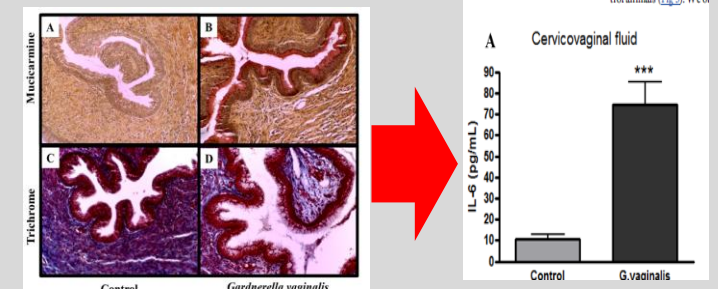
Proteoaminoglykane: Kollagenmetabolismus*



Fehlt: Der cervicovaginale Raum
Microbiom, Metabolom
Immunsystem, Biomechanik

Sierra et al. *PLoS ONE* 13e0191524. 2018

Therapie BV keine Wirkung PTB



*Schwahn et al. *AJOG* 1966; 94: 391-404 Uldbjerg et al. *AJOG* 1982;147: 662-6



FG Raten in Europa 4-12%

PRIMÄRE PRÄVENTION „Allostatic Load“

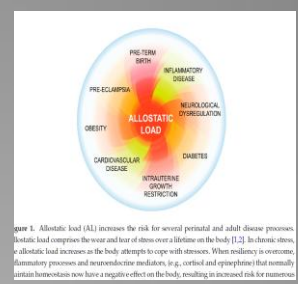


Figure 1. Allostatic load (AL) increases the risk for several perinatal and adult disease processes. Allostatic load comprises the wear and tear of stress over a lifetime on the body [1,2]. In these stressors, allostatic load increases as the body attempts to cope with stresses. When resiliency is overcome, inflammatory processes and neuroendocrine mediators, (e.g., cortisol and epinephrine) that normally maintain homeostasis now have a negative effect on the body, resulting in increased risk for numerous

Díez-Izquierdo et al. *Env. Res.* 2018; 160: 547-53

Transmission von Stress über Generationen

Physiologische Folgen „neuroendokriner Reaktionen auf chronischen Stress“ (McEwen and Stellar, 1993).

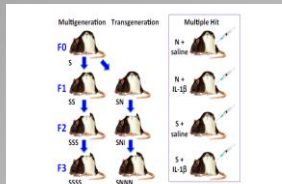


Figure 2. Allostatic load models in pregnant Long-Evans rats. We developed two longitudinal models: a multigenerational (left) and a transgenerational model (center), and a single generation full-F1 multiple hit model (right) that result in perinatal loss plus other adverse pregnancy outcomes. In the multigenerational model, pregnant dams in each generation are subjected to restraint and swim stressors (S) or gestational day (GD) 12-14. The transgenerational model differs in that only pregnant dams from the F0 generation are stressed; their daughters and granddaughters are not stressed (N).

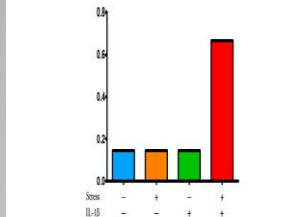
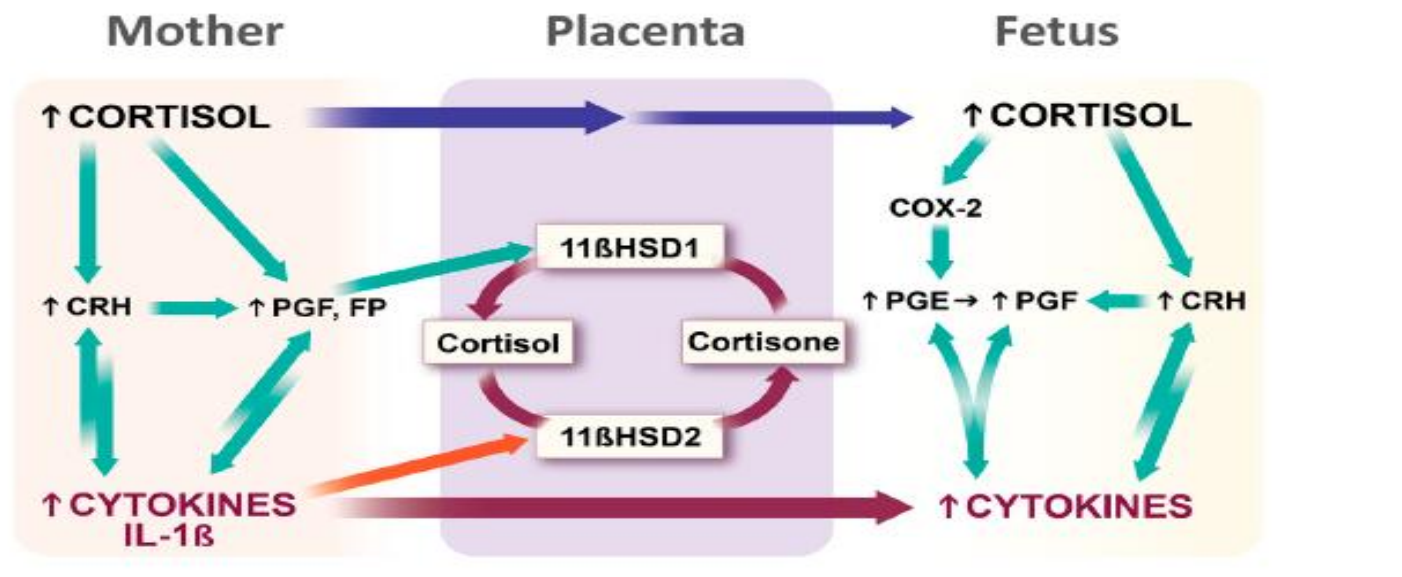
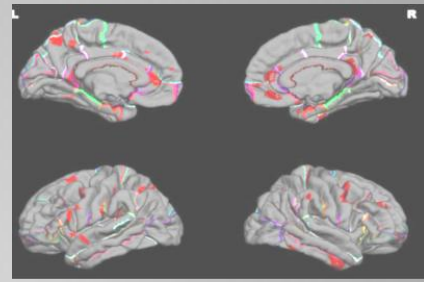


Figure 3. Adverse pregnancy outcomes in rats: frequency distribution. Two-hit hypothesis. Administration of stress (water swimming and restraint from gestational day (GD) 12-14) plus interleukin (IL-1β) (5 µg/kg, IP, GD 17-delivery; see Figure 2) to pregnant Long-Evans rats caused more pregnant dams to deliver early (most common outcome), deliver late or have other adverse pregnancy outcomes (delivery of fetuses with low birth weight, stillbirths, etc.).



Cortisol, Epinephrine, Reaktionen auf inflammatorische Prozesse HOMEOSTASE (?)

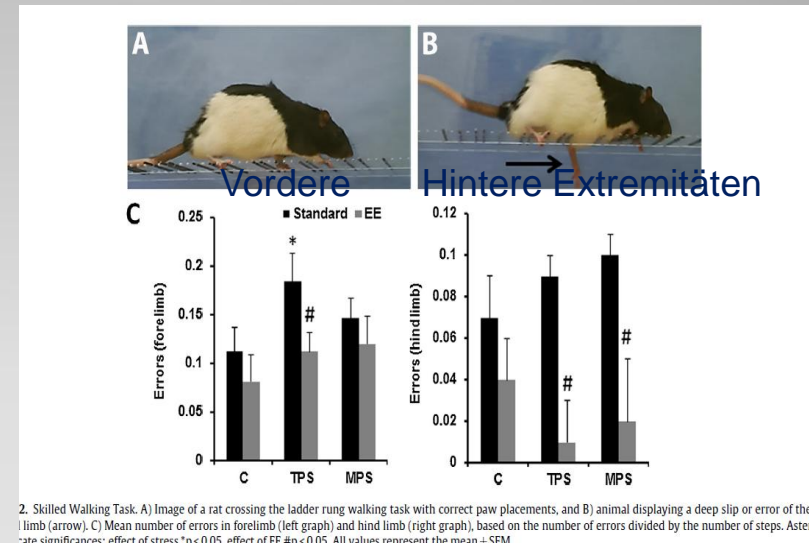
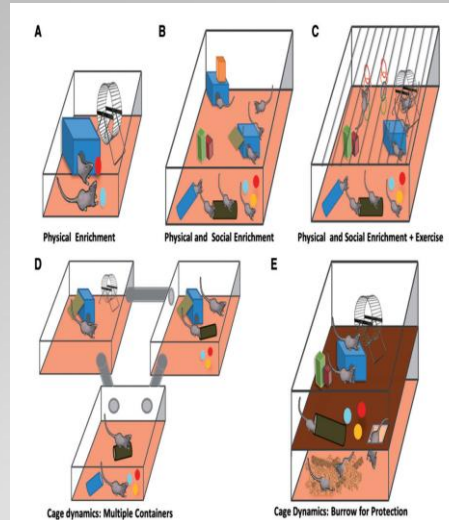
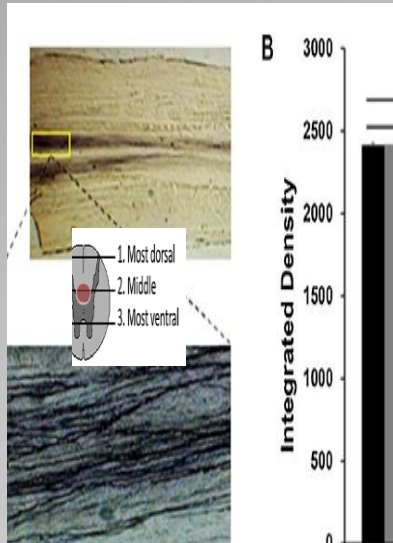


Cytokine: blockieren 11β-HSD2 / Cortisol – Cortison (inaktiv) **11βHSD2 schützt Fet vor Cortisol-Effekt**

„Two-hit hypothesis“: Anamnese mit induziertem Stress kombiniert mit Injektion von IL-18 verursacht Frühgeburten bis in 3. Generation. *Olson et al. Int. J. Mol. Sci.* 2015, 16, 29856–74

“Environmental Enrichment” wirkt Stress entgegen

Erhöhter Stress (über Generationen) führt zu verminderter axonaler Dichte im ZNS, GC-Rezeptoren, ängstlichem Verhalten, gestörter Koordination



C= Kein Stress, TPS= Stress von Eltern MPS= Stress über mehrer Generationen

EE vermindert die neuro-morphologischen Folgen von Stress/Familienanamnese.

Dies ist auch messbar (Stress Marker/miR-182 expression + brain-derived neurotrophic factor (BDNF)/ Neurotrophin-3 (NT-3) Regulation.

Mc Creary et al. Neuroscience Letters 2016; 632: 181–186

SEKUNDÄRE PRÄVENTION



- SUCHE

MM-Verschluss (n=7)

Pessar (147) vs. Vag. Progesteron (> 500)

Erste Langzeit-Untersuchung nach Pessar (3/4 J)

Mortalität: 5% vs 26%, aOR 0.14; [95% CI 0.04 to 0.50]

Bayley-III nach 2 J für 173/ 241 (72%) Überlebende



Tod oder schwere Behinderung 10% vs 29% P vs. C aOR 0.26 [95% CI 0.09 - 0.75]

Erster RCTs /TVS Vergleich Pessar- v.Progesteron (400 mg, n=300)

Dangh et al. AJOG 2018 suppl. 1 abstract 803 (late breaking news SMFM)

Women with a CL < 28 mm (TOP)

Outcome	Arabin Pessary	vag.Progesterone	RR (95%CI)
Delivery < 34 weeks	10/49 20.4%	16/34 44.0%	0.46 (0.24-0.89)
Delivery < 37 weeks	23/49 46.9%	26/36 72.2%	0.65 (0.45-0.93)
BW<2500 g	50/98 51.0%	51/72 70.8%	0.72 (0.23-0.82)
Admission NICU	14/90 15.6%	28/63 44.4%	0.35 (0.11-0.49)
RDS	12/90 13.3%	21/63 33.3%	0.40 (0.14-0.69)
Neonatal sepsis	6/90 6.7%	33/285 23.8%	0.28 (0.08-0.63)

Erster RCTs /TVS Vergleich Pessar- v.Progesteron (200 mg, n=300)

Cruz-Melguizo et al. Obstet Gynecol 2018; Epub ahead of print 7-9

Women with a CL < 25 mm,


Outcome	Arabin Pessary	vag.Progesterone	RR (95%CI)
Delivery < 34 weeks	18/127 14%	17/119 14.0%	-0.11% (-8.8.8.5%)

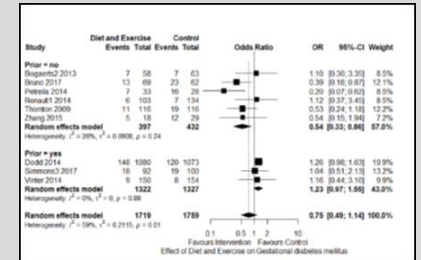
A cervical pessary was not inferior to vag. PG for preventing SPTB before 34 weeks



Die Zukunft evidenzbasierter Medizin

Prospektive Meta-Analysen

 Avoidable waste in the production and reporting of research evidence



PROMPT: PROspective Meta-Analysis for Pessary Trials

Feb/ 2016 under guidance George Saade / office Washington DC

CROWN : Core Outcomes in Women's Health



<<http://www.promptmaternity.org/prompt-symposium/>>

13 Core outcomes

Definierte cut-off values

Verschiedene Vergleiche

Collaboration Guidelines

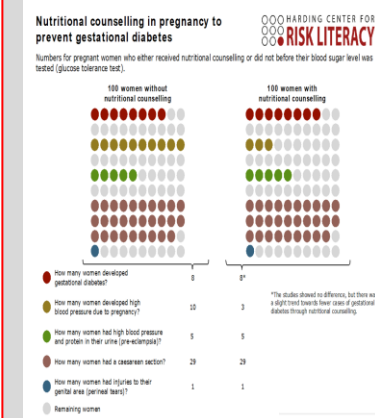
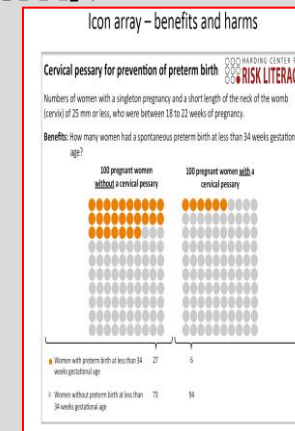
Ethik / Data Safety / Monitoring Committees / Autorenschaft

Kommunikation / Timeline, meeting schedules

Original Research

A Core Outcome Set for Evaluation of Interventions to Prevent Preterm Birth

Jannika van 't Hofst, MD, James M. N. Duffy, MD, Mandy Daly, MSc, Paula R. Williamson, PhD, Shireen Meher, MD, Elizabeth Thum, PhD, George R. Saade, MD, PhD, Zarko Alfirevic, MD, PhD, Ben Willem J. Mol, MD, PhD, and Khalid S. Khan, MD, PhD, on behalf of the Global Obstetrics Network (GONet)



The best answers to clinical problems will come from international collaboration.

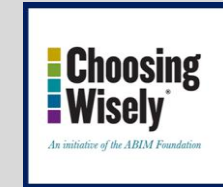
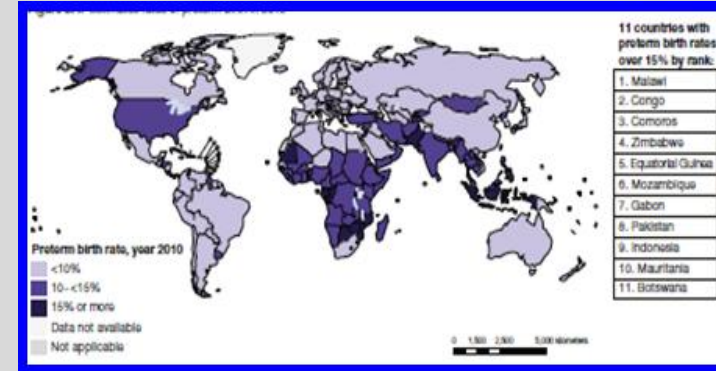
Globales Denken und Langzeitfolgen

O'Donnell and Meaney . *Fetal Origins of Mental Health. Am J Psych* 2017;174:319-28.

Black et al. *Early childhood development : science through the life course. Lancet.* 2017;389:77-90.



Land	N: Geburten < 37 SSW	Ranking	Rate FG	Ranking	Tote	Ranking
China	172 300	2	7,1	154	57 200	4
Deutschland	64 200	43	9.2	106	800	84
Indien	3 519 100	1	13.0	36	303 600	1



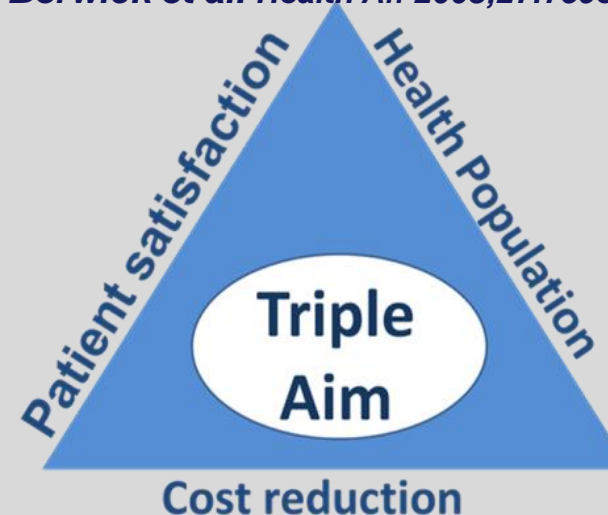
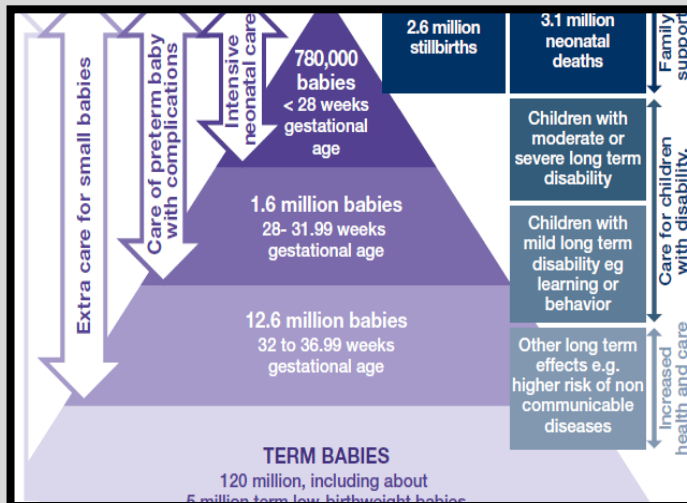
Statistik Frühgeburt: 1/10- 40% Mort.< 5 J

Blencowe et al. *Lancet*, 2012. 379: 2162-72

Berwick et al. *Health Aff* 2008;27:759e69

Bergman K et al.

J Am Acad Child Adol Psych. 2007;46:1454-63.



**Frühgeburten bedingen 2%,
maternalen Stress 17% Varianz
bei kognitiven Fähigkeiten !**
Die Folgen kommen erst bei
Exposition mit anderen
Belastungen zum Vorschein.



Rückblick und Ausblick



Deutsche Professoren sind eine schwer zu befriedigende Menschenklasse mit durchkreuzenden Interessen, Neid, Lust zu regieren und einseitigen Ansichten, wo jeder meint, dass nur er allein Förderung und Unterstützung verdiene.

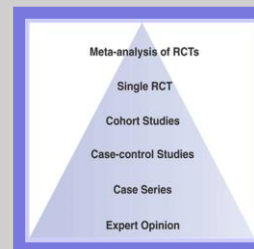
Wilhelm von Humboldt, 1809.



Zuerst die Beobachtungen, dann der Versuch, das Denken ohne Autorität, die Prüfung ohne Vorurteil. Mediziner kann nur der genannt werden, der als letzten Zweck seines Strebens das Heilen betrachtet.
Rudolf Virchow , 1821-1902

Die gefährlichste Weltanschauung ist die Weltanschauung derer, die die Welt nie angeschaut haben.

Alexander von Humboldt, 1811



I hatte einen Traum und träume noch ...

*Ich lebe mein Leben in wachsenden Ringen, die sich über die Dinge zieh'n.
Ich werde den letzten vielleicht nicht vollbringen, aber versuchen will ich ihn (Rilke).*



*Ikone 13.Jht,
Tretjakow Gallery*

*Gorki Theater Berlin
12-11-2017*

Irresponsible and responsible resource
management in obstetrics

Birgit Arabin, MD, PhD ^{a, b, *}

Best Practice & Research Clinical Obstetrics and Gynaecology xxx (2017) 1–20

Pregnancy: An underutilized window of
opportunity to improve long-term
maternal and infant health - An appeal
for continuous family care and
interdisciplinary communication-

Birgit Arabin^{1, 2*}, Ahmet A. Baschat^{3, 2}

Frühgeborene

*Charles Darwin
Albert Einstein
Johann W.
V.Goethe
Thomas Hardy
Thomas Hobbes
Victor Hugo
John Keats
D H Lawrence
Isaac Newton
Anna Pavlova
Pablo Picasso
Renoir
Franklin
Roosevelt
Jacques
Rousseau
Carol Thatcher
Mark Twain
Voltaire
Stevie Wonder*

85% von Publikation "wasted" (Lancet series).

Anerkennung geht zu denen, die den Status quo bewahren, nicht verbessern.

"Whether one day we speak with one voice, time will tell" ...

Arabin and Alfirevic UOG 2013

Fragen? bine.clara.angela@gmail.com