EBM...

JAN BLÁHA

KLINIKA ANESTEZIOLOGIE, RESUSCITACE
A INTENZIVNÍ MEDICÍNY

1. LÉKAŘSKÁ FAKULTA
Univerzita Karlova

VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

jan.blaha@vfn.cz

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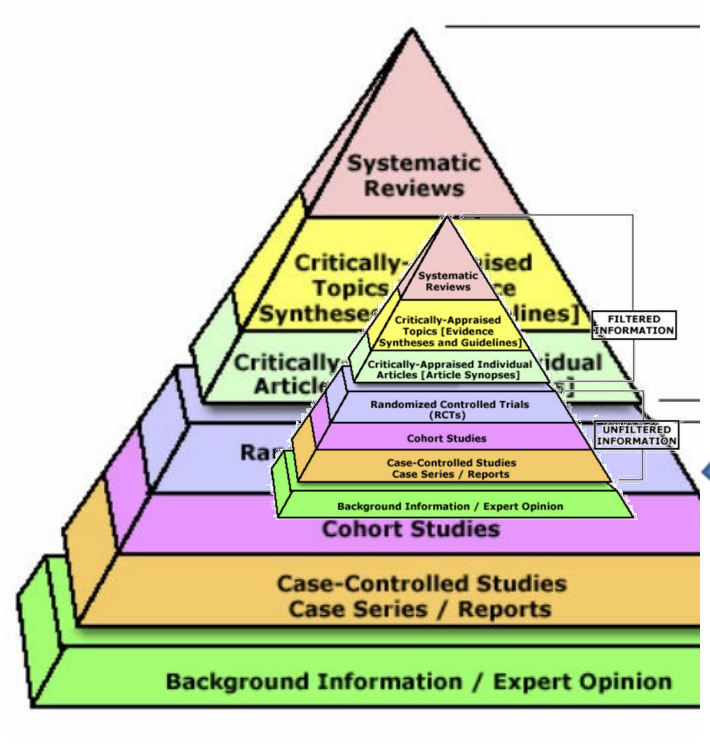
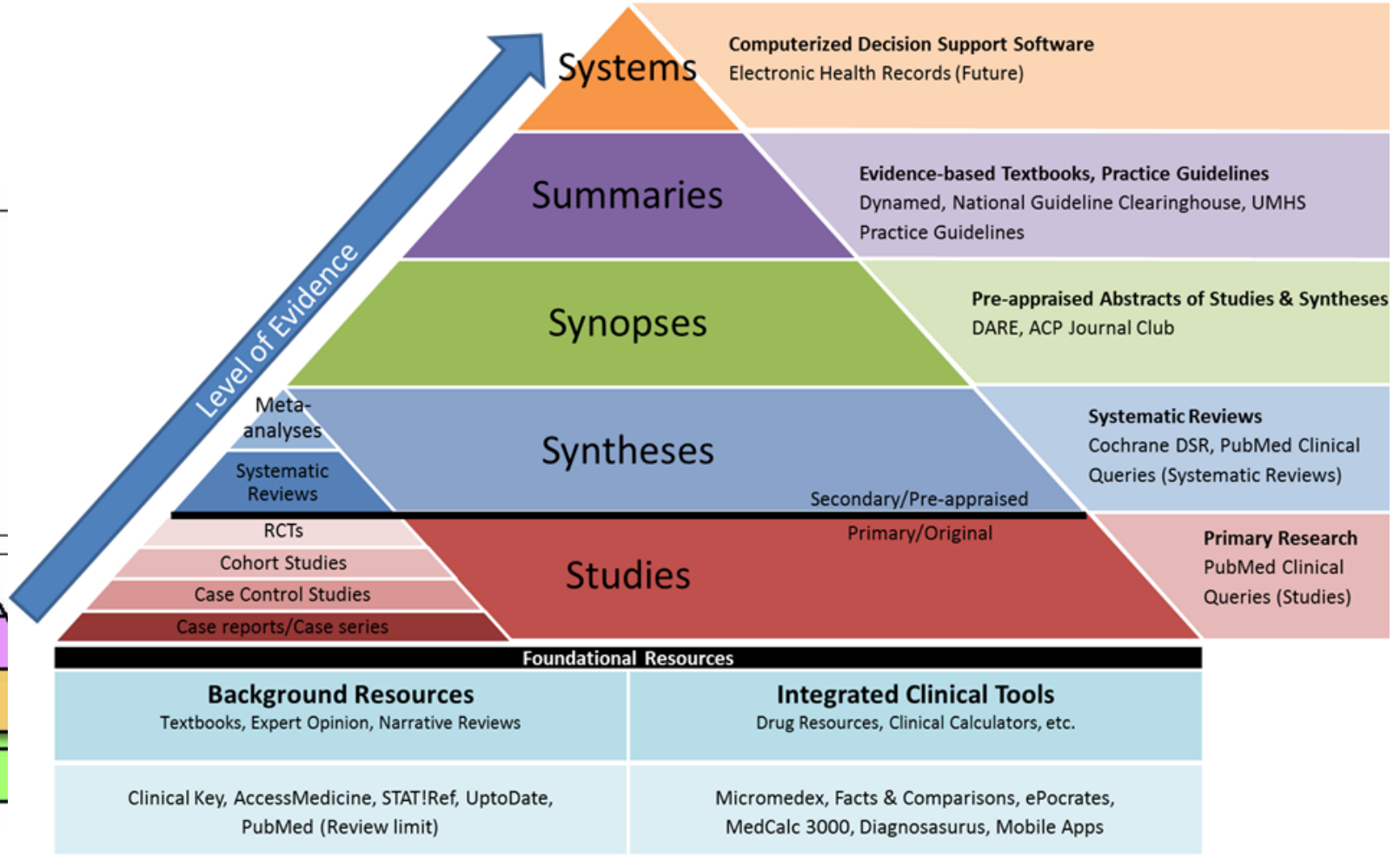
Evidence-based medicine

Evidence-based medicine (EBM, medicína založená na důkazech) je „*vědomé, zřetelné a soudné používání nejlepších současných důkazů při rozhodování o péči o jednotlivé pacienty*“.[1]





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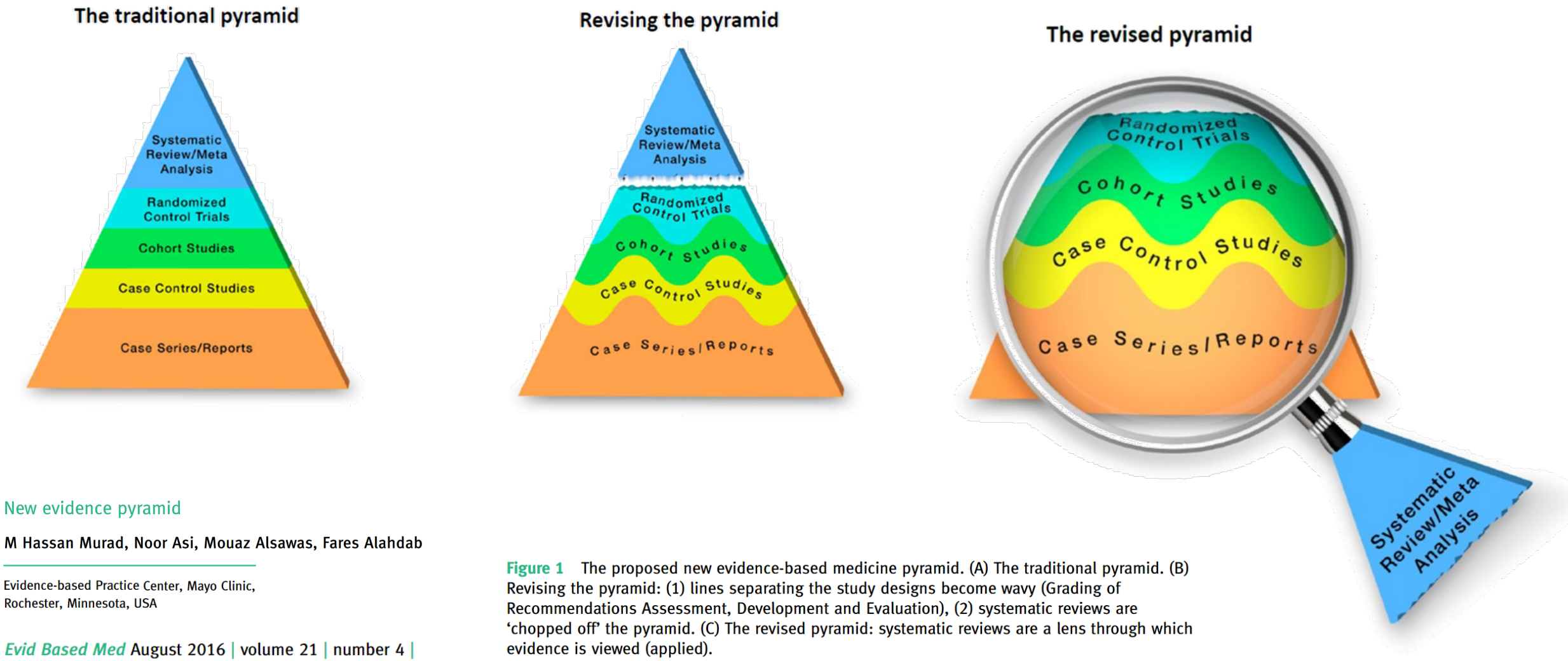


Figure 1 The proposed new evidence-based medicine pyramid. (A) The traditional pyramid. (B) Revising the pyramid: (1) lines separating the study designs become wavy (Grading of Recommendations Assessment, Development and Evaluation), (2) systematic reviews are 'chopped off' the pyramid. (C) The revised pyramid: systematic reviews are a lens through which evidence is viewed (applied).

New evidence pyramid

M Hassan Murad, Noor Asi, Mouaz Alsawas, Fares Alahdab

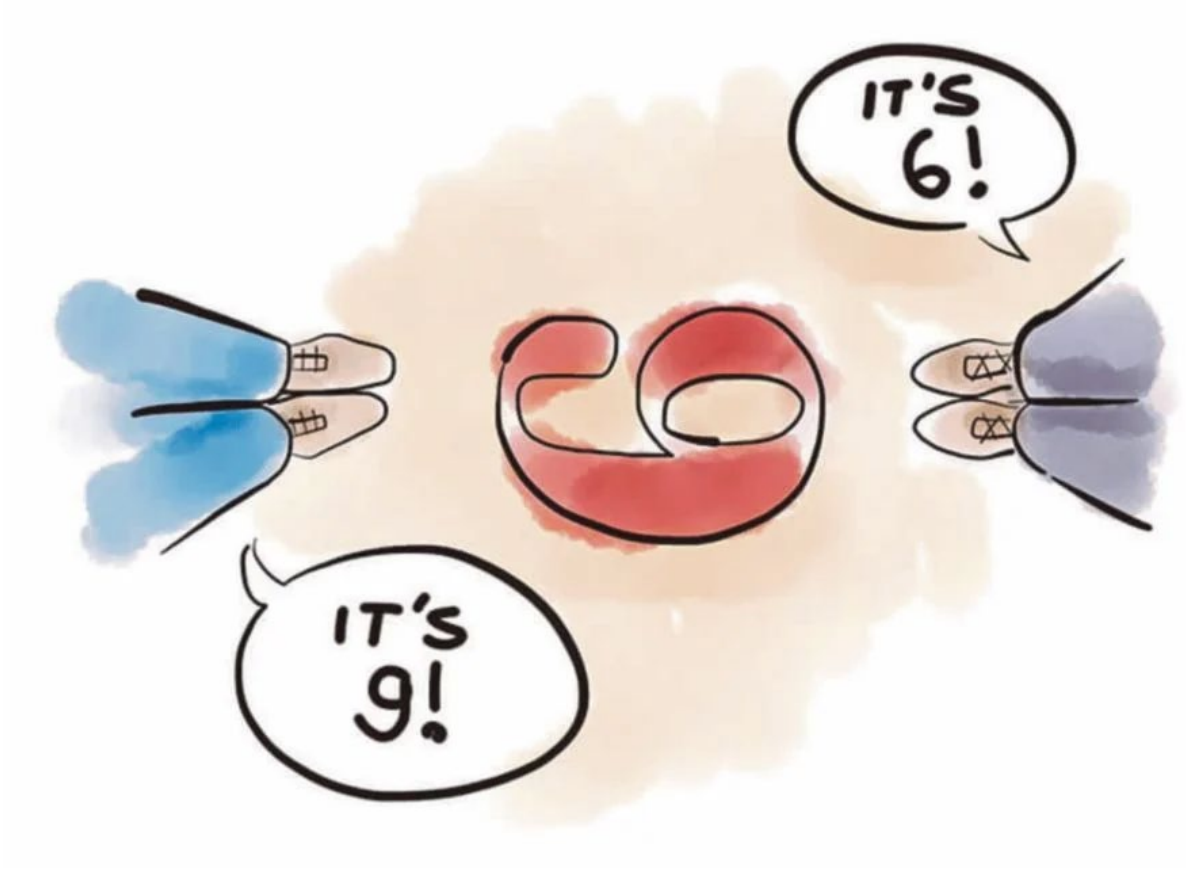
Evidence-based Practice Center, Mayo Clinic, Rochester, Minnesota, USA

EBM je nejlepší možný přístup,

který máme v současné době k dispozici!

Ale …

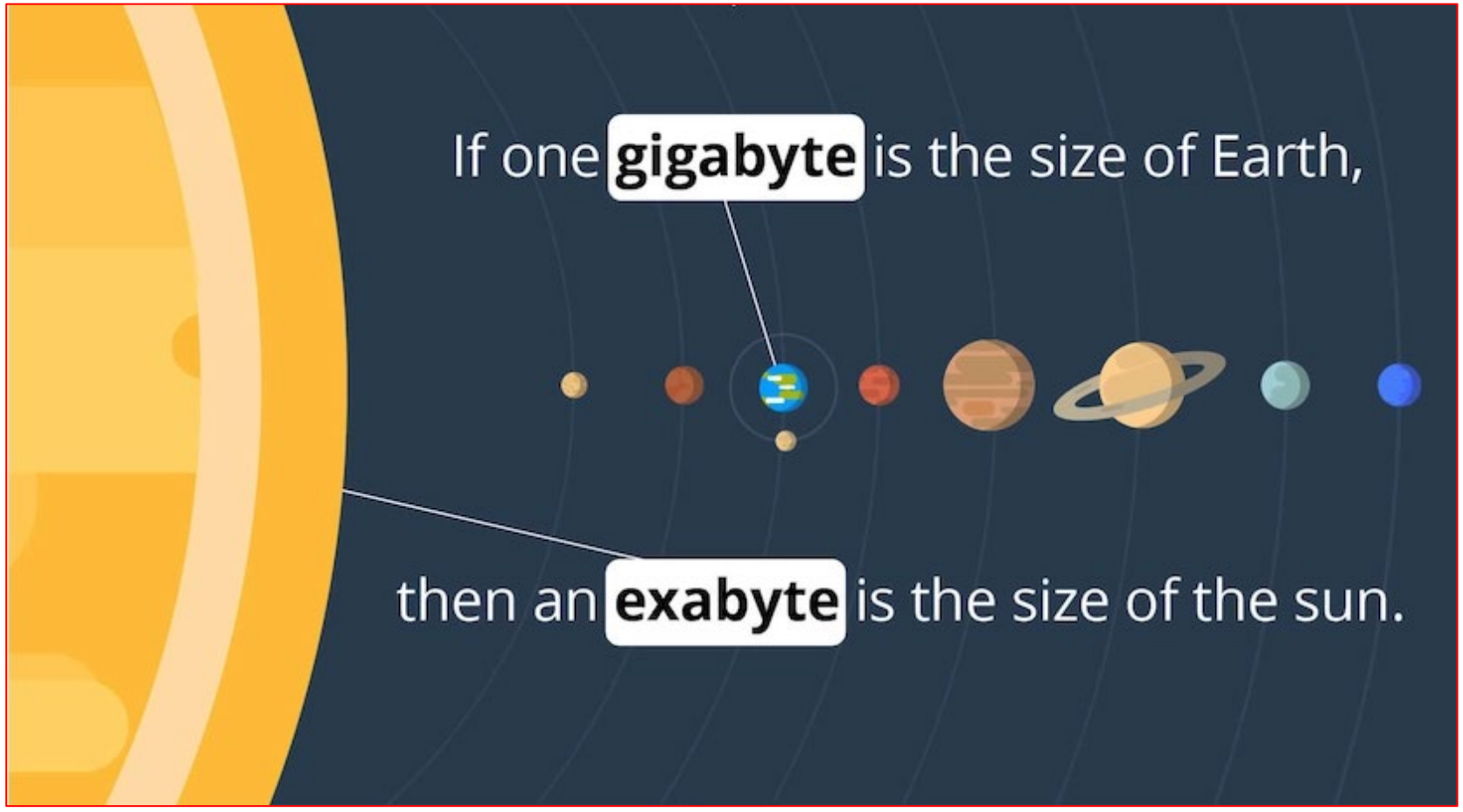

POTŘEBY A
PŘÁNÍ PACIENTA
EBM
VLASTNÍ
KLINICKÁ
ZKUŠENOST
NEJLEPŠÍ
VĚDECKÉ
POZNATKY
V DANÉ OBLASTI


IT'S
6!
IT'S
9!

WORLD ECONOMIC FORUM

2020

COMMITTED TO IMPROVING THE STATE OF THE WORLD



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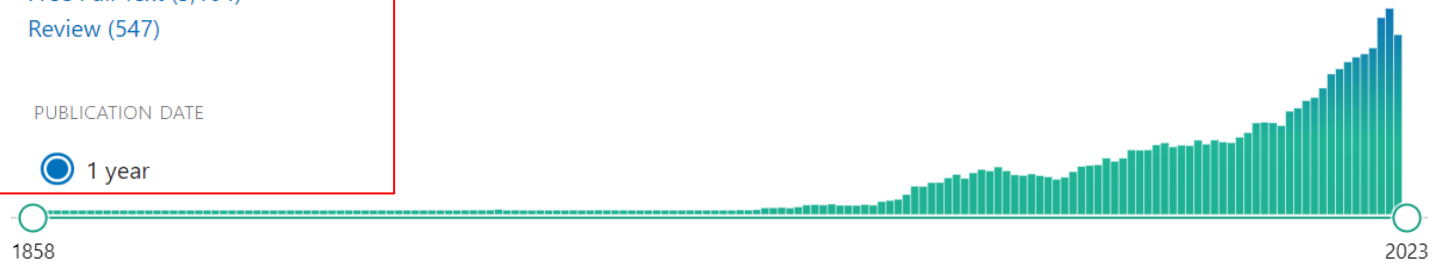

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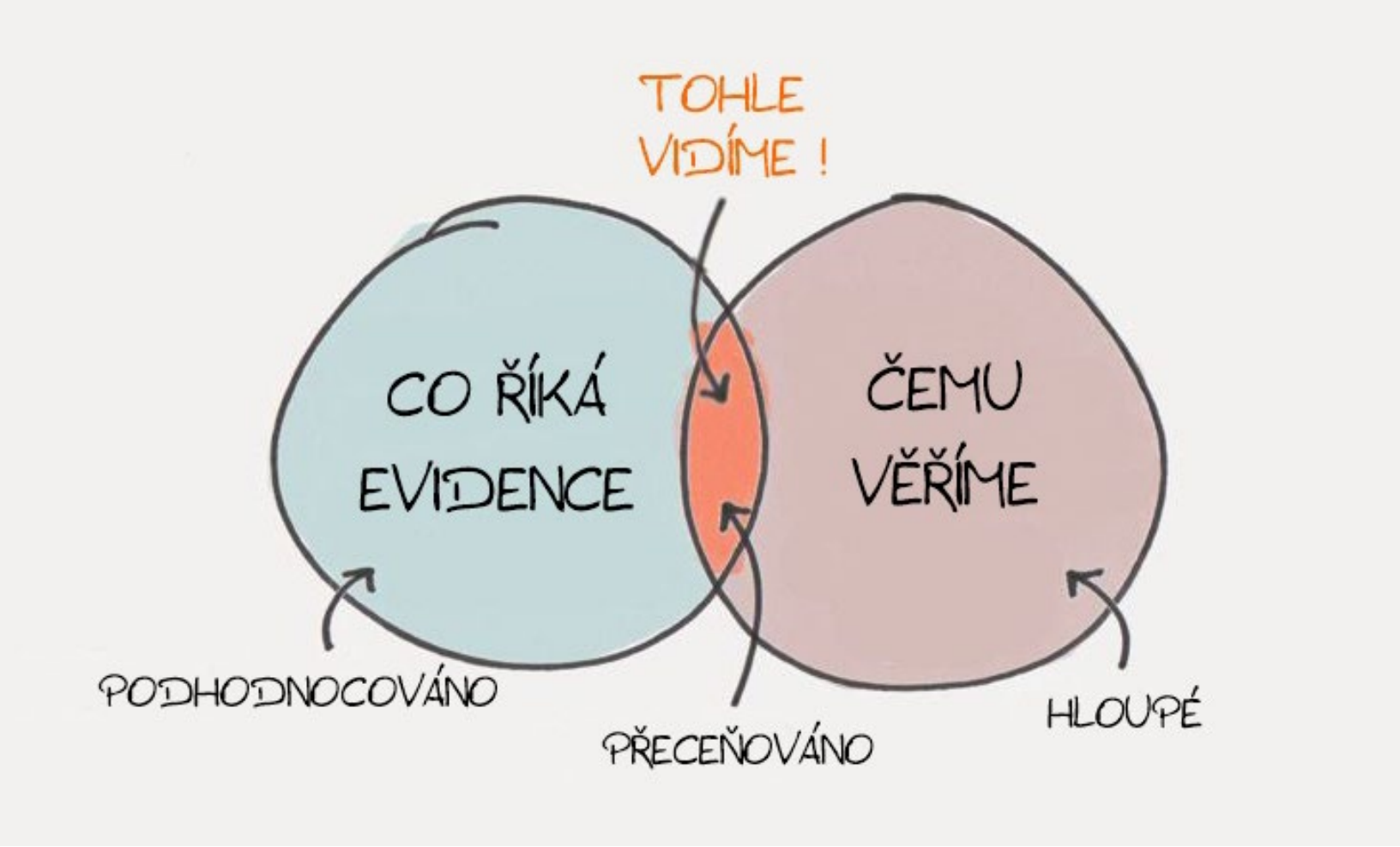
Máme tendenci se soustředit na informace, které potvrzují naše již existující názory.



“Atraumatic” Sprotte needle reduces the incidence of post-lumbar puncture headaches

Article abstract—Post-lumbar puncture headache (PLPH) is best explained by spinal fluid leakage due to delayed closure of a dural defect. In a prospective, randomized, double-blind study, taking into consideration all known methodological problems, the authors compared the incidence of PLPH using the “atraumatic” Sprotte needle vs the “traumatic” Quincke needle. Of the 230 patients included in the final analysis, 24.4% of patients in the “traumatic” group developed PLPH, whereas only 12.2% of patients in the “atraumatic” group did ($p < 0.05$). Therefore, use of the “atraumatic” Sprotte needle for lumbar puncture is recommended.

NEUROLOGY 2001;57:2310–2312

M. Strupp, MD; O. Schueler, MD; A. Straube, MD; S. Von Stuckrad–Barre; and T. Brandt, MD, FRCP

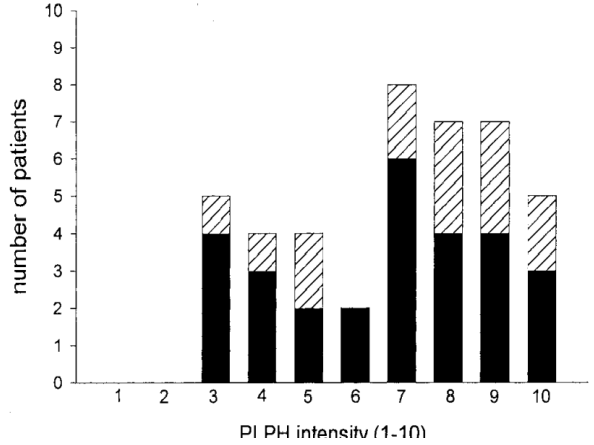


Figure 2. Intensity of the post-lumbar puncture headaches (PLPH). The complaints of the patients (mainly headache) were graded from 0 (no complaints) to 10 (major complaints). The mean value of the intensity of complaints (±SD) of the patients with the “traumatic needle” was 6.4 ± 2.3 (n = 28); it was 7.5 ± 2.2 for the patients with the “atraumatic needle” (n = 14), i.e., not significantly different. ■ = “traumatic needle”; ▨; = “atraumatic needle.”

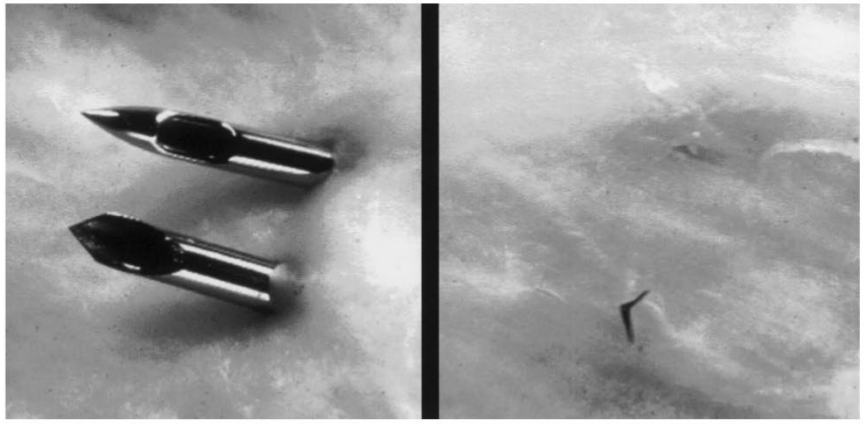
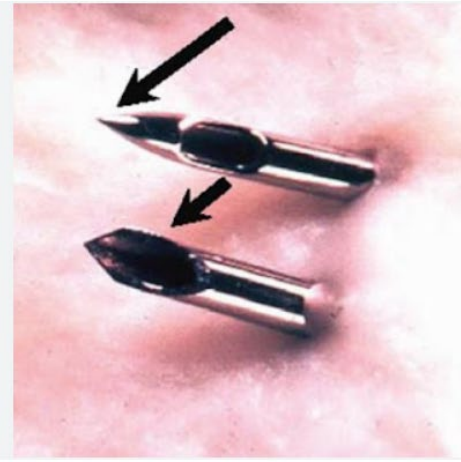
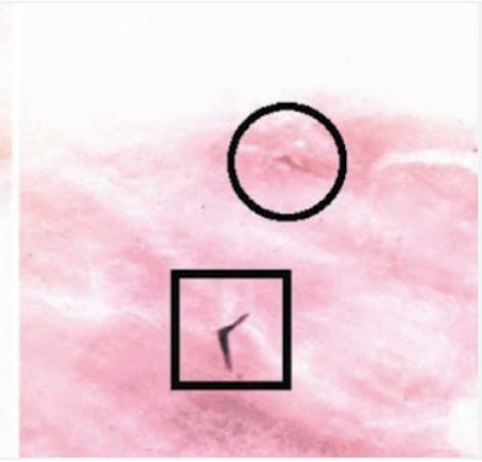


Figure 1. Two types of spinal needle tips: “Atraumatic Sprotte needle” (upper) and “traumatic Quincke needle” (lower) of the same diameter (left). As shown on the right, the atraumatic needle causes a smaller dural defect (upper) than the traumatic needle (lower). The smaller defect should theoretically result in a lower incidence of post-lumbar puncture headache.

Barts MS Blog





Multiple Sclerosis Research: It's OK to ask for an atraumatic needle

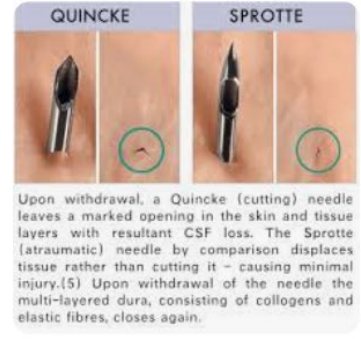
Navštívit

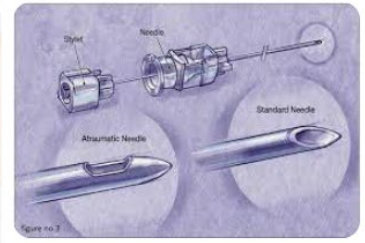
Autor: kschmierer

Zajímá vás, odkud tyto informace pocházejí? **Další informace**

Na obrázky se mohou vztahovat autorská práva. **Další informace**

Související obsah





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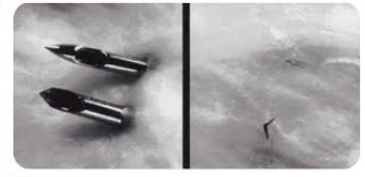

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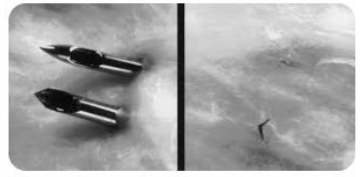
Hole in dural sac caused by penci…



Neurology - Neurology.org

Atraumatic” Sprotte needle reduc…

Fujirebio

How to perform a lumbar puncture | Fujirebio

LUMBAR PUNCTURE

The Pioneer of Atraumatic Lumbar Puncture

Together with Pajunk, Prof. Sprotte developed the Sprotte, the first atraumatic needle for lumbar puncture. The secret of its success can be found in its unique tip geometry and basic architecture. This design, developed especially for the requirements of dural puncture, allows for an atraumatic puncture of the ligamentary structures and optimises CSF flow while reducing the incidence of post-lumbar puncture headaches (PLPH).

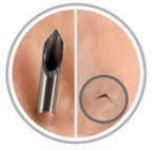
→ Sprotte decreases complications of lumbar puncture and increases the safety of application, and the efficiency of diagnostics.

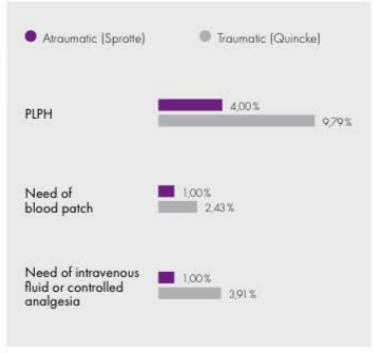
CLINICAL COMPARISON OF SPROTTE VS QUINCKE[6]

Sprotte: Evidence class 1, recommendation level A[5,6,7,8]

Sprotte – atraumatic needle
Leading technology for decreasing the incidence of post-lumbar puncture headaches.[5]

Quincke – cutting needle
One risk factor for post-lumbar puncture headaches is the use of a Quincke needle.[6]





STUDIES CONCLUSIONS

- Atraumatic lumbar puncture needles are safe to use[1,2,4,5,6,7,8]
- Require a minimal learning curve[5]
- Provide reliable results[6]
- Minimise side effects, complication, and recovery time[2]
- High savings potential by minimising process and treatment costs[3,8]
- Increase efficiency[3]

It´s time to change the needle.[1,2,11]

Highest Processing Quality

→ High quality stainless steel needle for increased stability

→ Smoothly polished and burr-free surface and inner lumen desgined for optimised gliding properties and CSF backflow

→ Consistent feel and reliable performance

Highest Processing Quality

Magnifying Hub (Only NRFit®)

Clear, magnifying needle hub allows for easy visualisation of blood or CSF.

→ Easier detection of CSF flashback

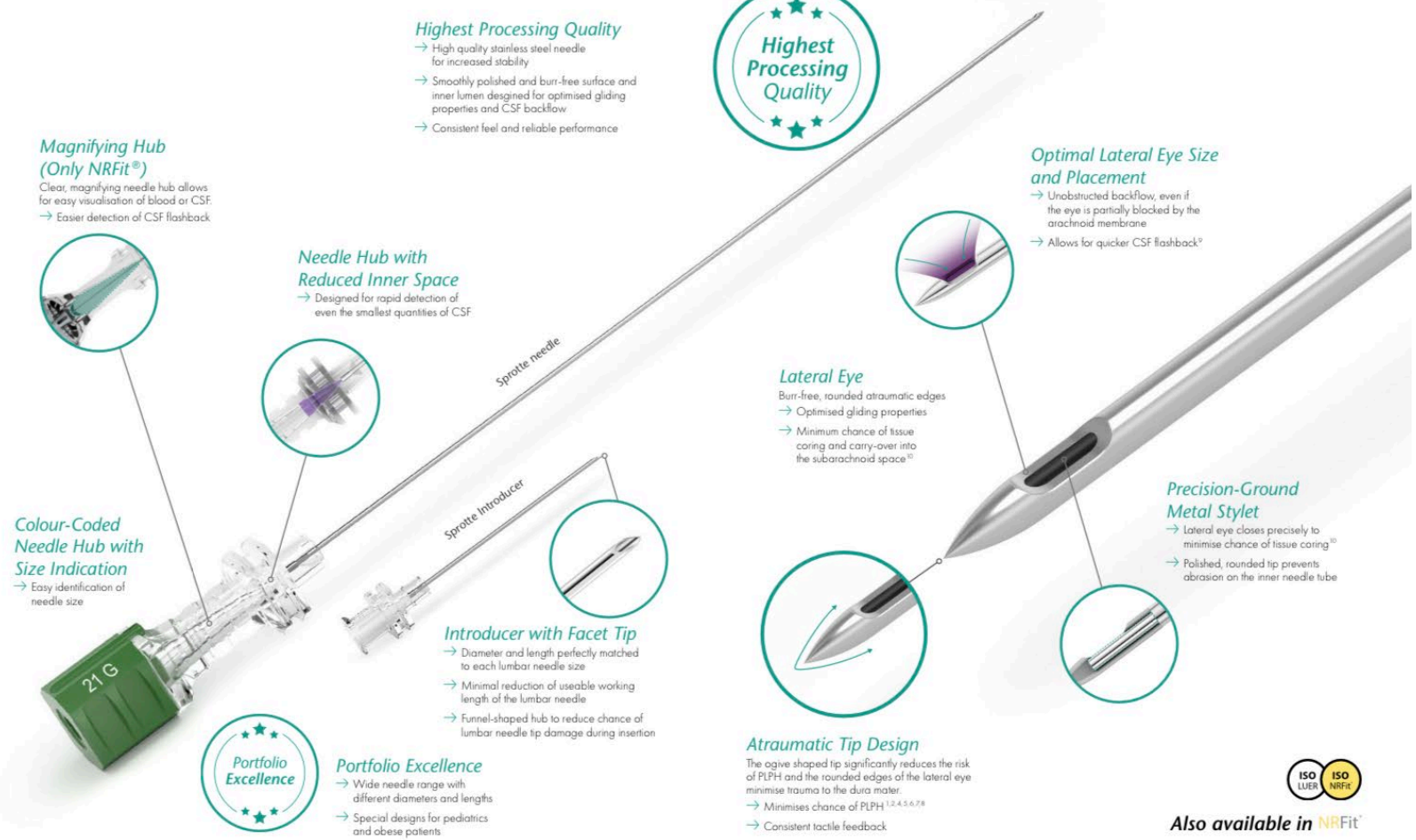
Needle Hub with Reduced Inner Space

→ Designed for rapid detection of even the smallest quantities of CSF

Optimal Lateral Eye Size and Placement

→ Unobstructed backflow, even if the eye is partially blocked by the arachnoid membrane

→ Allows for quicker CSF flashback[9]



Lateral Eye

Burr-free, rounded atraumatic edges

→ Optimised gliding properties

→ Minimum chance of tissue coring and carry-over into the subarachnoid space[10]

Colour-Coded Needle Hub with Size Indication

→ Easy identification of needle size

Introducer with Facet Tip

→ Diameter and length perfectly matched to each lumbar needle size

→ Minimal reduction of useable working length of the lumbar needle

→ Funnel-shaped hub to reduce chance of lumbar needle tip damage during insertion

Precision-Ground Metal Stylet

→ Lateral eye closes precisely to minimise chance of tissue coring[10]

→ Polished, rounded tip prevents abrasion on the inner needle tube

Portfolio Excellence

Portfolio Excellence

→ Wide needle range with different diameters and lengths

→ Special designs for pediatrics and obese patients

Atraumatic Tip Design

The ogive shaped tip significantly reduces the risk of PLPH and the rounded edges of the lateral eye minimise trauma to the dura mater.

→ Minimises chance of PLPH[1,2,4,5,6,7,8]

→ Consistent tactile feedback

ISO LUER ISO NRFit

Also available in NRFit

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Article abstract—Post-lumbar puncture headache (PLPH) is best explained by spinal fluid leakage due to delayed closure of a dural defect. In a prospective, randomized, double-blind study, taking into consideration all known methodological problems, the authors compared the incidence of PLPH using the "atraumatic" Sprotte needle vs the "traumatic" Quincke needle. Of the 230 patients included in the final analysis, 24.4% of patients in the "traumatic" group developed PLPH, whereas only 12.2% of patients in the "atraumatic" group did ($p < 0.05$). Therefore, use of the "atraumatic" Sprotte needle for lumbar puncture is recommended.

NEUROLOGY 2001;57:2310–2312

M. Strupp, MD; O. Schueler, MD; A. Straube, MD; S. Von Stuckrad–Barre; and T. Brandt, MD, FRCP

LP was performed with either an "atraumatic" Sprotte needle[5] (22 Gauge, 0.80 mm, 90 mm; Pajunk, Geisingen, Germany) or a "traumatic" Quincke needle[4] (22 Gauge, 0.80 mm, 90 mm; Braun, Melsungen, Germany) (see figure 1) while the patient was in a sitting position. All LP were performed by experienced neurologists who were unaware of the type of needle.

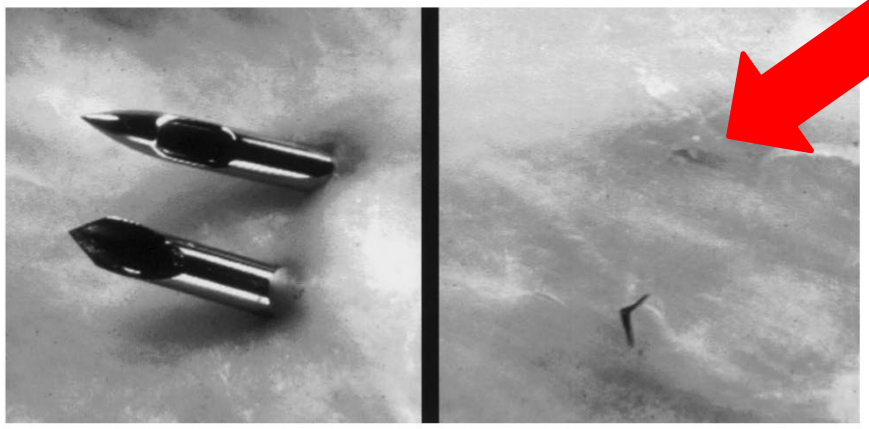


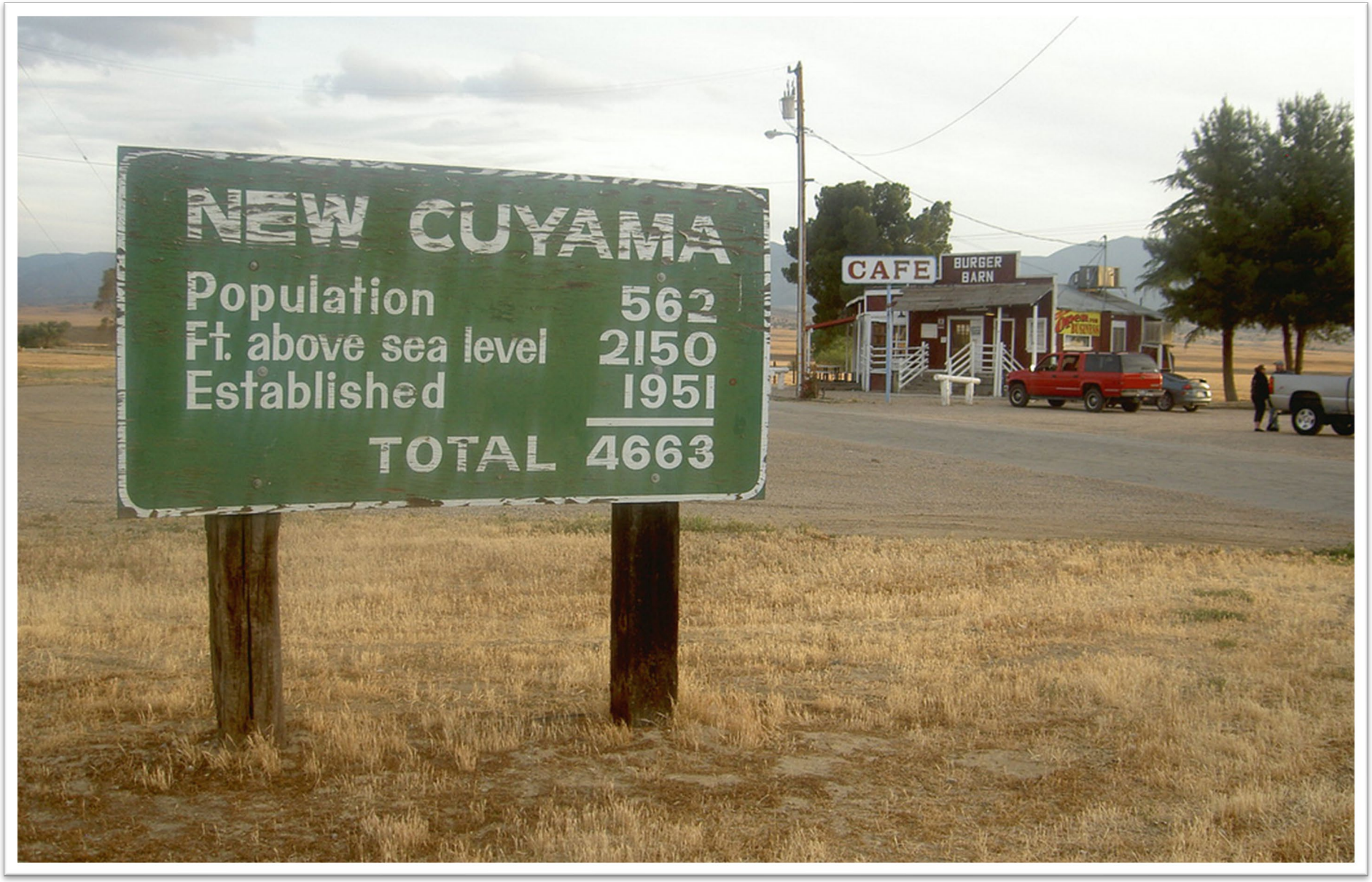
Figure 1. Two types of spinal needle tips: "Atraumatic Sprotte needle" (upper) and "traumatic Quincke needle" (lower) of the same diameter (left). As shown on the right, the atraumatic needle causes a smaller dural defect (upper) than the traumatic needle (lower). The smaller defect should theoretically result in a lower incidence of post-lumbar puncture headache.

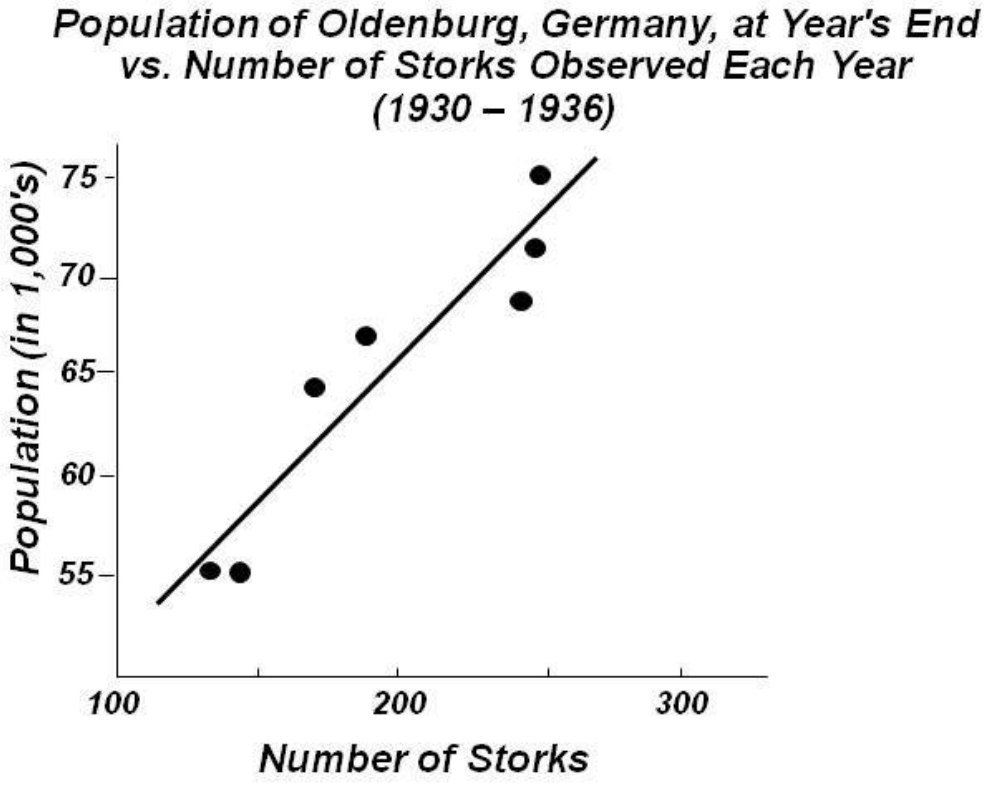
Table *Baseline characteristics and symptoms of patients undergoing lumbar puncture with atraumatic or standard needles*

Characteristic	Needle type	
	"atraumatic," n = 115	"traumatic," n = 115
Age, y	39.8 (12.8)	40.7 (11.5)
Females, %	64	63
Males, %	36	37
Body mass index, kg/m^2	23.3 (3.8)	23.3 (3.6)
Coffee consumption, cups/day		
Usually	1.6 (1.5)	1.8 (1.9)
Day of lumbar puncture	1.0 (1.2)	1.3 (1.8)
Days after lumbar puncture	1.4 (2.1)	1.6 (2.2)
Relative prevalence of migraine, %	21.3	24.6
Severity and prevalence of PLPH		
Mean	7.5 (2.2)	6.4 (2.3)
None, %	87.8	75.6
Mild, %	0.0	4.1
Moderate, %	4.9	12.2
Severe, %	7.3	8.1

Values are means (±SD) unless stated otherwise.

PLPH = Post-lumbar puncture headache.


NEW CUYAMA
Population 562
Ft. above sea level 2150
Established 1951
TOTAL 4663
CAFE
BURGER BARN



Source: Statistics for Experimenters, by Box, Hunter & Hunter

Paediatric and Perinatal Epidemiology 2004, **18**, 88–92

New evidence for the Theory of the Stork

Thomas Höfer[a], Hildegard Przyrembel[b] and Silvia Verleger[c]

[a]Federal Institute for Risk Assessment, Berlin, [b]Office of the National Breast Feeding Committee at BfR, Berlin, and [c]Independent Midwife, Berlin, Germany

Correspondence:
Dr Thomas Höfer, Federal Institute for Risk Assessment, Thielallee 88–92, D-14195 Berlin, Germany.
E-mail: thomas.hoefer@bfr.bund.de

Summary

Data from Berlin (Germany) show a significant correlation between the increase in the stork population around the city and the increase in deliveries outside city hospitals (out-of-hospital deliveries). However, there is no correlation between deliveries in hospital buildings (clinical deliveries) and the stork population. The decline in the number of pairs of storks in the German state of Lower Saxony between 1970 and 1985 correlated with the decrease of deliveries in that area. The nearly constant number of deliveries from 1985 to 1995 was associated with an unchanged stork population (no statistical significance). However, the relevance of the stork for the birth rate in that part of Germany remains unclear, because the number of out-of-hospital deliveries in this area is not well documented. A lack of statistical information on out-of-hospital deliveries in general is a severe handicap for further proof for the Theory of the Stork.

The intended value (disclaimer): This article is not intended to disprove the value of serious epidemiological investigations. It is an example of how studies based on popular belief and unsubstantiated theory, seconded by low quality references and supported by coincidental statistical association could lead to apparent scientific endorsement. Insofar it is a humorous case study for education in perinatal epidemiology.

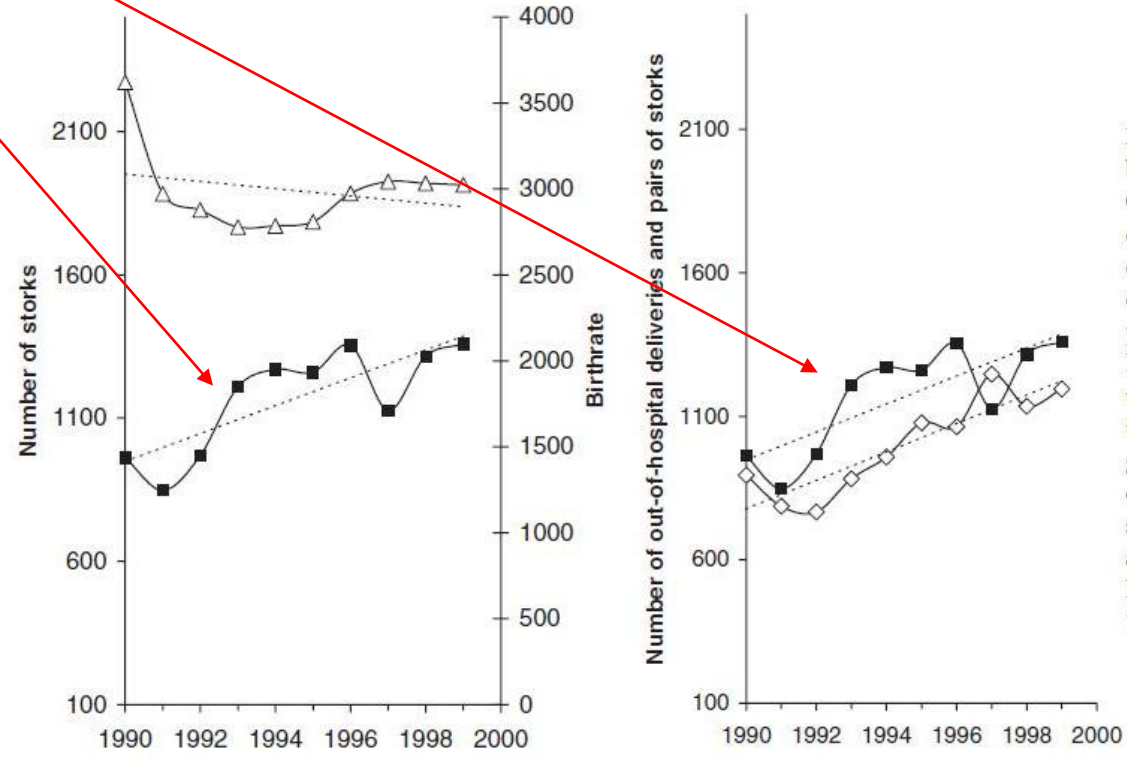
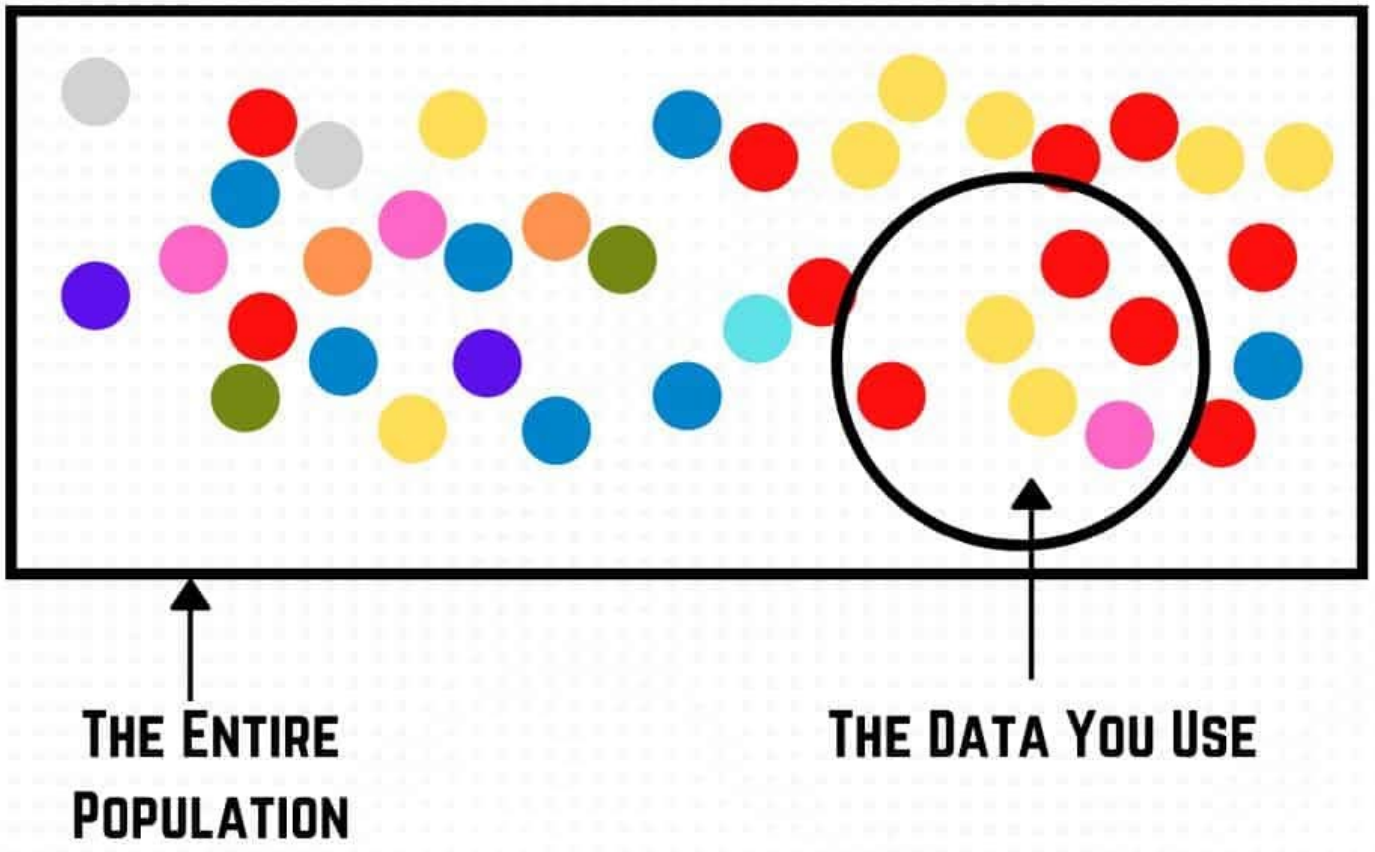
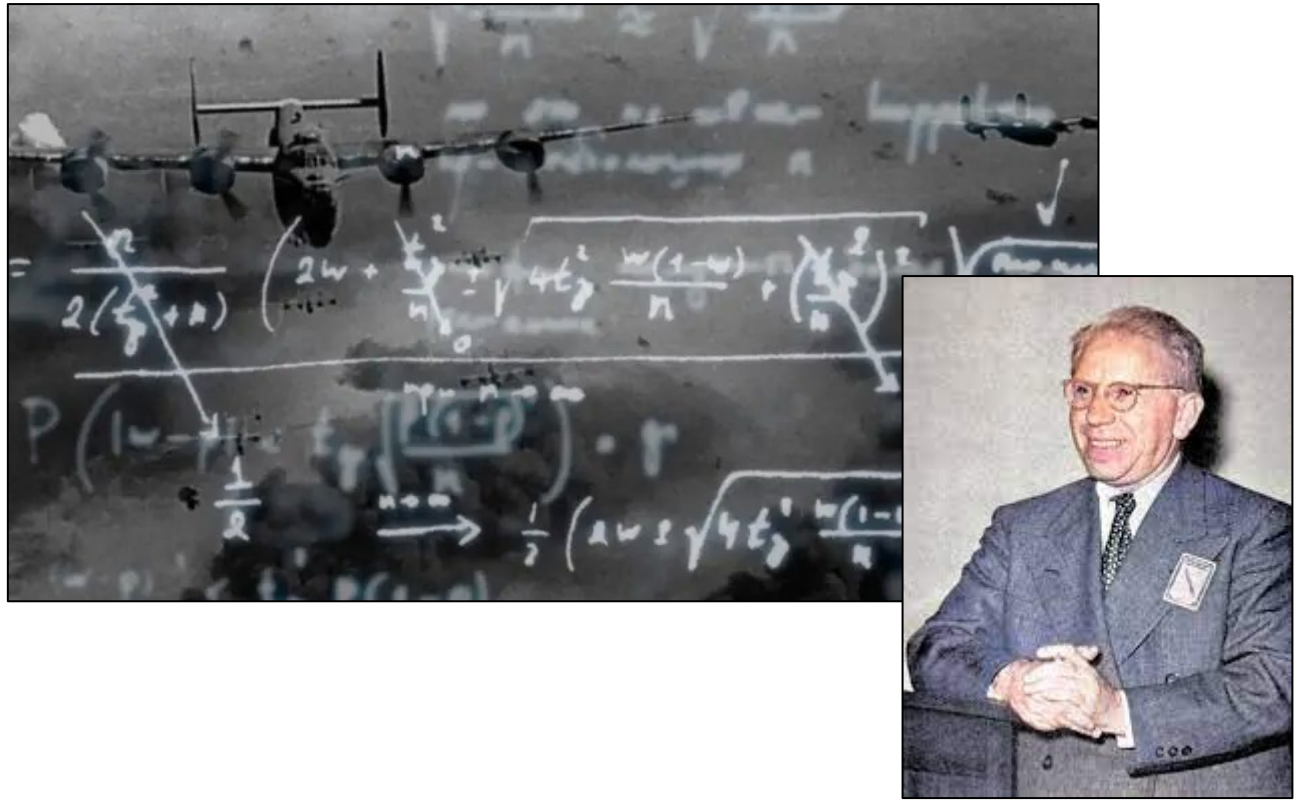


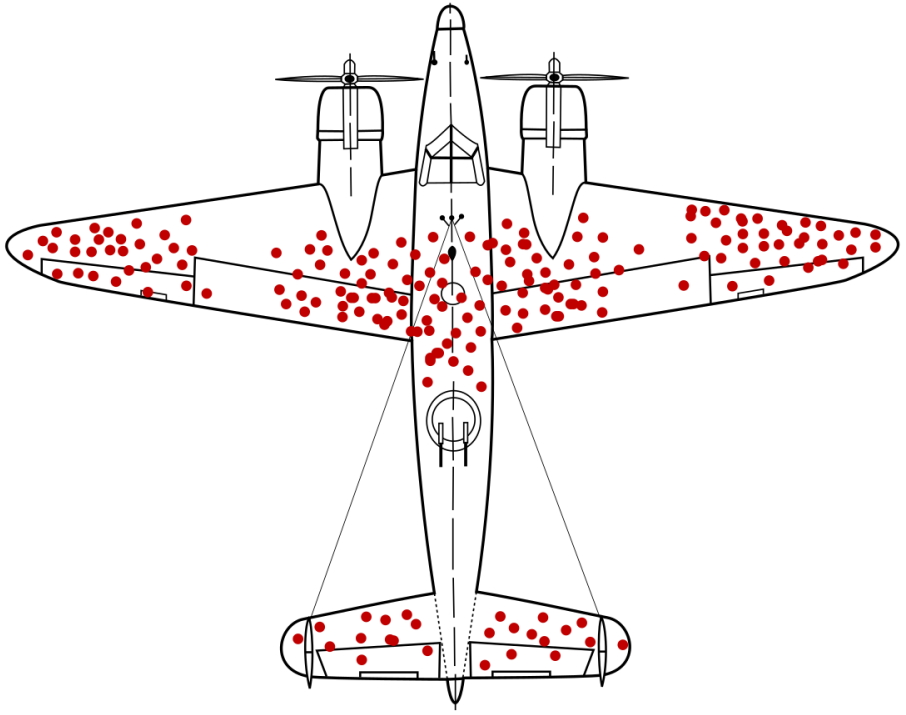
Figure 2. Storks in Brandenburg and the birthrates in Berlin, Germany (1990–99). Open triangles show number of clinical deliveries per year in Berlin. Open diamonds show number of out-of-hospital deliveries per year in Berlin. Number of pairs of storks are shown as full squares. Dotted lines represent linear regression trend ($y = mx + b$). For the convenience of the readers, two figures are presented. Left graph shows clinical deliveries against pairs of storks using two scalings, right graph shows numbers of out-of-hospital deliveries and pairs of storks both on the same scale. In both figures, data are from the years 1990–2000.

SAMPLING BIAS





Abraham Wald
1902-1950
americký matematik



BIAS PŘEŽIVŠÍCH

- Logická chyba soustředění se na entity, které prošly výběrem, zatímco přehlížíme ty, kteří ne. To může vést k nesprávným závěrům kvůli neúplným údajům.

$0.99\overline{9} = 1$

$$x = .99\overline{9}$$
$$10x = 9.99\overline{9}$$
$$9x = 9$$
$$x = 1$$

Pokud napíšeme rovnici že X=0,999… vynásobíme ji 10,
a odečteme vlevo X a vpravo 0,9999… (X se přece =0,999…)
tak dostaneme že 9X=9, a děleno 9 se X=1
tudíž **X=1=0,999…**

$$1/3 = .3\overline{3}$$
$$3 \cdot (1/3) = 3 \cdot (.3\overline{3})$$
$$1 = .99\overline{9}$$

Pokud 1/3 = 0,333…
tak když vynásobíme 3
dostaneme 3/3 = 0,999…
a tudíž **1=0,999…**

UTRACENO	ZŮSTATEK
20	30
15	15
9	6
6	0
50	**51**

„Jsou tři druhy lží:

lež

sprostá lež

a statistika“

Boldt's retraction count upped to 94, co-author takes legal action to prevent 95th

with 2 comments

We've found two recent retractions and an expression of concern for Joachim Boldt, former prominent anesthesiologist and currently *Retraction Watch* leaderboard's 2nd place titleholder. He now has 94 retractions.

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

One of the retracted articles contains falsified data, along with a researcher who didn't agree to be a co-author, according to an investigation by the Justus Liebig University Giessen, where Boldt used to work. The expression of concern is regarding some questionable data. The other new retraction is actually one of 88 papers that a group of editors agreed to retract back in 2011, after they were "unable to verify" approval by the Institutional Review Board (IRB) for the studies.

One of those 88 papers, we've discovered, has still has not been retracted. According to an editor at the journal, they haven't removed it because one of Boldt's co-authors has threatened them with legal action.
Read the rest of this entry »

„Jsou tři druhy lží:

lež

sprostá lež

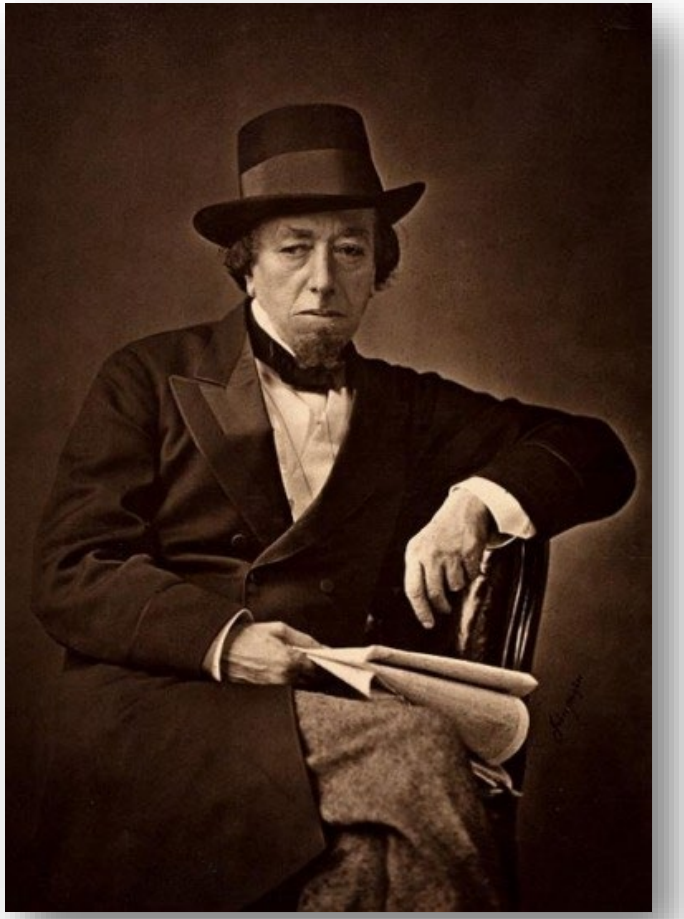
a statistika“

„Jsou tři druhy lží:

lež

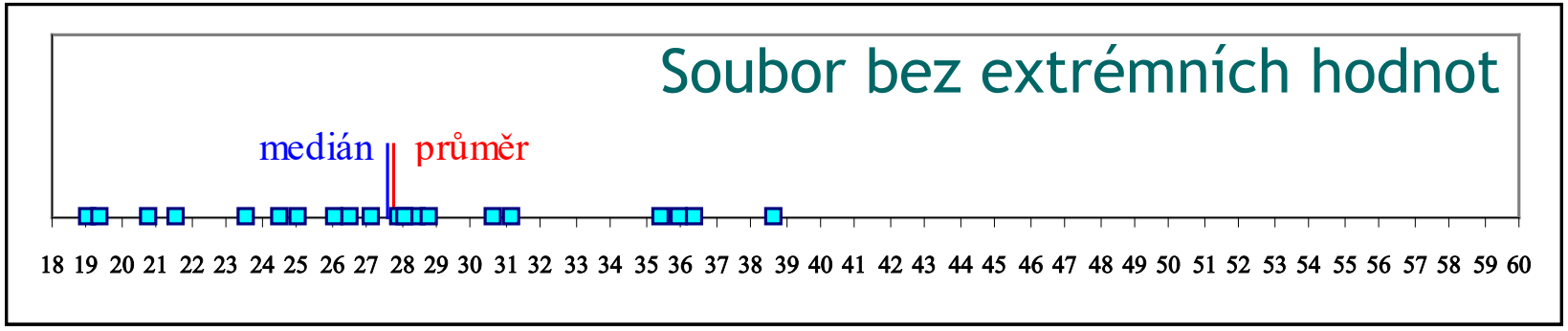
sprostá lež

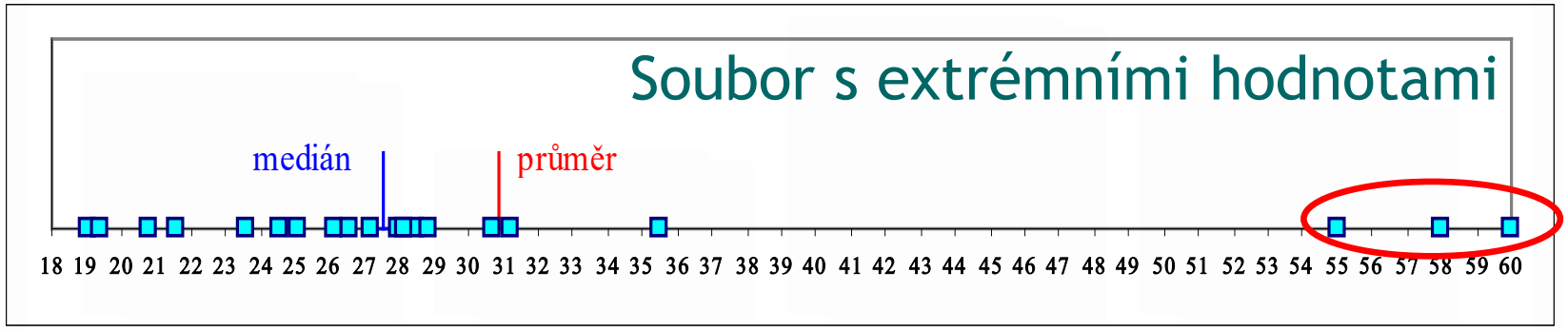
a statistika“



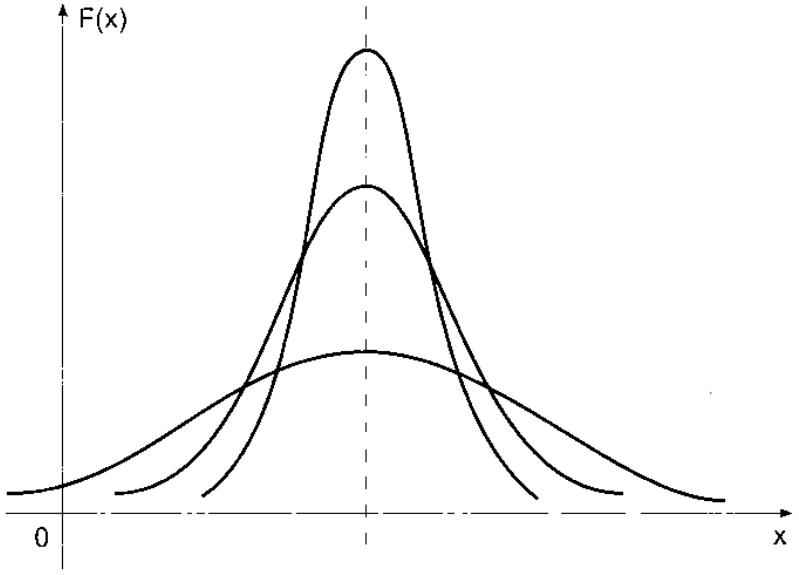
Benjamin Disraeli (1804 - 1881)

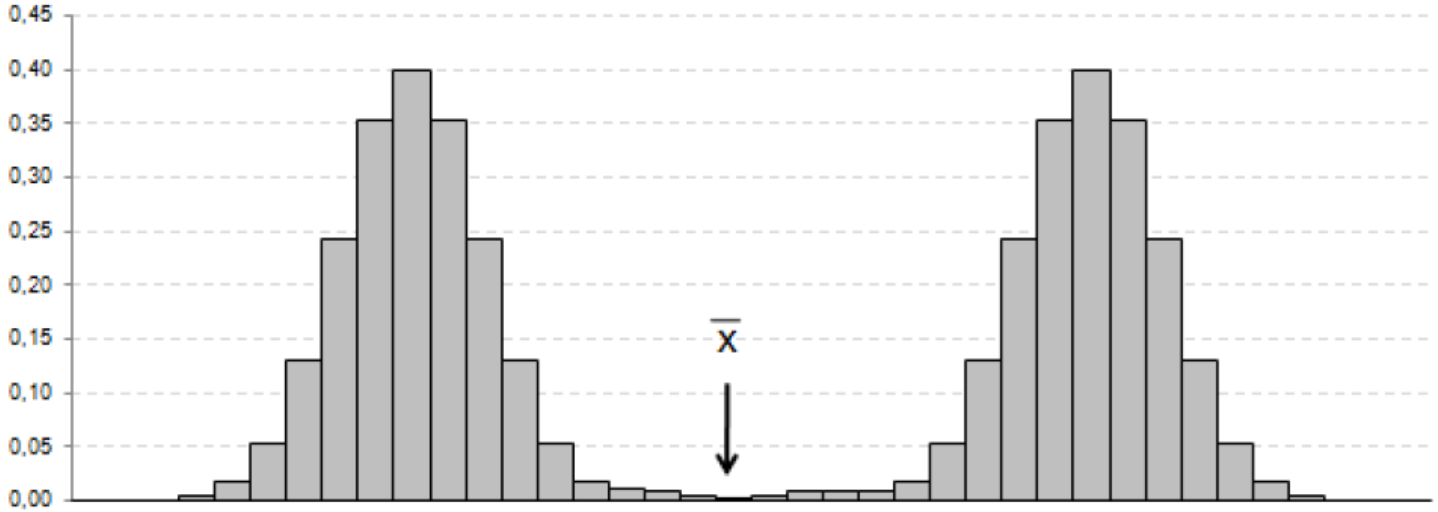
PRŮMĚR vs. MEDIÁN





PRŮMĚR vs. MEDIÁN

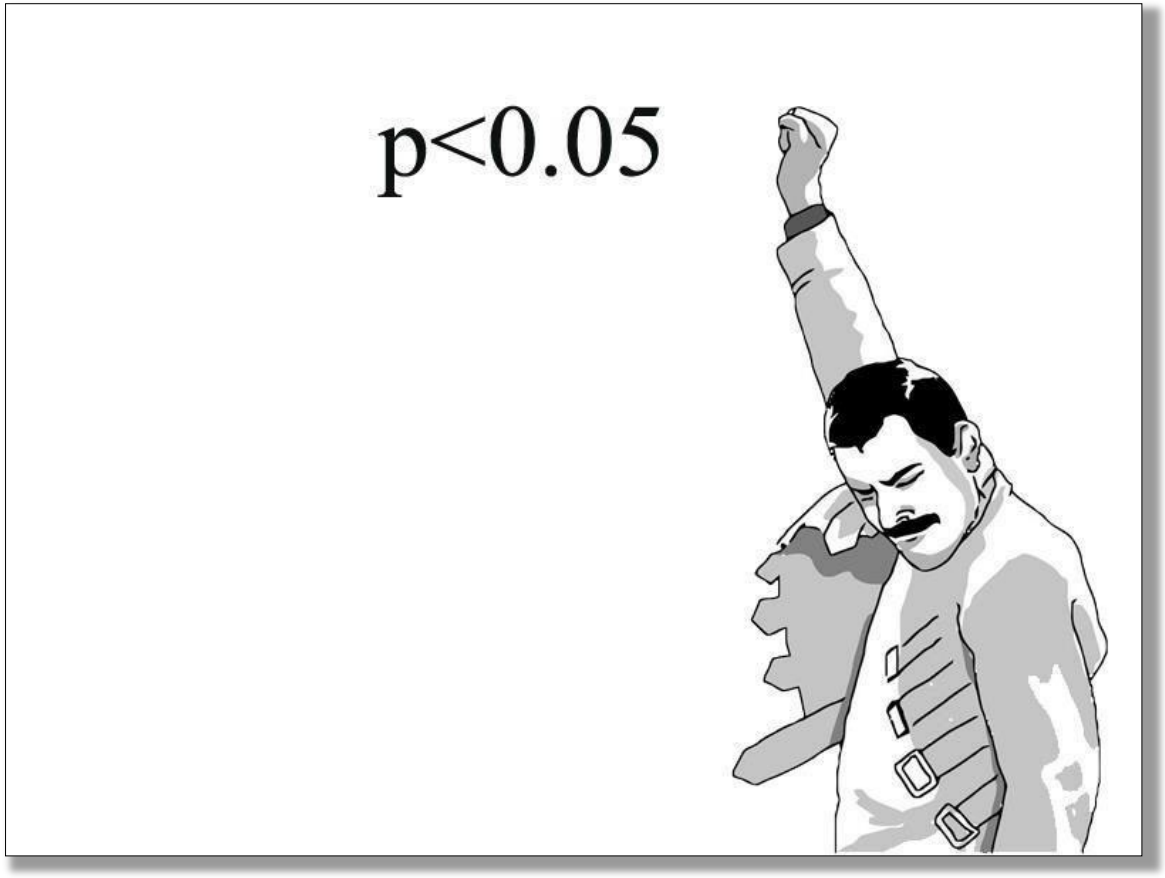




Musíme znát rozptyl hodnot - konfidenční interval CI 95%

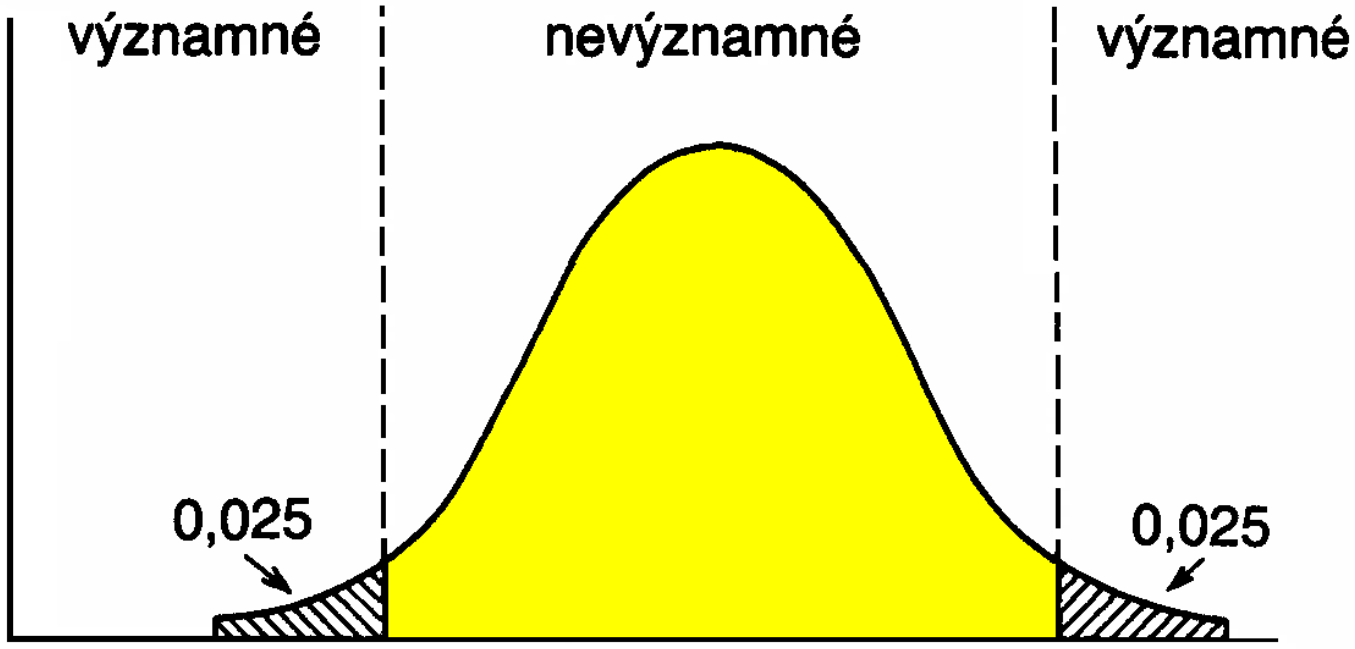

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh
Průměrný člověk má
jedno ňadro a jedno varle.
Des McHale
Emeritus Professor of Mathematics,
University College Cork

EVIDENCE BASED MEDICINE …



Hodnota **p** říká, jestli rozdíly mezi skupinami jsou větší než by bylo možné očekávat v důsledku náhodné variability.

P<0.05 zjednodušeně znamená, že akceptujeme 5% riziko chyby, že výsledek je pouze náhodný.



Ronald Aylmer Fisher
1890 – 1962

…zavedl v roce 1925 do statistiky hodnotu $\alpha = 0.05$

CAVE: neexistuje žádný vědecký důvod, proč volit právě tuto hodnotu, jde pouze o konvenci!

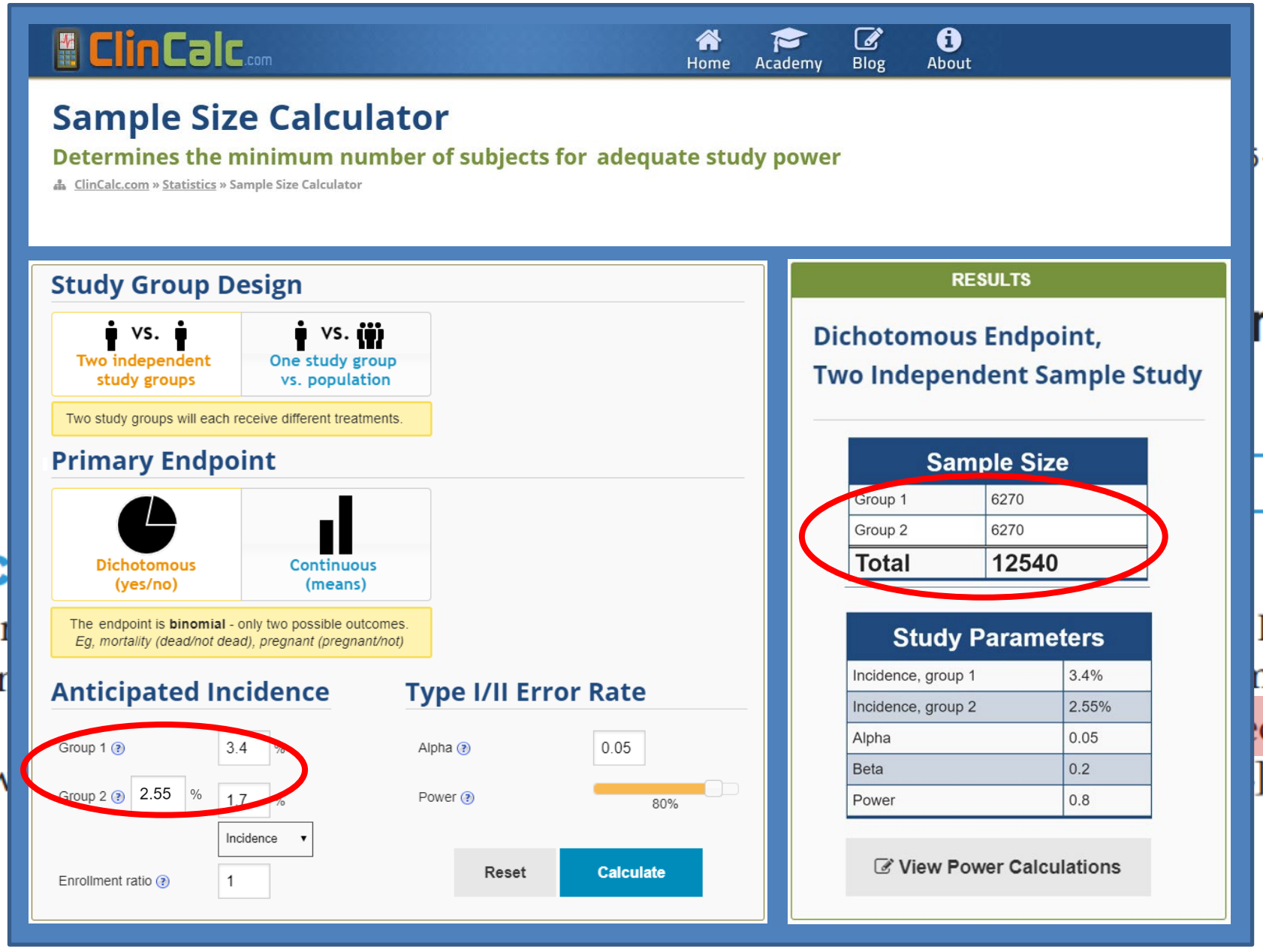
P=0.049 vs. P=0.051

Na čem závisí hodnota *p*

1. **na velikosti výběru** (s rostoucím *n* klesá)

2. **na velikosti odchylky skutečné hodnoty parametru od hodnoty předpokládaného hypotézou** (čím dále, tím je menší)

3. **na variabilitě uvnitř výběrů** (menší variabilita = menší P)



INTRODUC

Obstetric her
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hemorrhage
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In Africa and Asia,
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ORIGINAL ARTICLE

High-Frequency Oscillation for Acute Respiratory Distress Syndrome

Duncan Young, D.M., Sarah E. Lamb, D.Phil., Sanjoy Shah, M.D., Iain MacKenzie, M.D., William Tunnicliffe, M.Sc., Ranjit Lall, Ph.D., Kathy Rowan, D.Phil., and Brian H. Cuthbertson, M.D., for the OSCAR Study Group*

N Engl J Med 2013; 368:806-813

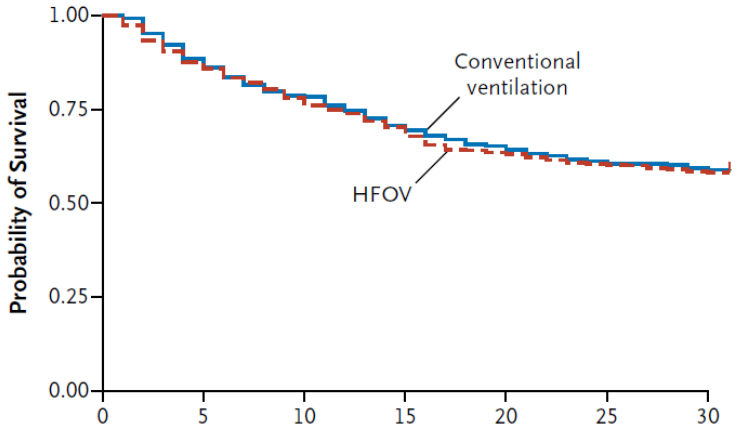


Figure 3. Kaplan–Meier Survival Estimates during the First 30 Study Days.

ABSTRACT

BACKGROUND

Patients with the acute respiratory distress syndrome (ARDS) require mechanical ventilation to maintain arterial oxygenation, but this treatment may produce secondary lung injury. High-frequency oscillatory ventilation (HFOV) may reduce this secondary damage.

METHODS

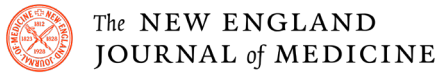
In a multicenter study, we randomly assigned adults requiring mechanical ventilation for ARDS to undergo either HFOV with a Novalung R100 ventilator (Metran) or usual ventilatory care. All the patients had a ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FIO_2) of 200 mm Hg (26.7 kPa) or less and an expected duration of ventilation of at least 2 days. The primary outcome was all-cause mortality 30 days after randomization.

RESULTS

There was no significant between-group difference in the primary outcome, which occurred in 166 of 398 patients (41.7%) in the HFOV group and 163 of 397 patients (41.1%) in the conventional-ventilation group (P=0.85 by the chi-square test). After adjustment for study center, sex, score on the Acute Physiology and Chronic Health Evaluation (APACHE) II, and the initial PaO_2:FIO_2 ratio, the odds ratio for survival in the conventional-ventilation group was 1.03 (95% confidence interval, 0.75 to 1.40; P=0.87 by logistic regression).

CONCLUSIONS

The use of HFOV had no significant effect on 30-day mortality in patients undergoing mechanical ventilation for ARDS. (Funded by the National Institute for Health Research Health Technology Assessment Programme; OSCAR Current Controlled Trials number, ISRCTN10416500.)



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NEW ENGLAND JOURNAL OF MEDICINE	MEDICINE, GENERAL & INTERNAL - SCIE	506,071	176.082	Q1
JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	MEDICINE, GENERAL & INTERNAL - SCIE	242,430	157.375	Q1
NATURE REVIEWS MOLECULAR CELL BIOLOGY	CELL BIOLOGY - SCIE	66,072	113.915	Q1
NATURE REVIEWS DRUG DISCOVERY	Multiple	47,615	112.288	Q1
NATURE REVIEWS IMMUNOLOGY	IMMUNOLOGY - SCIE	67,752	108.555	Q1
Lancet Respiratory Medicine	Multiple	29,214	102.642	Q1
BMJ-British Medical Journal	MEDICINE, GENERAL & INTERNAL - SCIE	183,671	96.216	Q1
NATURE MEDICINE	Multiple	141,867	87.244	Q1

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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Duncan Young, D.M., Sarah E. Lamb, D.Phil., Sanjoy Shah, M.D., Iain MacKenzie, M.D., William Tunnicliffe, M.Sc., Ranjit Lall, Ph.D., Kathy Rowan, D.Phil., and Brian H. Cuthbertson, M.D., for the OSCAR Study Group*

N Engl J Med 2013; 368:806-813

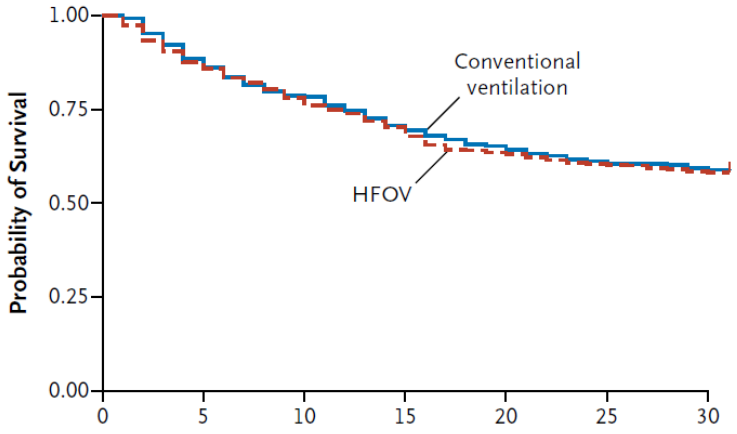

Figure 3. Kaplan–Meier Survival Estimates during the First 30 Study Days.

In conclusion, in a large effectiveness study, we were unable to find any benefit or harm from the use of HFOV in adult patients with ARDS. We recommend that this mode of ventilation not be used for routine care.

METHODS

In a multicenter study, we randomly assigned adults requiring mechanical ventilation for ARDS to undergo either HFOV with a Novalung R100 ventilator (Metran) or usual ventilatory care. All the patients had a ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FIO_2) of 200 mm Hg (26.7 kPa) or less and an expected duration of ventilation of at least 2 days. The primary outcome was all-cause mortality 30 days after randomization.

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In conclusion, in a large effectiveness study, we were unable to find any benefit or harm from the use of HFOV in adult patients with ARDS. We recommend that this mode of ventilation not be used for routine care.

METHODS

Study Design

We conducted a randomized, controlled trial of HFOV, as compared with conventional mechanical ventilation. Patients were recruited from adult general intensive care units (ICUs) in 12 university hospitals, 4 university-affiliated hospitals, and 13 district general hospitals in England, Wales, and Scotland. Three hospitals had previous experience with HFOV with the use of SensorMedics 3100B ventilators (Car
(in 20 hospitals
Appendix, avail
NEJM.org.

Z 29 nemocnic pouze 3 nemocnice měly předchozí zkušenost s použitým HFOV ventilátorem;

6 nemocnic mělo nějakou zkušenost a 20 nemocnic žádnou zkušenost s HFOV !

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 June 2013
EMA/349341/2013

PRAC recommends suspending marketing authorisati
for infusion solutions containing hydroxyethyl-starch

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) h
concluded following a review of the available evidence that the benefits of infusion solution
hydroxyethyl-starch (HES) no longer outweigh their risks and therefore recommended tha
marketing authorisations for these medicines be suspended.

Infusion solutions containing HES are medicines mainly used to replace lost blood volum
hypovolaemia (low blood volume caused by dehydration or blood loss) and hypovolaem
steep fall in blood pressure caused by drop in blood volume). They are used in critical
including patients with sepsis (bacterial infection of the blood) or burn or trauma inju
who are undergoing surgery.

The review of infusion solutions containing HES was triggered by the German medi
Federal Institute for Drugs and Medical Devices (BfArM), following three recent stu
compared HES with other products used for volume replacement called crystalloid
patients. The studies showed that patients with severe sepsis treated with HES
of kidney injury requiring dialysis. Two of the studies[1,2] also showed that in pati
there was a greater risk of mortality. The PRAC was therefore requested to ass
evidence and how it impacts on the risk-benefit balance of HES infusion soluti
of hypovolaemia and hypovolaemic shock.

The PRAC assessed data from the scientific literature and the data submitte
took advice from a group of external experts. The PRAC was of the opinion
crystalloids, patients treated with HES were at a greater risk of kidney inju
a greater risk of mortality. The PRAC also considered that the available d
benefit of HES in hypovolaemia, which did not justify its use considering
therefore concluded that the marketing authorisations for these medicin

[1] Perner, A. *et al.* Hydroxyethyl Starch 130/0.42 versus Ringer's acetate in severe
134.
[2] Brunkhorst, F.M. *et al.* Intensive insulin therapy and pentastarch resuscitation i
358(2):125-39.
[3] Myburgh, J.A. *et al.* Hydroxyethyl starch or saline for fluid resuscitation in inte
367(20):1901-11.

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 December 2013
EMA/809470/2013

Hydroxyethyl-starch solutions (HES) no longer to be used in patients with sepsis or burn injuries or in critically ill patients

HES will be available in restricted patient populations

On 23 October 2013, the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), endorsed by majority the recommendations of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which concluded that HES solutions must no longer be used to treat patients with sepsis (bacterial infection in the blood) or burn injuries or critically ill patients because of an increased risk of kidney injury and mortality.*

HES solutions may continue to be used in patients to treat hypovolaemia (low blood volume) caused by acute (sudden) blood loss, where treatment with alternative infusions solutions known as 'crystalloids' alone are not considered to be sufficient. In order to minimise potential risks in these patients, HES solutions should not be used for more than 24 hours and patients' kidney function should be monitored after HES administration. In addition to updating the product information, further studies should be carried out on the use of these medicines in elective surgery and trauma patients.

The review of HES solutions was carried out by the PRAC following the publication of studies showing an increased risk of mortality in patients with sepsis[1,2] and an increased risk of kidney injury requiring dialysis in critically ill patients[1,2,3] following treatment with HES solutions.

As the CMDh position was adopted by majority vote, it was sent to the European Commission, which endorsed it and, on 19 December 2013, adopted a final legally binding decision valid throughout the European Union (EU).

Information for patients

- *Because of the risk of kidney injury and mortality, HES solutions must no longer be used in patients with sepsis (bacterial infection in the blood) or burn injuries or critically ill patients.*
- *HES solutions may continue to be used to treat hypovolaemia (low blood volume) caused by acute (sudden) blood loss. However, the doctor should monitor the patient's kidney function after HES administration.*

** The CMDh is a medicines regulatory body representing the European Union (EU) Member States*

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
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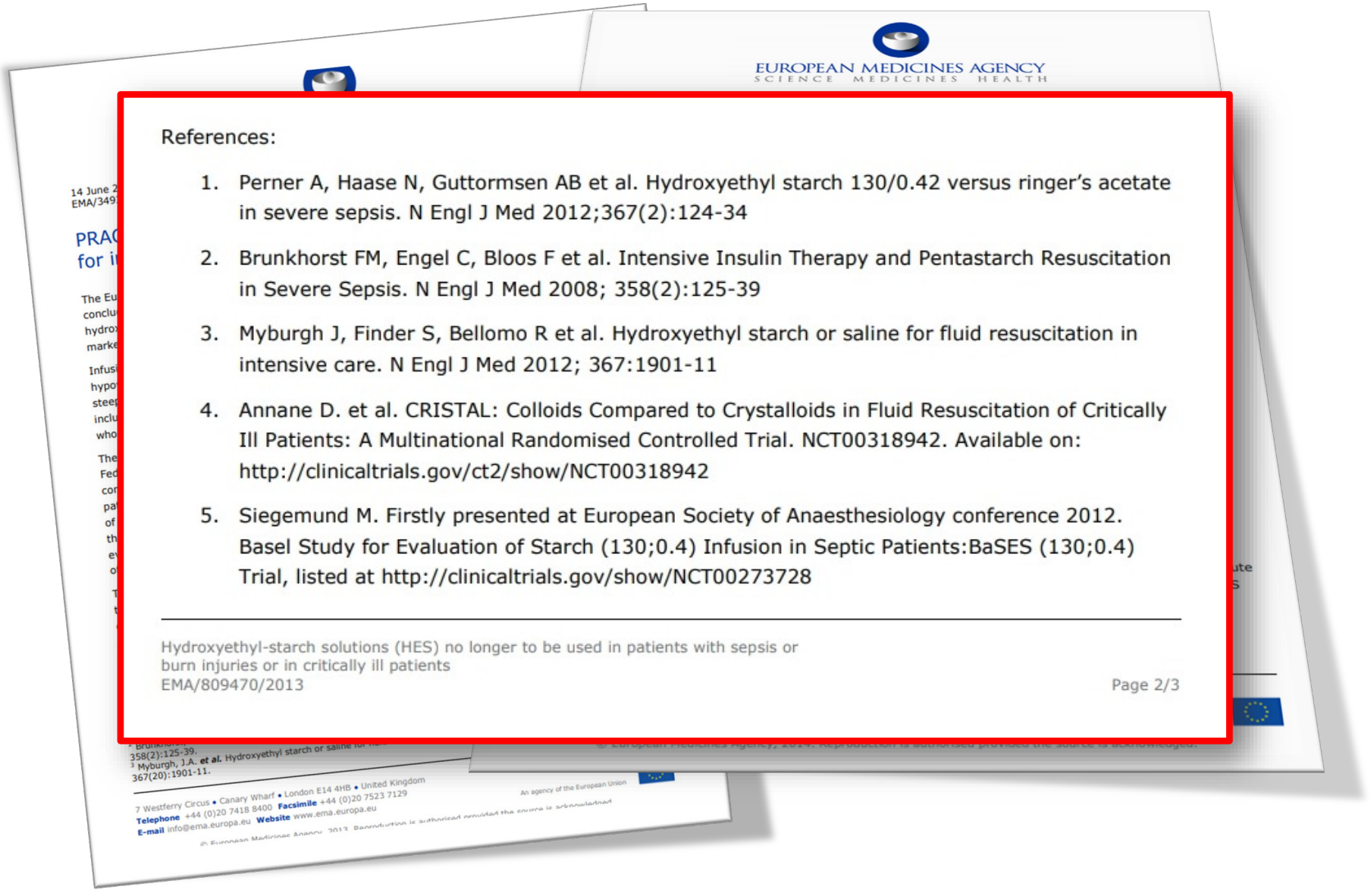


References:

1. Perner A, Haase N, Guttormsen AB et al. Hydroxyethyl starch 130/0.42 versus ringer's acetate in severe sepsis. N Engl J Med 2012;367(2):124-34
2. Brunkhorst FM, Engel C, Bloos F et al. Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis. N Engl J Med 2008; 358(2):125-39
3. Myburgh J, Finder S, Bellomo R et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med 2012; 367:1901-11
4. Annane D. et al. CRISTAL: Colloids Compared to Crystalloids in Fluid Resuscitation of Critically Ill Patients: A Multinational Randomised Controlled Trial. NCT00318942. Available on: http://clinicaltrials.gov/ct2/show/NCT00318942
5. Siegemund M. Firstly presented at European Society of Anaesthesiology conference 2012. Basel Study for Evaluation of Starch (130;0.4) Infusion in Septic Patients:BaSES (130;0.4) Trial, listed at http://clinicaltrials.gov/show/NCT00273728

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis

Outcome	HES 130/0.42 (N=398)	Ringer's Acetate (N=400)	Relative Risk (95% CI)	P Value
Primary outcome				
Dead or dependent on dialysis at day 90 — no. (%)	202 (51)	173 (43)	1.17 (1.01–1.36)	0.03
Dead at day 90 — no. (%)	201 (51)	172 (43)	1.17 (1.01–1.36)	0.03

více pacientů s HES muselo mít CRRT

HES má vyšší 90ti denní riziko smrti

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D., Andreas Meier-Hellmann, M.D., Max Ragaller, M.D., Norbert Weiler, M.D., Onnen Moerer, M.D., Matthias Gruendling, M.D., Michael Oppert, M.D., Stefan Grond, M.D., Derk Olthoff, M.D., Ulrich Jaschinski, M.D., Stefan John, M.D., Rolf Rossaint, M.D., Tobias Welte, M.D., Martin Schaefer, M.D., Peter Kern, M.D., Evelyn Kuhnt, M.Sc., Michael Kiehntopf, M.D., Christiane Hartog, M.D., Charles Natanson, M.D., Markus Loeffler, M.D., Ph.D., and Konrad Reinhart, M.D., for the German Competence Network Sepsis (SepNet)

ABSTRACT

BACKGROUND

The role of intensive insulin therapy in patients with severe sepsis is uncertain. Fluid resuscitation improves survival among patients with septic shock, but evidence is lacking to support the choice of either crystalloids or colloids.

METHODS

In a multicenter, two-by-two factorial trial, we randomly assigned patients with severe sepsis to receive either intensive insulin therapy to maintain euglycemia or conventional insulin therapy and either 10% pentastarch, a low-molecular-weight hydroxyethyl starch (HES 200/0.5), or modified Ringer's lactate for fluid resuscitation. The rate of death at 28 days and the mean score for organ failure were coprimary end points.

RESULTS

The trial was stopped early for safety reasons. Among 537 patients who could be evaluated, the mean morning blood glucose level was lower in the intensive-therapy group (112 mg per deciliter [6.2 mmol per liter]) than in the conventional-therapy group (151 mg per deciliter [8.4 mmol per liter], P<0.001). However, at 28 days, there was no significant difference between the two groups in the rate of death or the mean score for organ failure. The rate of severe hypoglycemia (glucose level, ≤40 mg per deciliter [2.2 mmol per liter]) was higher in the intensive-therapy group than in the conventional-therapy group (17 [6.3%] vs. 1 [0.4%], P<0.001). The rate of serious adverse events (10.9% vs. 5.2%, P=0.01). HES therapy was associated with higher rates of renal dysfunction and renal failure than was Ringer's lactate.

CONCLUSIONS

The use of intensive insulin therapy placed critically ill patients with sepsis at increased risk for serious adverse events related to hypoglycemia. As used in this study, HES was harmful, and its toxicity increased with accumulating doses. (ClinicalTrials.gov number, NCT00135473.)

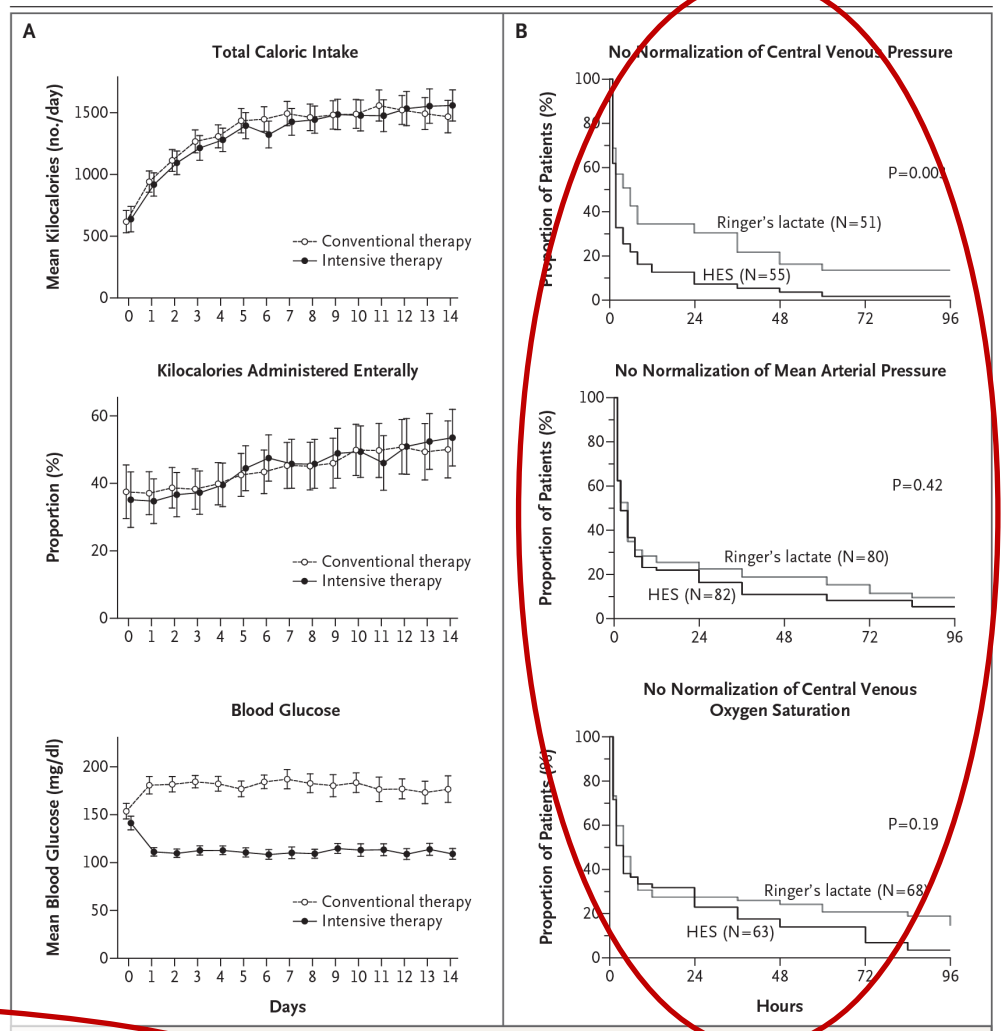


Figure 1. Nutrition, Blood Glucose, Systemic Pressures, and Central Venous Oxygen Saturation, According to the Type of Insulin and Fluid Therapy.

Panel A shows caloric intake and daily morning blood glucose levels in all 537 patients during the first 14 days of the study according to whether patients received intensive insulin therapy or conventional insulin therapy. Day 0 represents the time at randomization until the start of the next full 24-hour study day; I bars denote 95% confidence intervals. The mean daily caloric intake (both parenteral and enteral) and the fraction of kilocalories administered by the enteral route, respectively, were calculated only for days on which nutrition was given. The type of nutrition was similar in the two study groups. The mean morning blood glucose level in both study groups was calculated only for patients receiving insulin therapy on the respective study day (P<0.001). Panel B shows the results of volume resuscitation in patients receiving either 10% pentastarch, a low-molecular-weight hydroxyethyl starch (HES), or Ringer's lactate, with P values calculated by the log-rank test. Indicated are the proportions of patients who did not have normalization of hemodynamic values for central venous pressure, mean arterial pressure, and central venous oxygen saturation.

HES byl škodlivý a jeho toxicita se zvyšovala s dávkou

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

nebyl rozdíl v 90ti denní mortalitě

CONCLUSIONS

In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy. (Funded by the National Health and Medical Research Council of Australia and others; CHEST ClinicalTrials.gov number, NCT00935168.)

s HES více CRRT

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock

The CRISTAL Randomized Trial

Djillali Annane, MD, PhD; Shidasp Siami, MD; Samir Jaber, MD, PhD; Claude Martin, MD, PhD; Souheil Elatrous, MD; Adrien Descorps Declère, MD; Jean Charles Preiser, MD; Hervé Outin, MD; Gilles Troché, MD; Claire Charpentier, MD; Jean Louis Trouillet, MD; Antoine Kimmoun, MD; Xavier Forceville, MD, PhD; Michael Darmon, MD; Olivier Lesur, MD, PhD; Jean Reignier, MD; Fékri Abroug, MD; Philippe Berger, MD; Christophe Clec'h, MD, PhD; Joël Cousson, MD; Laure Thibault, MD; Sylvie Chevret, MD, PhD; for the CRISTAL Investigators

INTERVENTIONS Colloids (n = 1414; gelatins, dextrans, hydroxyethyl starches, or 4% or 20% of albumin) or crystalloids (n = 1443; isotonic or hypertonic saline or Ringer lactate solution) for all fluid interventions other than fluid maintenance throughout the ICU stay.

CONCLUSIONS AND RELEVANCE Among ICU patients with hypovolemia, the use of colloids vs crystalloids did not result in a significant difference in 28-day mortality. Although 90-day mortality was lower among patients receiving colloids, this finding should be considered exploratory and requires further study before reaching conclusions about efficacy.

stejná 28denní mortalita

JAMA. 2013;310(17):1809-1817

Intensive Care Med (2014) 40:927–934
DOI 10.1007/s00134-014-3311-y

SEVEN-DAY PROFILE PUBLICATION

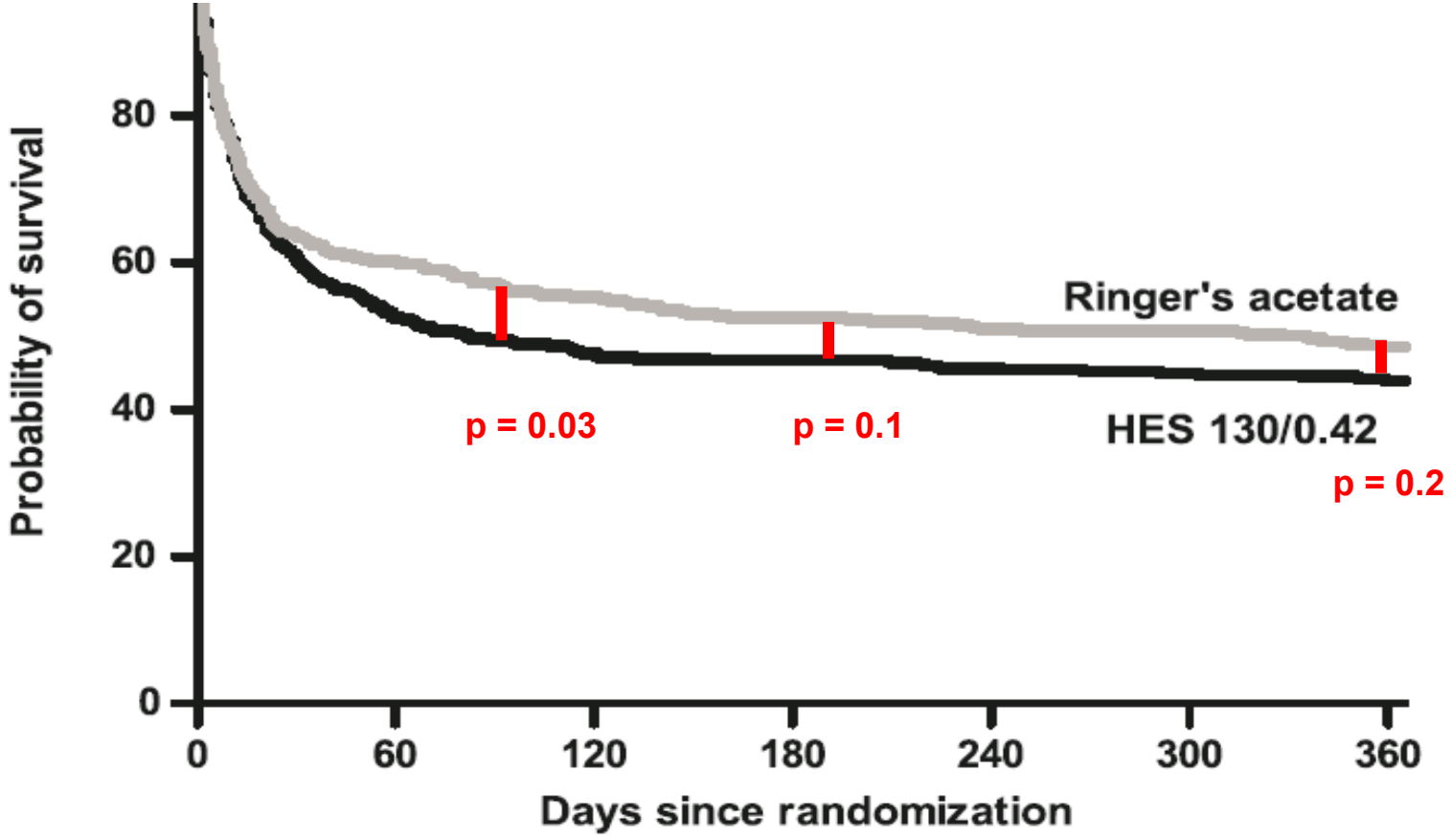
Anders Perner
Nicolai Haase
Per Winkel
Anne B. Guttormsen
Jyrki Tenhunen
Gudmundur Klemenzson
Rasmus G. Müller
Anders Åneman
Jørn Wetterslev

Long-term outcomes in patients with severe sepsis randomised to resuscitation with hydroxyethyl starch 130/0.42 or Ringer's acetate

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis



ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D., Andreas Meier-Hellmann, M.D., Max Ragaller, M.D., Norbert Weiler, M.D., Onnen Moerer, M.D., Matthias Gruendling, M.D., Michael Oppert, M.D., Stefan Grond, M.D., Derk Olthoff, M.D., Ulrich Jaschinski, M.D., Stefan John, M.D., Rolf Rossaint, M.D., Tobias Welte, M.D., Martin Schaefer, M.D., Peter Kern, M.D., Evelyn Kuhnt, M.Sc., Michael Kiehntopf, M.D., Christiane Hartog, M.D., Charles Natanson, M.D., Markus Loeffler, M.D., Ph.D., and Konrad Reinhart, M.D., for the German Competence Network Sepsis (SepNet)

ABSTRACT

BACKGROUND

The role of intensive insulin therapy in patients with severe sepsis is uncertain. Fluid resuscitation improves survival among patients with septic shock, but evidence is lacking to support the choice of either crystalloids or colloids.

METHODS

In a multicenter, two-by-two factorial trial, we randomly assigned patients with severe sepsis to receive either intensive insulin therapy to maintain euglycemia or conventional insulin therapy and either 10% pentastarch, a low-molecular-weight hydroxyethyl starch (HES 200/0.5), or modified Ringer's lactate for fluid resuscitation. The rate of death at 28 days and the mean score for organ failure were coprimary end points.

RESULTS

The trial was stopped early for safety reasons. Among 537 patients who could be evaluated, the mean morning blood glucose level was lower in the intensive-therapy group (112 mg per deciliter [6.2 mmol per liter]) than in the conventional-therapy group (151 mg per deciliter [8.4 mmol per liter], P<0.001). However, at 28 days, there was no significant difference between the two groups in the rate of death or the mean score for organ failure. The rate of severe hypoglycemia (glucose level, ≤40 mg per deciliter [2.2 mmol per liter]) was higher in the intensive-therapy group than in the conventional-therapy group (17 [6.3%] vs. 1 [0.4%], P<0.001). The rate of serious adverse events (10.9% vs. 5.2%, P=0.01). HES therapy was associated with higher rates of renal dysfunction and renal replacement therapy than was Ringer's lactate.

CONCLUSIONS

The use of intensive insulin therapy placed critically ill patients with sepsis at increased risk for serious adverse events related to hypoglycemia. As used in this study, HES was harmful, and its toxicity increased with accumulating doses. (ClinicalTrials.gov number, NCT00135473.)

HES byl škodlivý a jeho toxicita se zvyšovala s dávkou

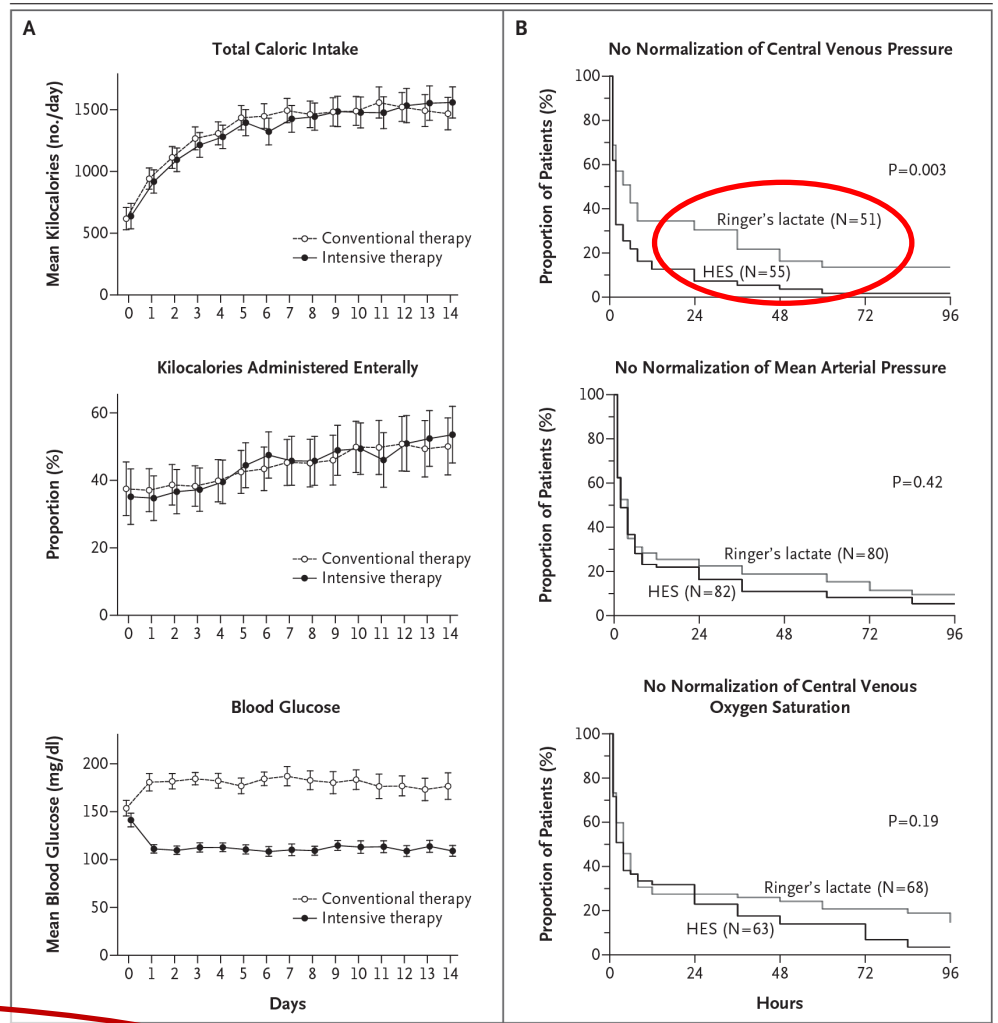


Figure 1. Nutrition, Blood Glucose, Systemic Pressures, and Central Venous Oxygen Saturation, According to the Type of Insulin and Fluid Therapy.

Panel A shows caloric intake and daily morning blood glucose levels in all 537 patients during the first 14 days of the study according to whether patients received intensive insulin therapy or conventional insulin therapy. Day 0 represents the time at randomization until the start of the next full 24-hour study day; I bars denote 95% confidence intervals. The mean daily caloric intake (both parenteral and enteral) and the fraction of kilocalories administered by the enteral route, respectively, were calculated only for days on which nutrition was given. The type of nutrition was similar in the two study groups. The mean morning blood glucose level in both study groups was calculated only for patients receiving insulin therapy on the respective study day (P<0.001). Panel B shows the results of volume resuscitation in patients receiving either 10% pentastarch, a low-molecular-weight hydroxyethyl starch (HES), or Ringer's lactate, with P values calculated by the log-rank test. Indicated are the proportions of patients who did not have normalization of hemodynamic values for central venous pressure, mean arterial pressure, and central venous oxygen saturation.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

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Nutrition and Blood Glucose Control

Data regarding nutritional intake and blood glucose levels are shown in Figure 1 and in Table 4 of the Supplementary Appendix. In the intensive-therapy group, 243 of 247 patients (98.4%) received insulin on at least one study day for glucose values above the target range (>110 mg per deciliter), whereas only 215 of 290 patients (74.1%) in the conventional-therapy group needed insulin because glucose values were outside the target range (>200 mg per deciliter) (P<0.001). During the study period, mean morning blood glucose levels were lower in the intensive-therapy group (mean, 112 mg per deciliter [6.2 mmol per liter]; 95% CI, 110 to 114 [6.1 to 6.3]) than in the conventional-therapy group (mean, 151 mg per deciliter [8.4 mmol per liter]; 95% CI, 148 to 155 [8.2 to 8.6]; P<0.001).

Table 2. (Continued.)

Variable	Insulin Therapy				Fluid Resuscitation		
	All Patients (N=537)	Conventional (N=290)	Intensive (N=247)	P Value†	Ringer's Lactate (N=275)	HES (N=262)	P Value‡
Hypoglycemia (≤40 mg/dl)				<0.001			0.85
No. of patients/total no.	54/537	12/290	42/247		27/275	27/262	
Percent (95% CI)	10.1 (7.5–12.6)	4.1 (2.9–6.4)	17.0 (12.3–21.7)		9.8 (6.3–13.3)	10.3 (6.6–14.0)	

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

nebyl rozdíl v 90ti denní mortalitě

CONCLUSIONS

In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy. (Funded by the National Health and Medical Research Council of Australia and others; CHEST ClinicalTrials.gov number, NCT00935168.)

s HES více CRRT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	HES (N=3358)	Saline (N=3384)
Age — yr	63.1±17.0	62.9±16.9
Male sex — no./total no. (%)	2030/3356 (60.5)	2041/3384 (60.3)
Weight — kg	79.4±21.0	78.6±20.8
Source of admission to ICU — no./total no. (%)		
Emergency department	930/3353 (27.7)	931/3379 (27.6)
Hospital floor	659/3353 (19.7)	668/3379 (19.8)
Another ICU	53/3353 (1.6)	41/3379 (1.2)
Another hospital	315/3353 (9.4)	306/3379 (9.1)
Operating room		
After emergency surgery	625/3353 (18.6)	630/3379 (18.6)
After elective surgery	771/3353 (23.0)	803/3379 (23.8)
Diagnosis on admission — no./total no. (%)		
Surgical cases	1426/3353 (42.5)	1450/3379 (42.9)
Nonsurgical cases	1920/3353 (57.3)	1926/3379 (57.0)
APACHE II score — median (interquartile range)†	17.0 (12.0–22.0)	17.0 (12.0–23.0)
Time from ICU admission to randomization — hr	10.9±156.5	11.4±165.4

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Predefined subgroups — no./total no. (%)		
RIFLE criteria for acute kidney injury‡	522/1449 (36.0)	511/1421 (36.0)
Sepsis	979/3355 (29.2)	958/3376 (28.4)
Trauma	267/3358 (8.0)	265/3384 (7.8)
Traumatic brain injury	28/3338 (0.8)	30/3365 (0.9)
APACHE II score ≥25	597/3335 (17.9)	624/3356 (18.6)
Receipt of HES before randomization	509/3347 (15.2)	508/3372 (15.1)

* Plus–minus values are means ±SD. There were no significant differences between the groups except for central venous pressure ($P<0.001$) and lactate level ($P<0.05$). To convert the values for creatinine to milligrams per deciliter, divide by 88.4. HES denotes hydroxyethyl starch, and ICU intensive care unit.

† Scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II range from 0 to 71, with higher scores indicating an increased risk of death.

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock

The CRISTAL Randomized Trial

Djillali Annane, MD, PhD; Shidasp Siami, MD; Samir Jaber, MD, PhD; Claude Martin, MD, PhD; Souheil Elatrous, MD; Adrien Descorps Declère, MD; Jean Charles Preiser, MD; Hervé Outin, MD; Gilles Troché, MD; Claire Charpentier, MD; Jean Louis Trouillet, MD; Antoine Kimmoun, MD; Xavier Forceville, MD, PhD; Michael Darmon, MD; Olivier Lesur, MD, PhD; Jean Reignier, MD; Fékri Abroug, MD; Philippe Berger, MD; Christophe Clec'h, MD, PhD; Joël Cousson, MD; Laure Thibault, MD; Sylvie Chevret, MD, PhD; for the CRISTAL Investigators

INTERVENTIONS Colloids (n = 1414; gelatins, dextran[illegible] of albumin) or crystalloids (n = 1443; isotonic or [illegible] for all fluid interventions other than fluid mainte[illegible]

Ačkoli 90denní mortalita byla nižší u pacientů dostávajících koloidy, tento výsledek by měl být považován pouze za průzkumný…

CONCLUSIONS AND RELEVANCE Among ICU patients with hypovolemia, the [illegible] of colloids vs crystalloids did not result in a significant difference in 28-day mortality. Although 90-day mortality was lower among patients receiving colloids, this finding should be considered exploratory and requires further study before reaching conclusions about efficacy.

stejná 28denní mortalita

JAMA. 2013;310(17):1809-1817

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effects of Fluid Resuscitat on Mortality in Critically Ill With Hypovolemic Shock

The CRISTAL Randomized

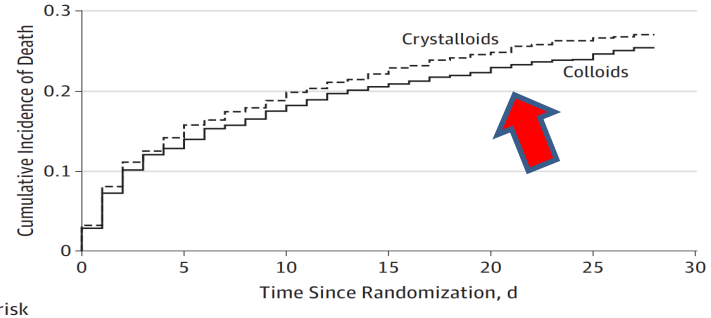
RESULTS

Dichotomous Endpoint, Two Independent Sample Study

Sample Size	
Group 1	11855
Group 2	11855
Total	**23710**

Study Parameters	
Incidence, group 1	25.4%
Incidence, group 2	27%
Alpha	0.05
Beta	0.2
Power	0.8

Figure 2. Cumulative Incidence of Death Within First 28 Days After Randomization



No. at risk

Colloids	1414	1233	1167	1124	1099	1076
Crystalloids	1443	1239	1172	1124	1089	1064

Table 2. Study Outcomes by Treatment Group

	No. (%) of Patients			
	Colloids (n = 1414)	Crystalloids (n = 1443)	RR (95% CI)	*P* Value[a]
Death				
Within 28 d	359 (25.4)	390 (27.0)	0.96 (0.88 to 1.04)	.26
Within 90 d	434 (30.7)	493 (34.2)	0.92 (0.86 to 0.99)	.03
In ICU	355 (25.1)	405 (28.1)	0.92 (0.85 to 1.00)	.06
In hospital	426 (30.1)	471 (32.6)	0.94 (0.87 to 1.02)	.07

JAMA. 2013;310(17):1809-1817

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D., Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D., Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H., Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

ABSTRACT

BACKGROUND

In 2013, New York began requiring hospitals to follow protocols for the early identification and treatment of sepsis. However, there is controversy about whether more rapid treatment of sepsis improves outcomes in patients.

METHODS

We studied data from patients with sepsis and septic shock that were reported to the New York State Department of Health from April 1, 2014, to June 30, 2016. Patients had a sepsis protocol initiated within 6 hours after arrival in the emergency department and had all items in a 3-hour bundle of care for patients with sepsis (i.e., blood cultures, broad-spectrum antibiotic agents, and lactate measurement) completed within 12 hours. Multilevel models were used to assess the associations between the time until completion of the 3-hour bundle and risk-adjusted mortality. We also examined the times to the administration of antibiotics and to the completion of an initial bolus of intravenous fluid.

RESULTS

Among 49,331 patients at 149 hospitals, 40,696 (82.5%) had the 3-hour bundle completed within 3 hours. The median time to completion of the 3-hour bundle was 1.30 hours (interquartile range, 0.65 to 2.35), the median time to the administration of antibiotics was 0.95 hours (interquartile range, 0.35 to 1.95), and the median time to completion of the fluid bolus was 2.56 hours (interquartile range, 1.33 to 4.20). Among patients who had the 3-hour bundle completed within 12 hours, a longer time to the completion of the bundle was associated with higher risk-adjusted in-hospital mortality (odds ratio, 1.04 per hour; 95% confidence interval [CI], 1.02 to 1.05; P<0.001), as was a longer time to the administration of antibiotics (odds ratio, 1.04 per hour; 95% CI, 1.03 to 1.06; P<0.001) but not a longer time to the completion of a bolus of intravenous fluids (odds ratio, 1.01 per hour; 95% CI, 0.99 to 1.02; P=0.21).

CONCLUSIONS

More rapid completion of a 3-hour bundle of sepsis care and rapid administration of antibiotics, but not rapid completion of an initial bolus of intravenous fluids, were associated with lower risk-adjusted in-hospital mortality. (Funded by the National Institutes of Health and others.)

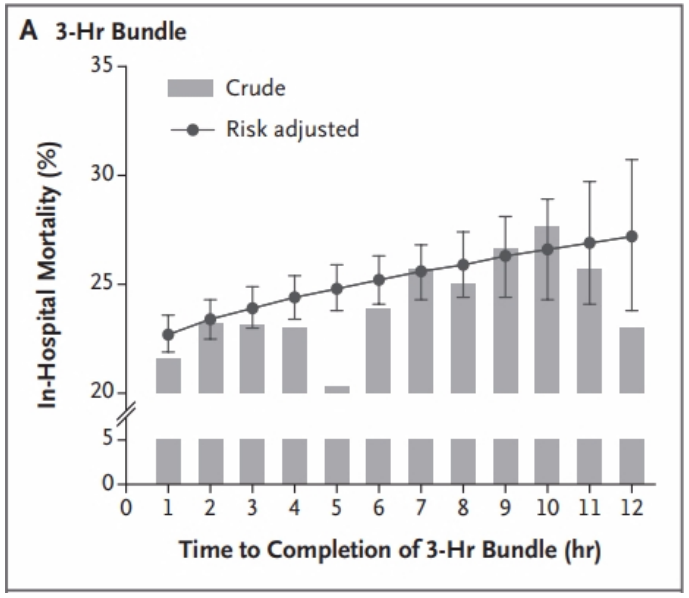
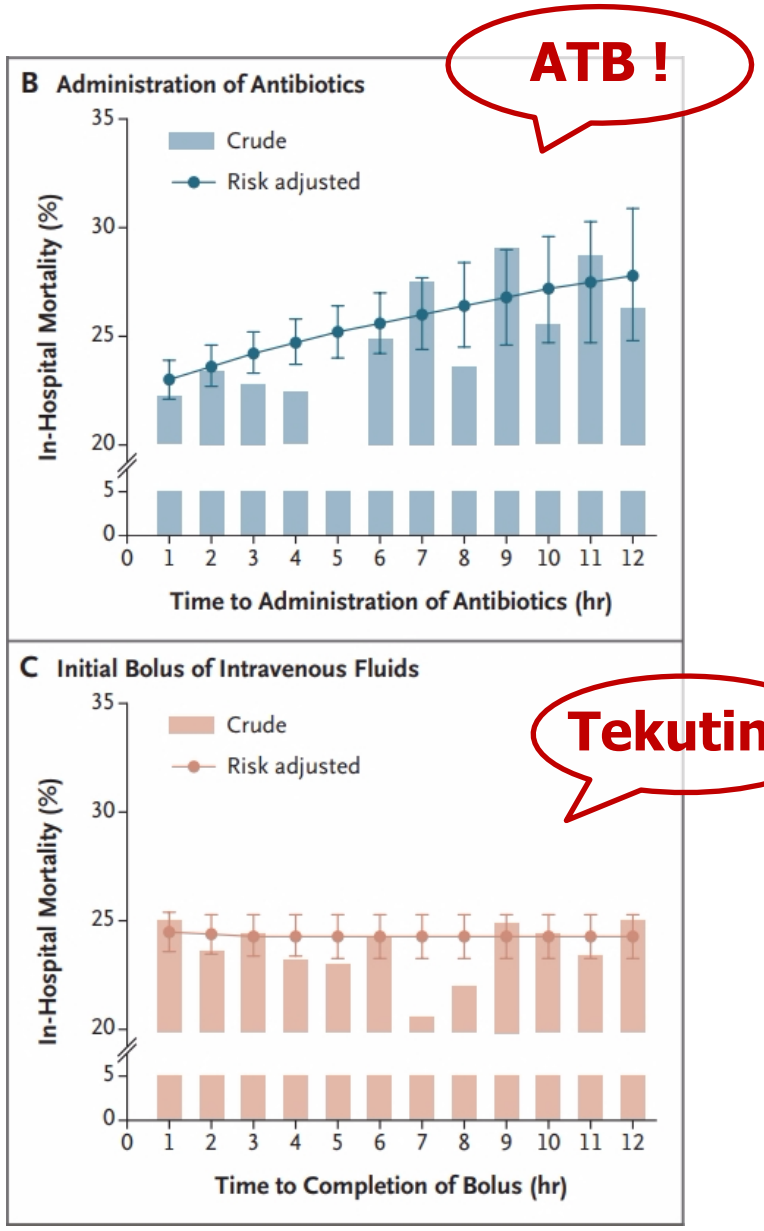


Figure 3. Crude In-Hospital Mortality and Predicted Risks of In-Hospital Death.

Shown are the crude in-hospital mortality and predicted risks of in-hospital death, with adjustment for covariates across a range of time after protocol initiation, for the completion of the 3-hour bundle of sepsis care (Panel A), the administration of broad-spectrum antibiotics (Panel B), and the completion of the initial bolus of intravenous fluids (Panel C) in a typical patient. I bars represent 95% confidence intervals.



Sepsis in European intensive care units: Results of the SOAP study*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators

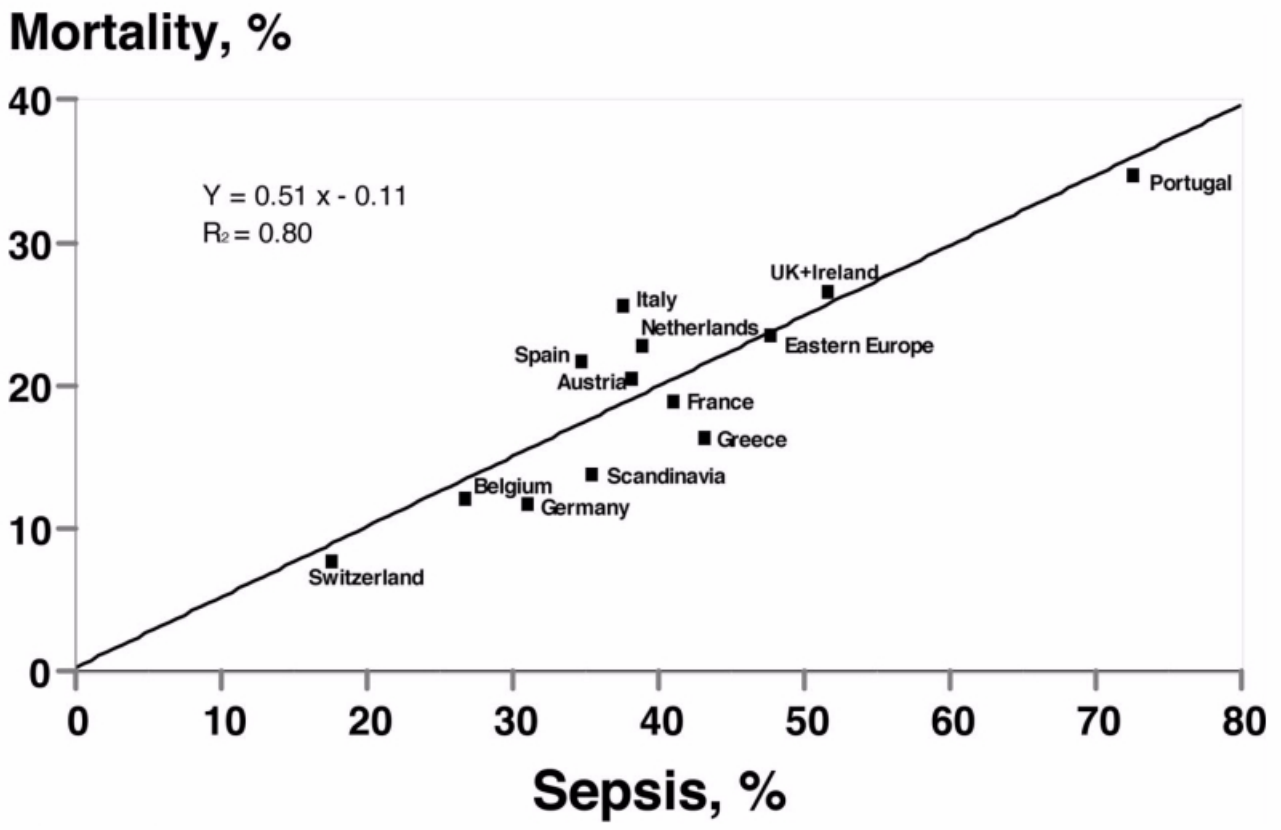


Figure 2. Relationship between intensive care unit mortality rates for all patients and frequency of sepsis in the various European countries.

EMINENCE-BASED

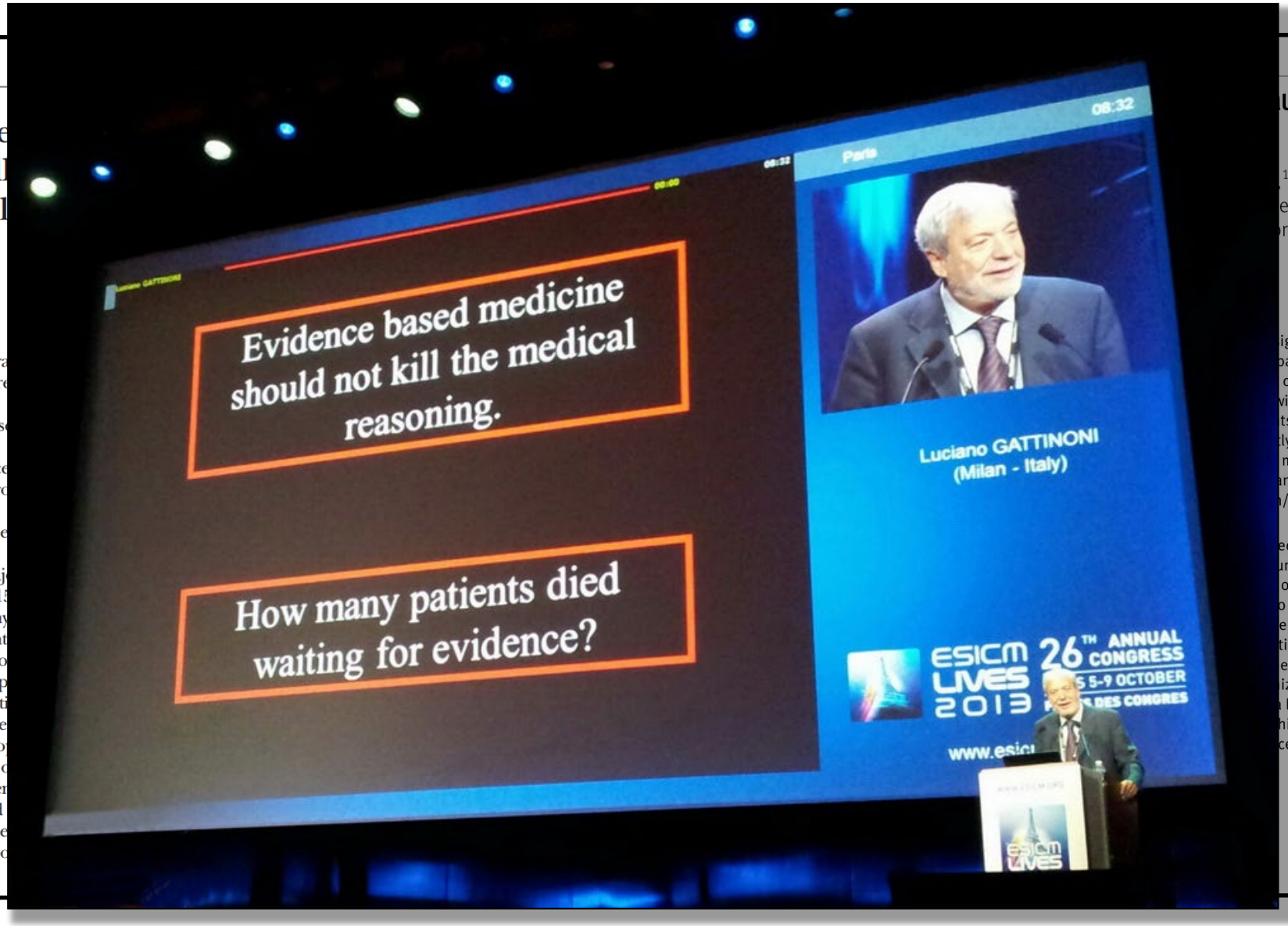
EVIDENCE-BASED

Parachute use to pre
to gravitational chall
randomised controll

Gordon C S Smith, Jill P Pell

Abstract

Objectives To determine whether para
effective in preventing major trauma re
gravitational challenge.
Design Systematic review of randomis
trials.
Data sources: Medline, Web of Science
the Cochrane Library databases; appro
sites and citation lists.
Study selection: Studies showing the e
a parachute during free fall.
Main outcome measure Death or maj
defined as an injury severity score >1
Results We were unable to identify any
controlled trials of parachute interven
Conclusions As with many interventio
prevent ill health, the effectiveness of p
not been subjected to rigorous evaluati
randomised controlled trials. Advocate
based medicine have criticised the ado
interventions evaluated by using only
data. We think that everyone might ben
radical protagonists of evidence based
organised and participated in a double
randomised, placebo controlled, crosso
parachute.



BMJ 2003;327:1459-61

uma when jumping

[1] Daniel B Kramer,[1]
eier,[3] Dhruv S Kazi,[1]
rs

ignificantly reduce death
parachute *v* 0% for control;
consistent across multiple
with individuals screened but
ts included in the study were
ly lower altitude (mean of
mean of 9146 m for non-
nd lower velocity (mean of 0
/h; P<0.001).

educe death or major
mping from aircraft in the first
of this intervention. However,
o enroll participants on small
e ground, suggesting cautious
titude jumps. When beliefs
ess of an intervention exist in
ized trials might selectively
lower perceived likelihood
ning the applicability of the
ce.

BMJ 2018;363:k5094

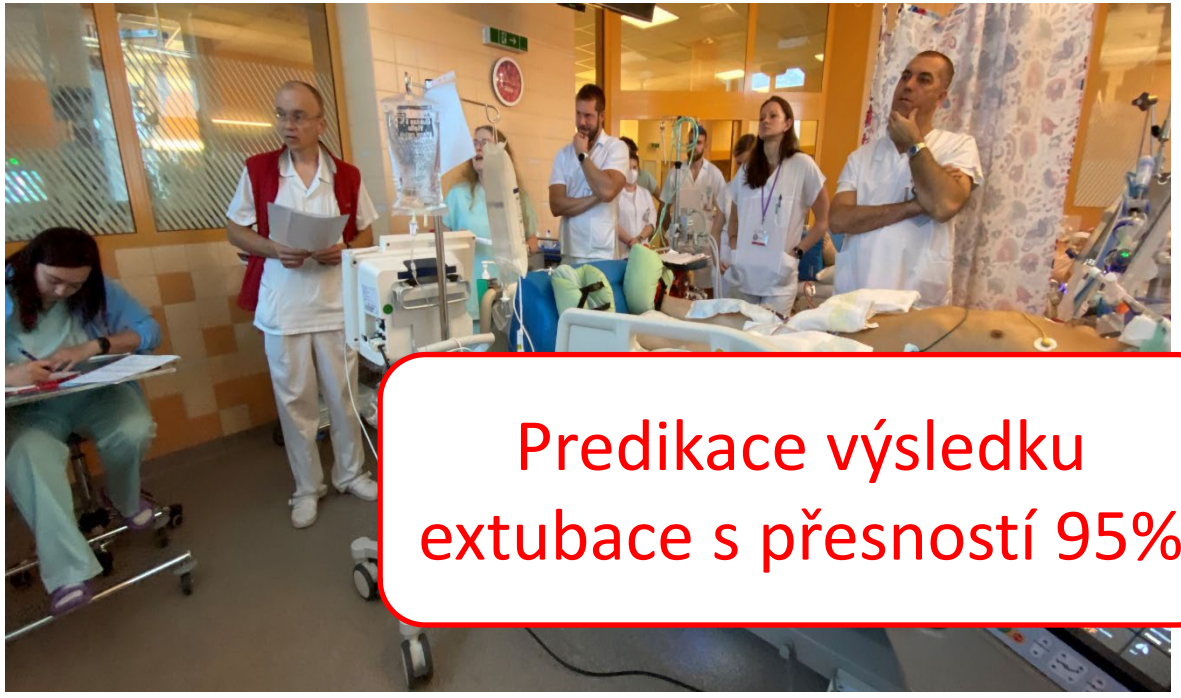
Computer Methods and Programs in Biomedicine 200 (2021) 105869

A Machine Learning decision-making tool for extubation in Intensive Care Unit patients

Alexandre Fabregat[a], Mónica Magret[b], Josep Anton Ferré[a], Anton Vernet[a], Neus Guasch[b], Alejandro Rodríguez[b], Josep Gómez[b,*], María Bodí[b]

[a] Department of Mechanical Engineering, Universitat Rovira i Virgili. Av. Països Catalans, 26 (43007) Tarragona, Spain
[b] Hospital Universitari de Tarragona Joan XXIII Institut d'Investigaci, Sanitária Pere Virgili, Universitat Rovira i Virgili. C/. Tarragona, Spain

Conclusions: Machine Learning-based tools have been found to accurately predict the extubation outcome in critical patients with invasive mechanical ventilation. The use of this important predictive capability to assess the extubation decision could potentially reduce the rate of extubation failure, currently at 9%. With about 40% of critically ill patients eventually receiving invasive mechanical ventilation during their stay and given the serious potential complications associated to reintubation, the excellent predictive ability of the model presented here suggests that Machine Learning techniques could significantly improve the clinical outcomes of critical patients.



Predikace výsledku extubace s přesností 95%

Table 1 List and characteristics of the variables used as model predictors.

Variable	Units	Symbol	Type	Comments
Time under IMV	h	Δt	I	
Ventilation mode	-	V-Mode	I	
Tidal Volume	L	V_T	I	
Heart Rate	m^{-1}	HR	I	
Respiratory rate	m^{-1}	RR	I	
Peak inspiratory pressure	cmH_2O	P_{IP}	I	
Plateau Pressure	cmH_2O	P_{PLAT}	I	
O_2 saturation to inspired fraction ratio	-	SpFiO2	I	
Respiratory rate-oxygenation index	min	ROX	II	SpFiO2/RR
Rapid Shallow Breathing Index	L^{-1}	RSBI	II	RR/V_T
Number of previous MV events	-	NPE	III	
Total Cumulative Dose (sedatives and analgesics)	mg	TCD	III	
Total Given Dose (sedatives and analgesics)	mg	TGD	III	
Glasgow Coma Scale	-	GCS	III	
Richmond Agitation-Sedation Scale	-	RASS	III	
Age at admission to ICU	yr	AGE	IV	
APACHE II score	-	APACHEII	IV	
Body Mass Index at admission to ICU	kgm^{-2}	BMI	IV	
Gender	-	GENDER	IV	Categorical
SEMICYUC code	-	ICUAR	IV	Categorical

Table 4
Mean accuracy and AUROC for each classifier using a classification threshold of 0.5 and undersampling for class imbalance.

Classifier	% Accuracy	% AUROC
SVM	94.6	98.3
GBM	89.6	96.1
LDA	72.4	79.4

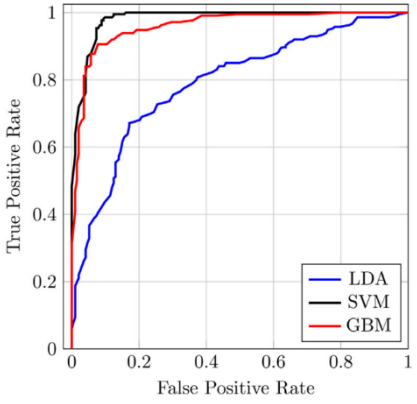


Fig. 2. Mean ROC curve for SVM, GBM and LDA classifiers.

OPEN

Mortality prediction of patients in intensive care units using machine learning algorithms based on electronic health records

Min Hyuk Choi[1], Dokyun Kim[1], Eui Jun Choi[2], Yeo Jin Jung[2], Yong Jun Choi[3], Jae Hwa Cho[3] & Seok Hoon Jeong[1]✉

Improving predictive models for intensive care unit (ICU) inpatients requires a new strategy that periodically includes the latest clinical data and can be updated to reflect local characteristics. We extracted data from all adult patients admitted to the ICUs of two university hospitals with different characteristics from 2006 to 2020, and a total of 85,146 patients were included in this study. Machine learning algorithms were trained to predict in-hospital mortality. The predictive performance of conventional scoring models and machine learning algorithms was assessed by the area under the receiver operating characteristic curve (AUROC). The conventional scoring models had hardly predictive powers, with the highest AUROC of 0.810 for hospital G) showing the highest AUROC among them. The best performing machine learning models achieved an AUROC of 0.977 (0.973–0.980) in hospital S and 0.955 (0.950–0.961) in hospital G. The use of ML models in conjunction with conventional scoring systems can provide more useful information for predicting the prognosis of critically ill patients. In this study, we suggest that the predictive model can be made more robust by training with the individual data of each hospital.

AUROC of 0.977 (0.973–0.980)

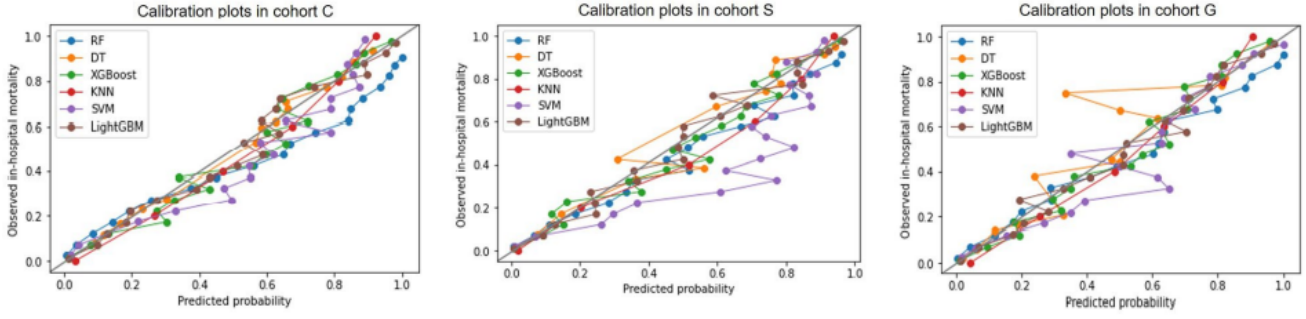


Figure 2. Comparison of machine learning-based in-hospital mortality prediction models.

The calibration plots show the agreement of between predicted probability and observed in-hospital mortality. The black line at 45 degrees indicates perfect calibration where the predicted and observed probabilities are equal.

Admission variables (obtained within 24 h of ICU admission)	Hospital S				Hospital G				
	Overall (N = 61,589)	No hospital mortality (N = 54,313)	Hospital mortality (N = 7276)	P*	Overall (N = 23,557)	No hospital mortality (N = 19,458)	Hospital mortality (N = 4099)	P*	P†
Age, years	67 [57–74]	66 [57–74]	67 [56–76]	< 0.001	65 [53–75]	64 [52–74]	70 [58–78]	< 0.001	< 0.001
Sex				0.004				0.174	< 0.001
Female	22,744 (36.9%)	19,944 (36.7%)	2800 (38.5%)		9034 (38.3%)	7501 (38.5%)	1533 (37.4%)		
Male	38,845 (63.1%)	34,369 (63.3%)	4476 (61.5%)		14,523 (61.7%)	11,957 (61.5%)	2566 (62.6%)		
Types of admission				< 0.001				< 0.001	< 0.001
Medical	39,560 (64.2%)	34,232 (63.0%)	5328 (73.2%)		11,365 (48.2%)	9073 (46.6%)	2292 (55.9%)		
Surgical	22,029 (35.8%)	20,081 (37.0%)	1948 (26.8%)		12,192 (51.8%)	10,385 (53.4%)	1807 (44.1%)		
Year of admission				< 0.001				< 0.001	0.033
2006–2010	16,531 (26.8%)	14,422 (26.6%)	2109 (29.0%)		6379 (27.1%)	5322 (27.4%)	1057 (25.8%)		
2011–2015	20,945 (34.0%)	18,371 (33.8%)	2574 (35.4%)		8179 (34.7%)	6637 (34.1%)	1542 (37.6%)		
2016–2020	24,113 (39.2%)	21,520 (39.6%)	2593 (35.6%)		8999 (38.2%)	7499 (38.5%)	1500 (36.6%)		
Conventional scoring systems									
APACHE II	13 [10–17]	13 [10–16]	19 [13–26]	< 0.001	16 [11–21]	15 [10–19]	22 [18–28]	< 0.001	< 0.001
APACHE III	55 [47–65]	54 [46–63]	74 [57–96]	< 0.001	60 [50–74]	57 [48–69]	79 [66–95]	< 0.001	< 0.001
SAPS II	34 [28–42]	33 [27–40]	48 [36–64]	< 0.001	37 [29–48]	35 [27–44]	52 [42–64]	< 0.001	< 0.001
SAPS III	47 [40–55]	46 [40–53]	59 [50–70]	< 0.001	51 [43–61]	49 [42–57]	65 [56–74]	< 0.001	< 0.001
MPM0 II	2 [2–2]	2 [2–2]	2 [1–3]	< 0.001	2 [1, 2]	1 [1, 2]	2 [1–3]	< 0.001	< 0.001
MPM0 III	2 [2–3]	2 [2, 3]	2 [1–3]	< 0.001	2 [1, 2]	2 [1, 2]	2 [2–4]	< 0.001	< 0.001
SOFA	4 [2–8]	4 [2–7]	7 [4–11]	< 0.001	6 [3–9]	6 [2–9]	10 [7–12]	< 0.001	< 0.001
Pitt bacteremia score	1 [0–4]	1 [0–4]	2 [0–5]	< 0.001	3 [1–5]	3 [1–4]	5 [3–7]	< 0.001	< 0.001
Underlying comorbidities									
Charlson comorbidity index	5 [4–6]	5 [4–6]	5 [4–7]	< 0.001	5 [3–6]	4 [3–6]	5 [4–7]	< 0.001	< 0.001
Cancer	5137 (8.3%)	3101 (5.7%)	2036 (28.0%)	< 0.001	4239 (18.0%)	3002 (15.4%)	1237 (30.2%)	< 0.001	< 0.001
Cerebrovascular diseases	14,373 (23.3%)	13,433 (24.7%)	940 (12.9%)	< 0.001	4533 (19.2%)	3716 (19.1%)	817 (19.9%)	0.226	< 0.001
Diabetes mellitus	16,696 (27.1%)	15,126 (27.8%)	1570 (21.6%)	< 0.001	4086 (17.3%)	3391 (17.4%)	695 (17.0%)	0.482	< 0.001
Hypertension	28,407 (46.1%)	26,538 (48.9%)	1869 (25.7%)	< 0.001	5406 (22.9%)	4677 (24.0%)	729 (17.8%)	< 0.001	< 0.001
Chronic pulmonary diseases	1832 (3.0%)	1364 (2.5%)	468 (6.4%)	< 0.001	541 (2.3%)	332 (1.7%)	209 (5.1%)	< 0.001	< 0.001
Hemiplegia	2041 (3.3%)	1900 (3.5%)	141 (1.9%)	< 0.001	1650 (7.0%)	1500 (7.7%)	150 (3.7%)	< 0.001	< 0.001
Liver diseases	2080 (3.4%)	1235 (2.3%)	845 (11.6%)	< 0.001	1248 (5.3%)	922 (4.7%)	326 (8.0%)	< 0.001	< 0.001
Myocardial infarction	11,682 (19.0%)	10,888 (20.0%)	794 (10.9%)	< 0.001	2886 (12.3%)	2482 (12.8%)	404 (9.9%)	< 0.001	< 0.001
Renal diseases	3462 (5.6%)	2798 (5.2%)	664 (9.1%)	< 0.001	1367 (5.8%)	981 (5.0%)	386 (9.4%)	< 0.001	0.313
Ulcer	1168 (1.9%)	926 (1.7%)	242 (3.3%)	< 0.001	485 (2.1%)	370 (1.9%)	115 (2.8%)	< 0.001	0.131
Transplantation	766 (1.2%)	265 (0.5%)	501 (6.9%)	< 0.001	203 (0.9%)	153 (0.8%)	50 (1.2%)	0.008	< 0.001
Ventilator use	10,537 (17.1%)	8895 (16.4%)	1642 (22.6%)	< 0.001	5957 (25.3%)	4745 (24.4%)	1212 (29.6%)	< 0.001	< 0.001
Vasopressor use	21,448 (34.8%)	18,089 (33.3%)	3359 (46.2%)	< 0.001	11,708 (49.7%)	8439 (43.4%)	3269 (79.8%)	< 0.001	< 0.001
Cardiac arrest	809 (1.3%)	694 (1.3%)	115 (1.6%)	0.038	1228 (5.2%)	414 (2.1%)	814 (19.9%)	< 0.001	< 0.001
Bacterial infection on ICU admission									
Site of infection				< 0.001				< 0.001	< 0.001
Multiple sites	843 (1.4%)	108 (0.2%)	735 (10.1%)		275 (1.2%)	906 (4.7%)	529 (12.9%)		
Lungs	428 (0.7%)	283 (0.5%)	145 (2.0%)		1435 (6.1%)	383 (2.0%)	238 (5.8%)		
Bloodstream	251 (0.4%)	119 (0.2%)	132 (1.8%)		183 (0.8%)	110 (0.6%)	73 (1.8%)		
Urinary tract	503 (0.8%)	363 (0.7%)	140 (1.9%)		621 (2.6%)	383 (2.0%)	238 (5.8%)		
CNS	3 (0.0%)	0 (0.0%)	3 (0.0%)		0 (0.0%)	165 (0.8%)	110 (2.7%)		
Abdomen	27 (0.0%)	19 (0.0%)	8 (0.1%)		156 (0.7%)	103 (0.5%)	53 (1.3%)		
None	59,521 (96.6%)	53,418 (98.4%)	6103 (83.9%)		20,887 (88.7%)	17,791 (91.4%)	3096 (75.5%)		
Antibiotic use at ICU admission (may be multiple)	28,255 (45.9%)	22,754 (41.9%)	5501 (75.6%)	< 0.001	16,867 (71.6%)	13,110 (67.4%)	3757 (91.7%)	< 0.001	< 0.001
3rd-generation cephalosporins	6788 (11.0%)	4947 (9.1%)	1841 (25.3%)	< 0.001	5649 (24.0%)	4490 (23.1%)	1159 (28.3%)	< 0.001	< 0.001
4th-generation cephalosporins	450 (0.7%)	30 (0.1%)	420 (5.8%)	< 0.001	591 (2.5%)	296 (1.5%)	295 (7.2%)	< 0.001	< 0.001
Beta lactam/beta lactamase inhibitors	8744 (14.2%)	5646 (10.4%)	3098 (42.6%)	< 0.001	6362 (27.0%)	4401 (22.6%)	1961 (47.8%)	< 0.001	< 0.001
Carbapenems	2300 (3.7%)	587 (1.1%)	1713 (23.5%)	< 0.001	2524 (10.7%)	1409 (7.2%)	1115 (27.2%)	< 0.001	< 0.001
Glycopeptides	7144 (11.6%)	4280 (7.9%)	2864 (39.4%)	< 0.001	3526 (15.0%)	2182 (11.2%)	1344 (32.8%)	< 0.001	< 0.001
Penicillins	3389 (5.5%)	3082 (5.7%)	307 (4.2%)	< 0.001	211 (0.9%)	150 (0.8%)	61 (1.5%)	< 0.001	< 0.001
Quinolones	3926 (6.4%)	1773 (3.3%)	2153 (29.6%)	< 0.001	4369 (18.5%)	2845 (14.6%)	1524 (37.2%)	< 0.001	< 0.001

Machine-learning Algorithm to Predict Hypotension Based on High-fidelity Arterial Pressure Waveform Analysis

Feras Hatib, Ph.D., Zhongping Jian, Ph.D., Sai Buddi, Ph.D., Christine Lee, M.S., Jos Settels, M.S., Karen Sibert, M.D., F.A.S.A., Joseph Rinehart, M.D., Maxime Cannesson, M.D., Ph.D.

ABSTRACT

Background: With appropriate algorithms, computers can learn to detect patterns and associations in large data sets. The authors' goal was to apply machine learning to arterial pressure waveforms and create an algorithm to predict hypotension. The algorithm detects early alteration in waveforms that can herald the weakening of cardiovascular compensatory mechanisms affecting preload, afterload, and contractility.

Methods: The algorithm was dev ist- ing of 1,334 patients' records wit (2) a prospective, local hospital coho rial waveform recording and 1,923 ep gh- fidelity arterial pressure waveform lg). Receiver-operating characteristic ean arterial pressure less than 65 mmHg.

Results: Using 3,022 individual features per cardiac cycle, the algorithm predicted arterial hypotension with a sensitivity and specificity of 88% (85 to 90%) and 87% (85 to 90%) 15 min before a hypotensive event (area under the curve, 0.95 [0.94 to 0.95]); 89% (87 to 91%) and 90% (87 to 92%) 10 min before (area under the curve, 0.95 [0.95 to 0.96]); 92% (90 to 94%) and 92% (90 to 94%) 5 min before (area under the curve, 0.97 [0.97 to 0.98]).

Conclusions: The results demonstrate that a machine-learning algorithm can be trained, with large data sets of high-fidelity arterial waveforms, to predict hypotension in surgical patients' records. (ANESTHESIOLOGY 2018; 129:663-74)

Sensitivita i specificita 88%
15 min před začátkem události

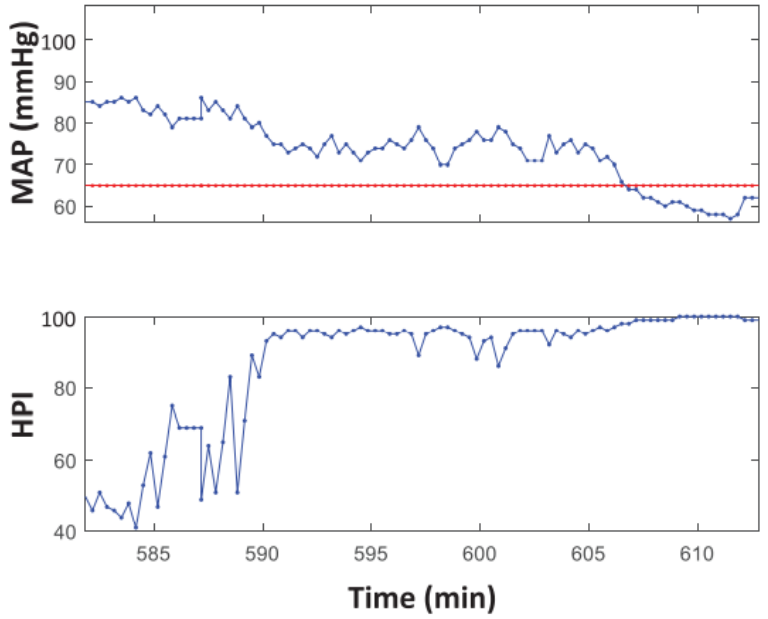


Fig. 5. One illustrative patient record showing the association between the algorithm output (Hypotension Prediction Index [HPI]) and the evolution of mean arterial pressure (MAP) over time.


KROMĚ MNE...
Everybody lies.
HOUSE M.D.

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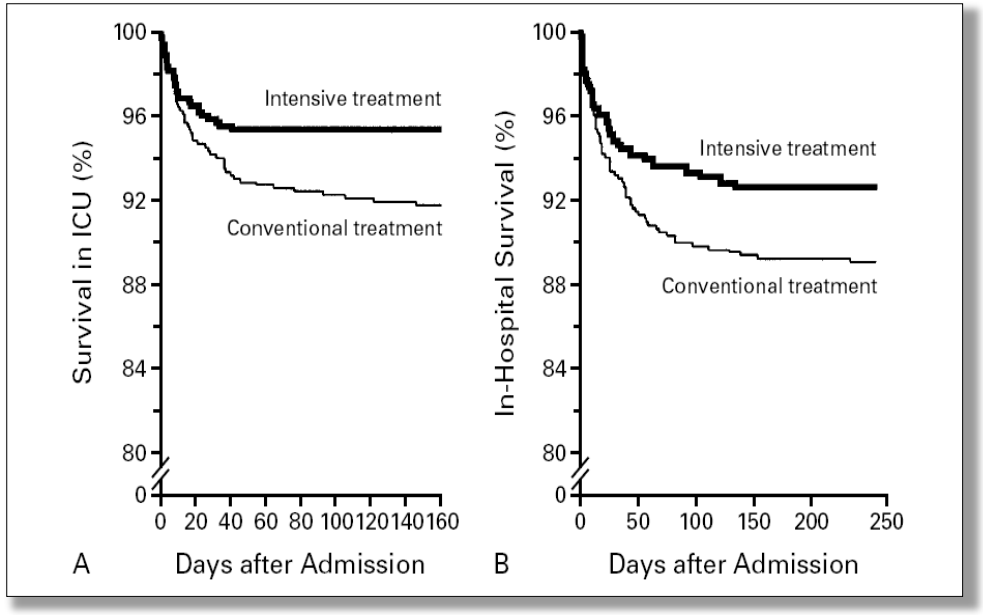
INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.SC., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.



METHODS

Study Population

All adults receiving mechanical ventilation who were admitted to our intensive care unit (which is dedicated primarily but not exclusively to surgical patients) between February 2, 2000, and January 18, 2001, were eligible for enrollment in the study after written informed consent had been obtained from the closest family member. Only 14 patients were excluded: 5 who were participating in other trials, and 9 who were moribund or for whom there were do-not-resuscitate orders. The protocol was approved by the institutional review board.

Four patients had renal failure requiring dialysis before admission. Among the patients who were admitted to the intensive care unit after cardiac surg had undergone coronar nt, and 14 percent nt of the patients h re- ceiving treatment with cose level on admission exceeded the upper limit of the normal range after an overnight fast (110 mg per deciliter [6.1 mmol per liter]) in 75 percent of the patients but was in the nonfasting diabetic range (>200 mg per deciliter [11.1 mmol per liter]) in only 12 percent.[21,22]

72% pacientů
bylo po kardiochirurgickém výkonu

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 2, 2006 VOL. 354 NO. 5

Intensive Insulin Therapy in the Medical ICU

Greet Van den Berghe, M.D., Ph.D., Alexander Wilmer, M.D., Ph.D., Greet Hermans, M.D., Wouter Meersseman, M.D., Pieter J. Wouters, M.Sc., Ilse Milants, R.N., Eric Van Wijngaerden, M.D., Ph.D., Herman Bobbaers, M.D., Ph.D., and Roger Bouillon, M.D., Ph.D.

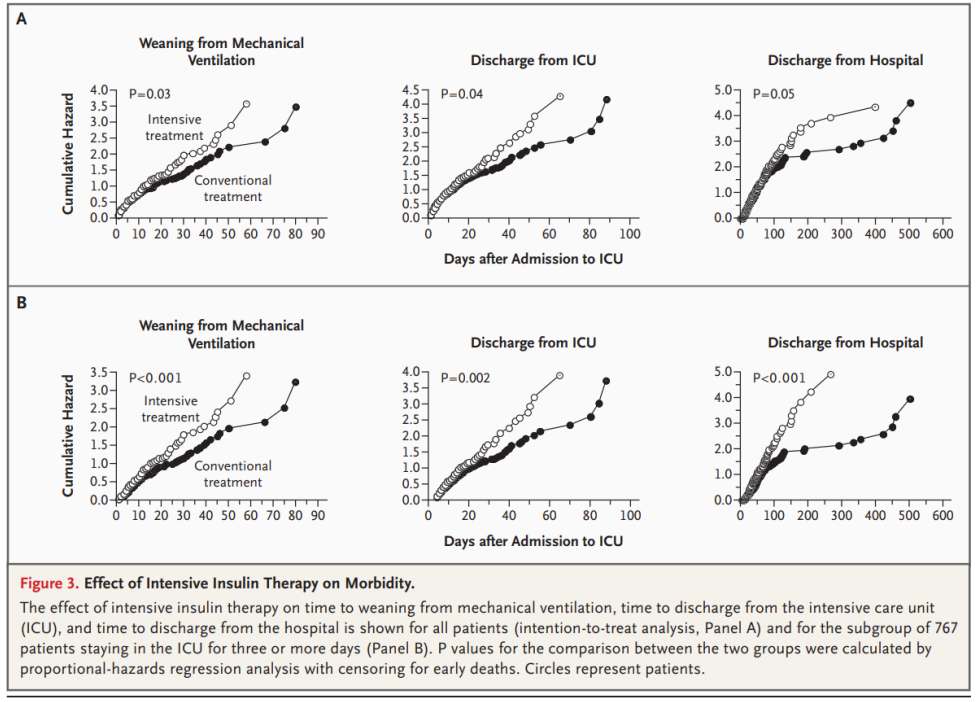


Figure 3. Effect of Intensive Insulin Therapy on Morbidity.

The effect of intensive insulin therapy on time to weaning from mechanical ventilation, time to discharge from the intensive care unit (ICU), and time to discharge from the hospital is shown for all patients (intention-to-treat analysis, Panel A) and for the subgroup of 767 patients staying in the ICU for three or more days (Panel B). P values for the comparison between the two groups were calculated by proportional-hazards regression analysis with censoring for early deaths. Circles represent patients.

Efekt pouze u pacientů
s pobytem na ICU >3 dny

RESULTS

In the intention-to-treat a… …n therapy reduced blood glucose levels but did not significantly reduce in-hospital mortality (40.0 percent in the conventional-treatment group vs. 37.3 percent in the intensive-treatment group, P=0.33). However, morbidity was significantly reduced by the prevention of newly acquired kidney injury, accelerated weaning from mechanical ventilation, and accelerated discharge from the ICU and the hospital. Although length of stay in the ICU could not be predicted on admission, among 433 patients who stayed in the ICU for less than three days, mortality was greater among those receiving intensive insulin therapy. In contrast, among 767 patients who stayed in the ICU for three or more days, in-hospital mortality in the 386 who received intensive insulin therapy was reduced from 52.5 to 43.0 percent (P=0.009) and morbidity was also reduced.

CONCLUSIONS

Intensive insulin therapy significantly reduced morbidity but not mortality among all patients in the medical ICU. Although the risk of subsequent death and disease was reduced in patients treated for three or more days, these patients could not be identified before therapy. Further studies are needed to confirm these preliminary data. (ClinicalTrials.gov number, NCT00115479.)

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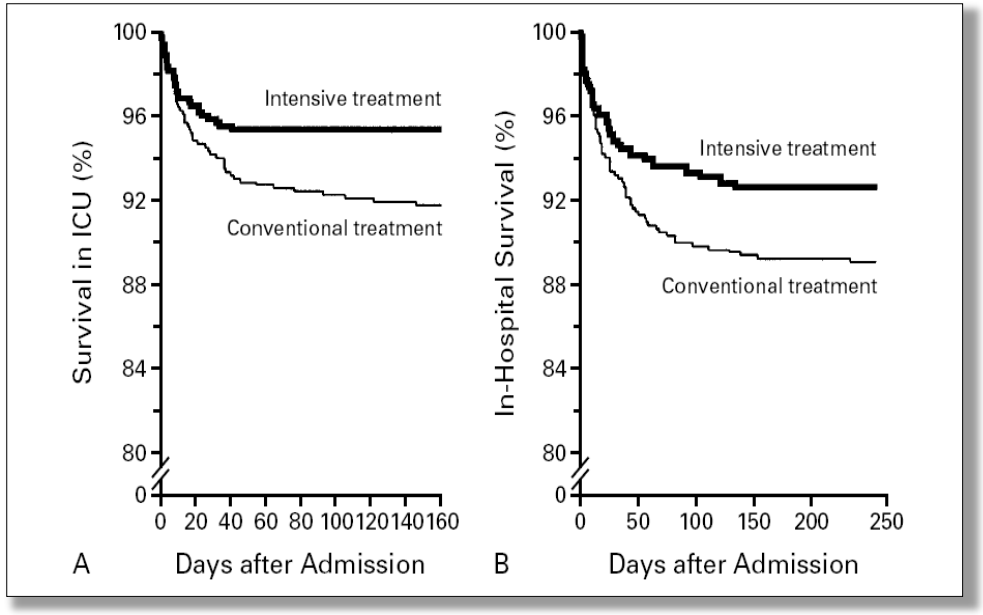

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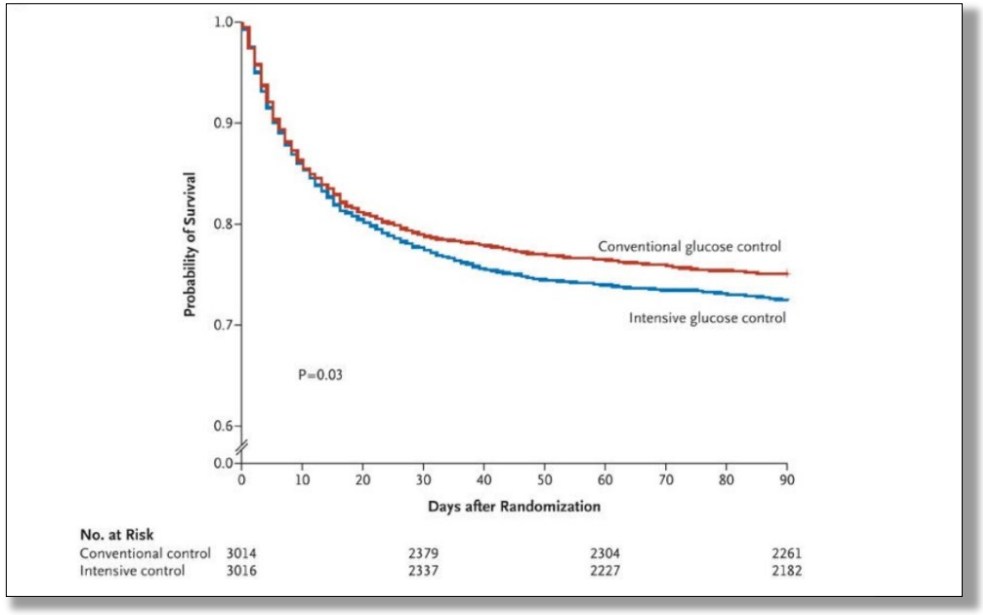
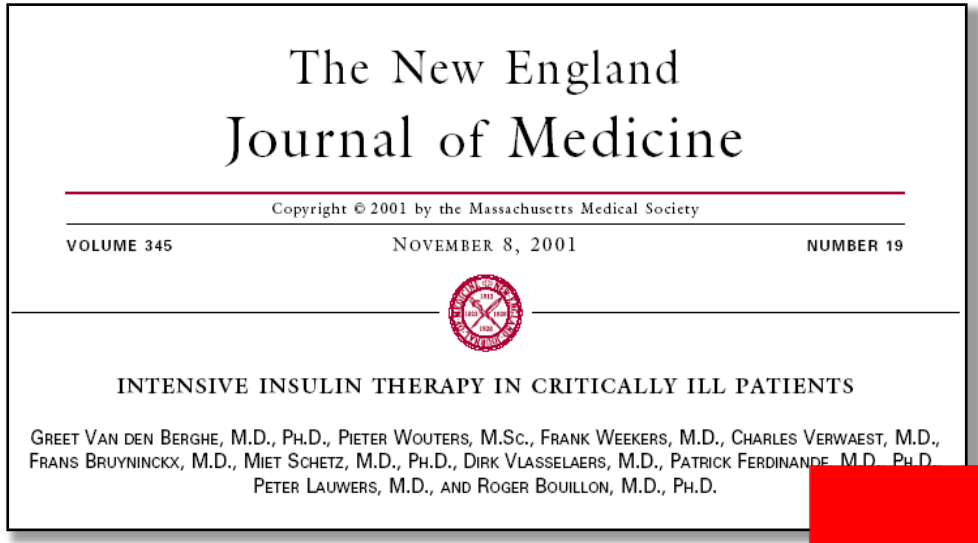
Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*





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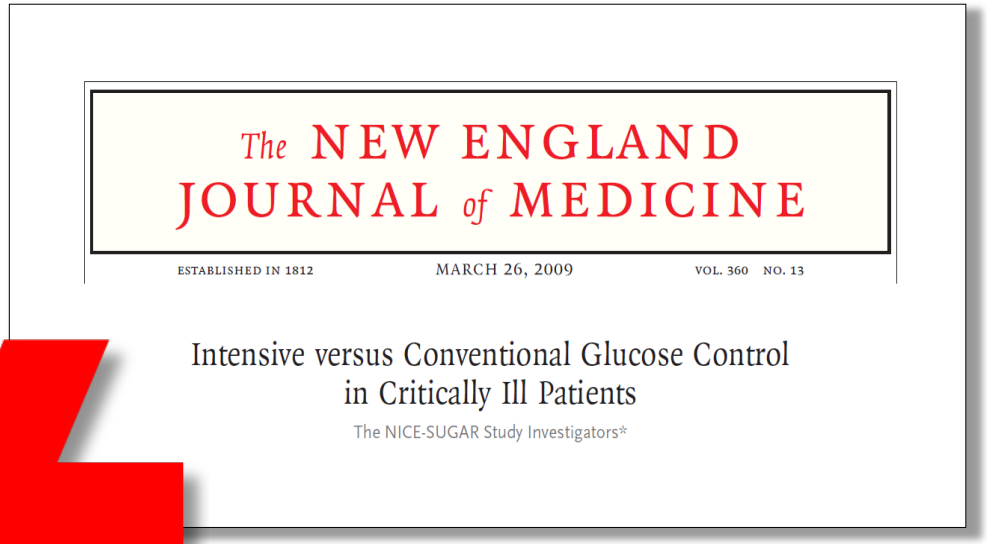

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Intensive versus Conventional Glucose Control in Critically Ill Patients

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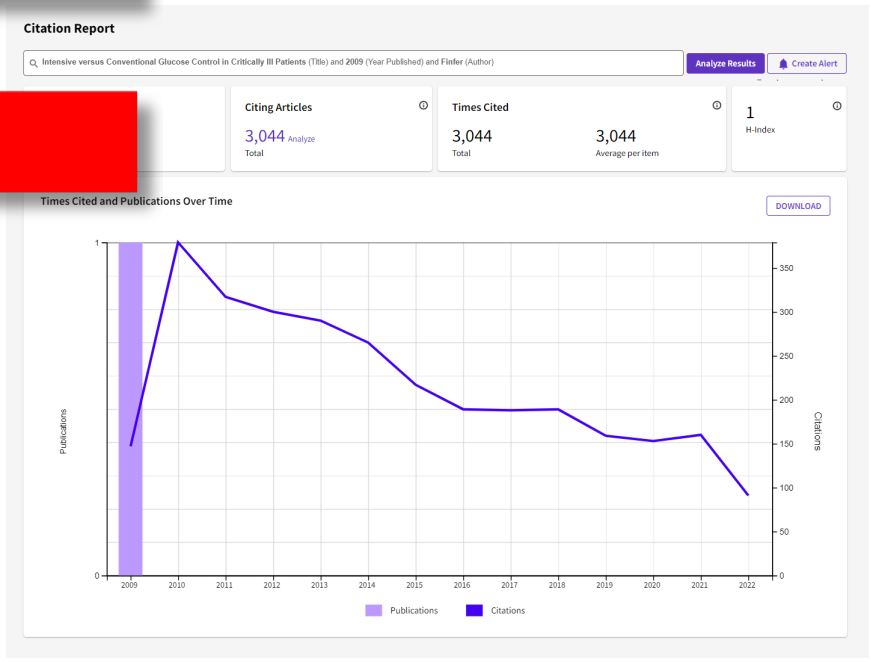

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Intensive versus Conventional Glucose Control in Critically Ill Patients

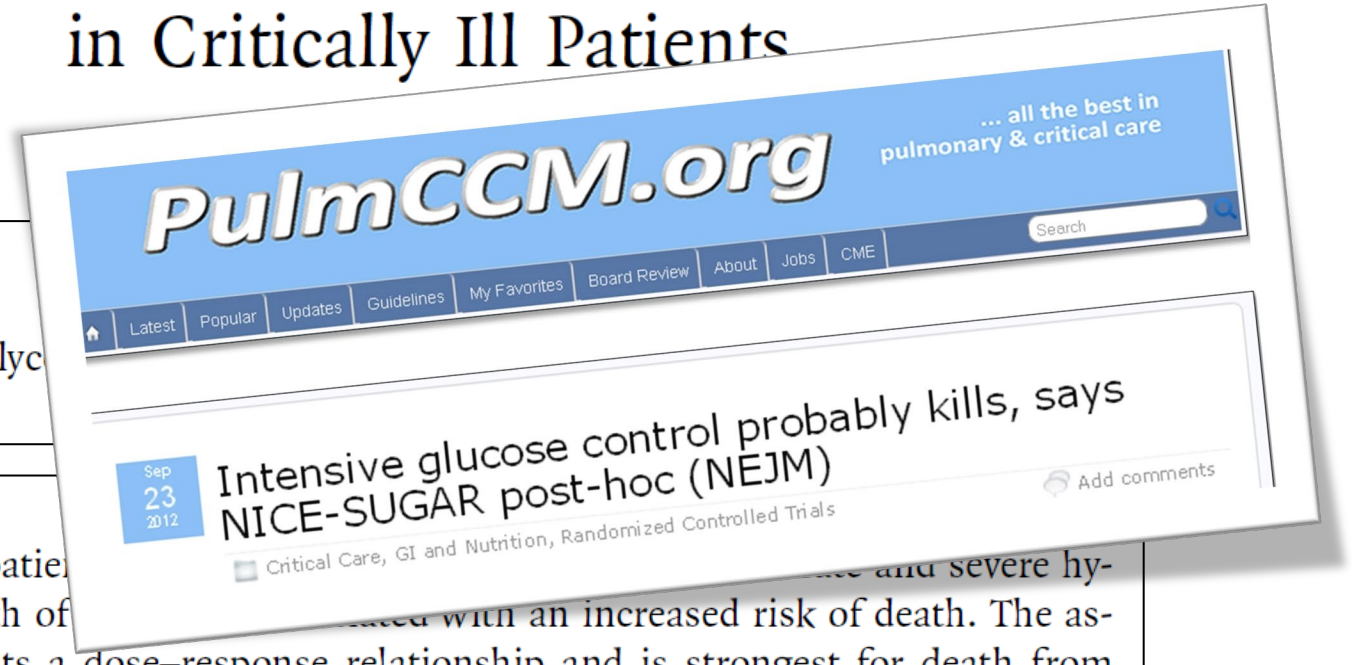
The NICE-SUGAR Study Investigators*

Table 3. Outcomes and Adverse Events.*

Outcome Measure	Intensive Glucose Control	Conventional Glucose Control	Odds Ratio or Absolute Difference (95% CI)†	Statistical Test	P Value
Death — no. of patients/total no. (%)				Logistic regression	
At day 90	829/3010 (27.5)	751/3012 (24.9)	1.14 (1.02 to 1.28)		0.02
At day 28	670/3010 (22.3)	627/3012 (20.8)	1.09 (0.96 to 1.23)		0.17
Severe hypoglycemia — no. of patients/total no. (%)	206/3016 (6.8)	15/3014 (0.5)	14.7 (9.0 to 25.9)	Logistic regression	<0.001
Days in ICU — median (IQR)	6 (2 to 11)	6 (2 to 11)	0	Log-rank test	0.84
Days in hospital — median (IQR)	17 (8 to 35)	17 (8 to 35)	0	Log-rank test	0.86
Mechanical ventilation — no. of patients/total no. (%)	2894/3014 (96.0)	2872/3014 (95.3)	0.7 (–0.3 to 1.76)	Pearson's test	0.17
Days of mechanical ventilation	6.6±6.6	6.6±6.5	0	Wilcoxon rank-sum test	0.56
Renal-replacement therapy — no. of patients/total no. (%)	465/3014 (15.4)	438/3014 (14.5)	0.9 (–0.9 to 2.7)	Pearson's test	0.34
Days of renal-replacement therapy	0.8±2.6	0.8±2.8	0	Wilcoxon rank-sum test	0.39

ORIGINAL ARTICLE

Hypoglycemia and Risk of Death in Critically Ill Patients

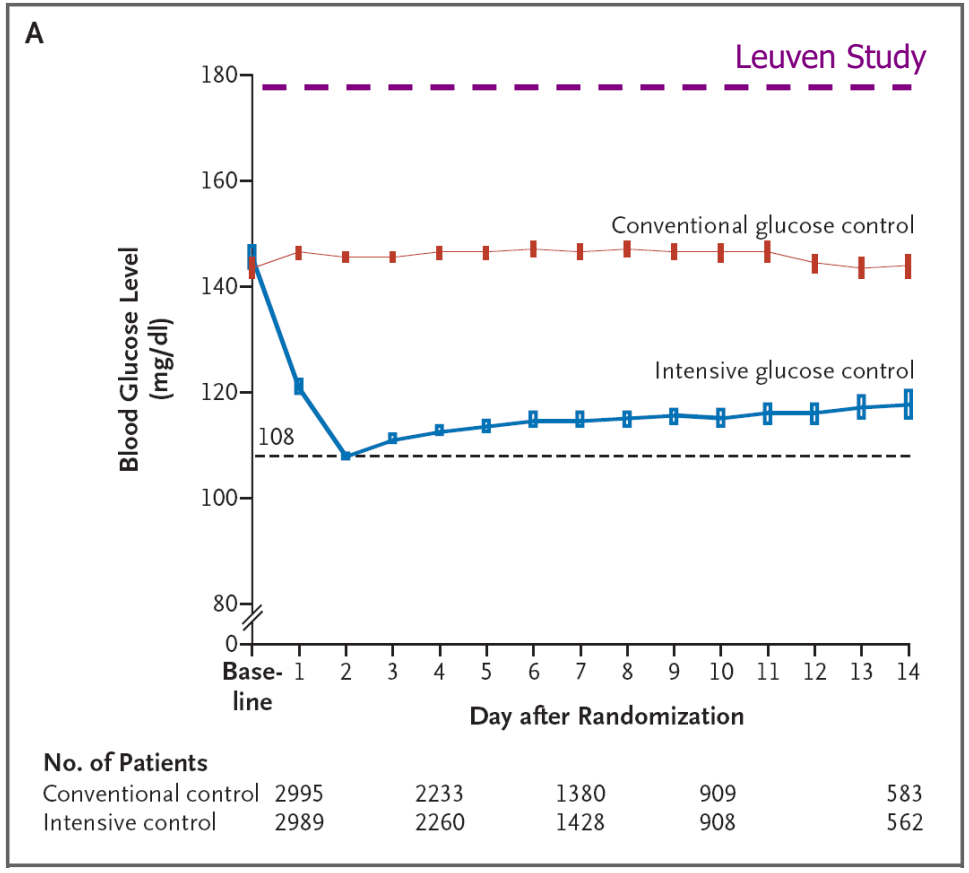


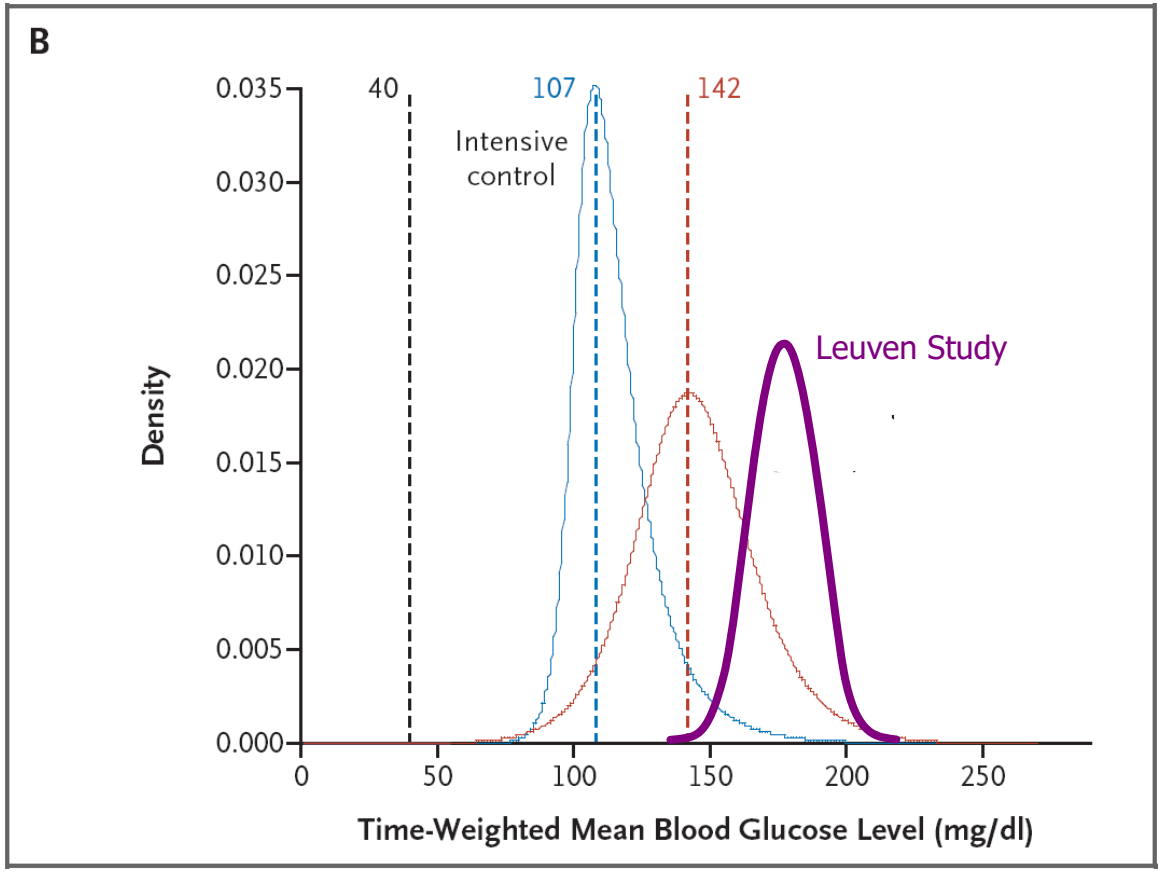
BACKGROUND

Whether hypoglyc

CONCLUSIONS

In critically ill patie severe hypoglycemia, both of with an increased risk of death. The association exhibits a dose–response relationship and is strongest for death from distributive shock. However, these data cannot prove a causal relationship. (Funded by the Australian National Health and Medical Research Council and others; NICE-SUGAR ClinicalTrials.gov number, NCT00220987.)





The NICE-SUGAR Study Investigators. N Engl J Med 2009;360:1283-97

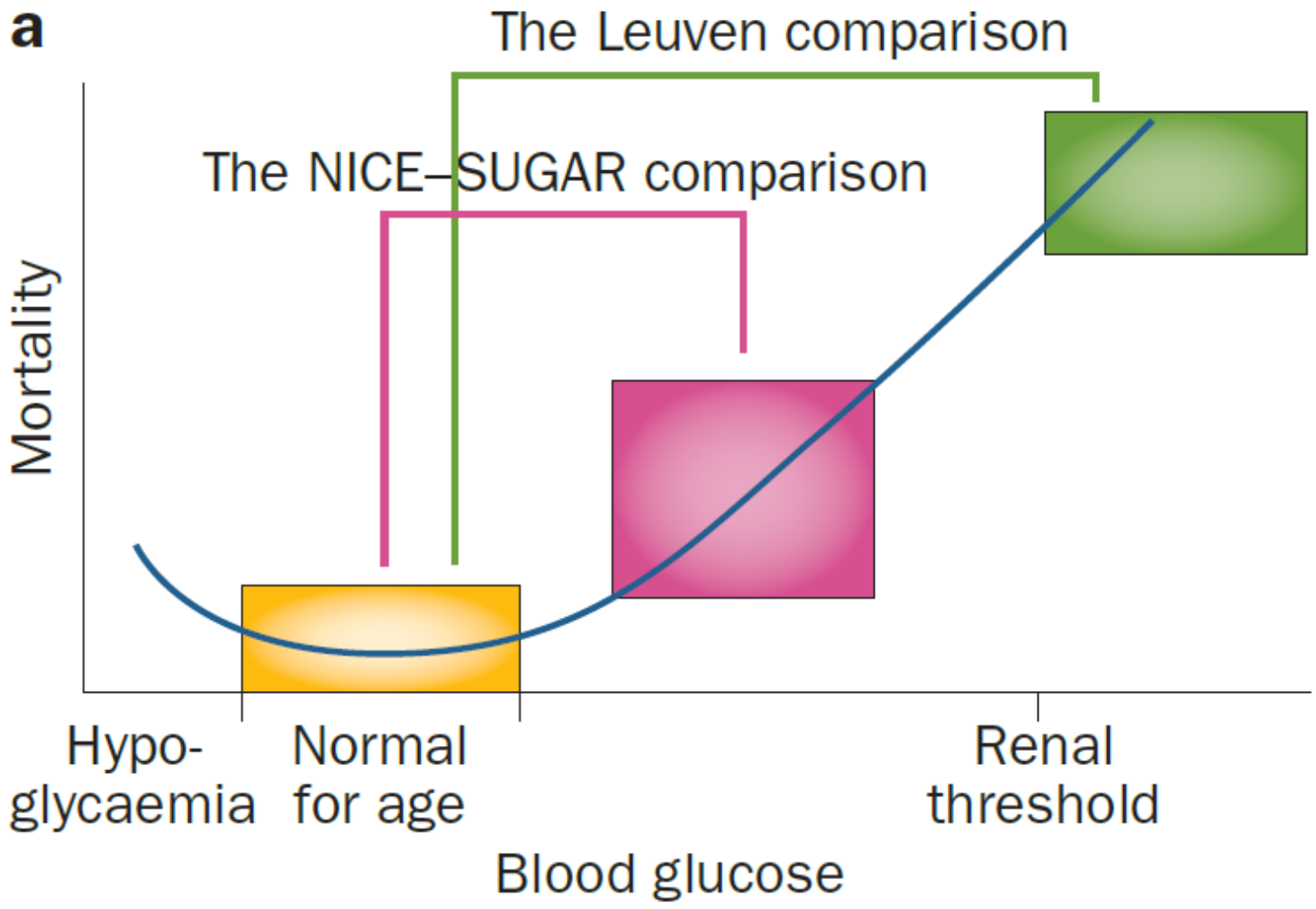


Figure 1 | Different designs of key intervention trials and expected outcome benefits. **a** | The NICE–SUGAR trial was executed in the flatter part of the J-shaped association curve between blood glucose and risk of death. A very small benefit aimed at lowering blood glucose further down from an intermediate level to strict normoglycaemia was hereby traded off against a similar risk of harm by hypoglycaemia, particularly when using inaccurate tools. Permission obtained from The Endocrine Society © Van den Berghe, G. *et al. J. Clin. Endocrinol. Metab.* **94**, 3163–3170 (2009).

Van den Berghe, G. Nat. Rev. Endocrinol 2012. 8;374–378

Table 1
Key differences between the Leuven studies[8,10] and NICE-SUGAR[16].

	Leuven adult studies	NICE-SUGAR
Number of patients	2748	6104
Setting	2 × 1 centre	42 centres
Patient sample (% of admissions)	60%(medical), 95%(surgical)	15%
Methodological aspects		
Comparator group target	10–12 mmol/L (180–215 mg/dL)	7.8–10 mmol/L (140–180 mg/dL)
Intervention target	<6.1 mmol/L (<110 mg/dL)	<6.0 mmol/L (<108 mg/dL)
Blood sampling site	Predominantly arterial line	Arterial/venous/capillary
Glucose measurement tool	ABL Radiometer bloodgas analyzer (surgical)	Not standardized
	HemoCue (medical)	All types glucometers allowed
Insulin infusion	Continuous only via central line	Continuous + bolus via all routes
	Syringe pump	All types of pumps allowed
Nurse instructions	Guideline + Intuitive decision making	A strict "if-then" algorithm
Feeding route first week	Parenteral + Enteral	Enteral only
Average kcal received during ICUstay	1100 kcal/day	880 kcal/day
Therapy compliance		
Blood glucose target reached	70%	<50%
Overlap in blood glucose between two groups	<10%	>50%
Outcome		
Hypoglycaemia	× 6	× 13
Morbidity	Reduced organ failure and infections	Neutral
Mortality	Lowered by absolute 3%	Increased by absolute 3%
Therapy withdrawal policy	Late	Early

D. Mesotten, G. Van den Berghe / Best Practice & Research Clinical Anaesthesiology 23 (2009) 421-9

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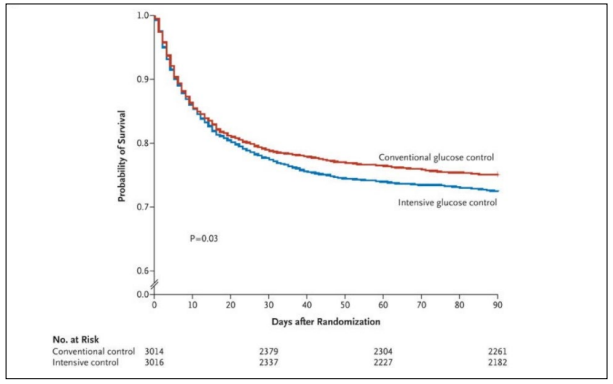
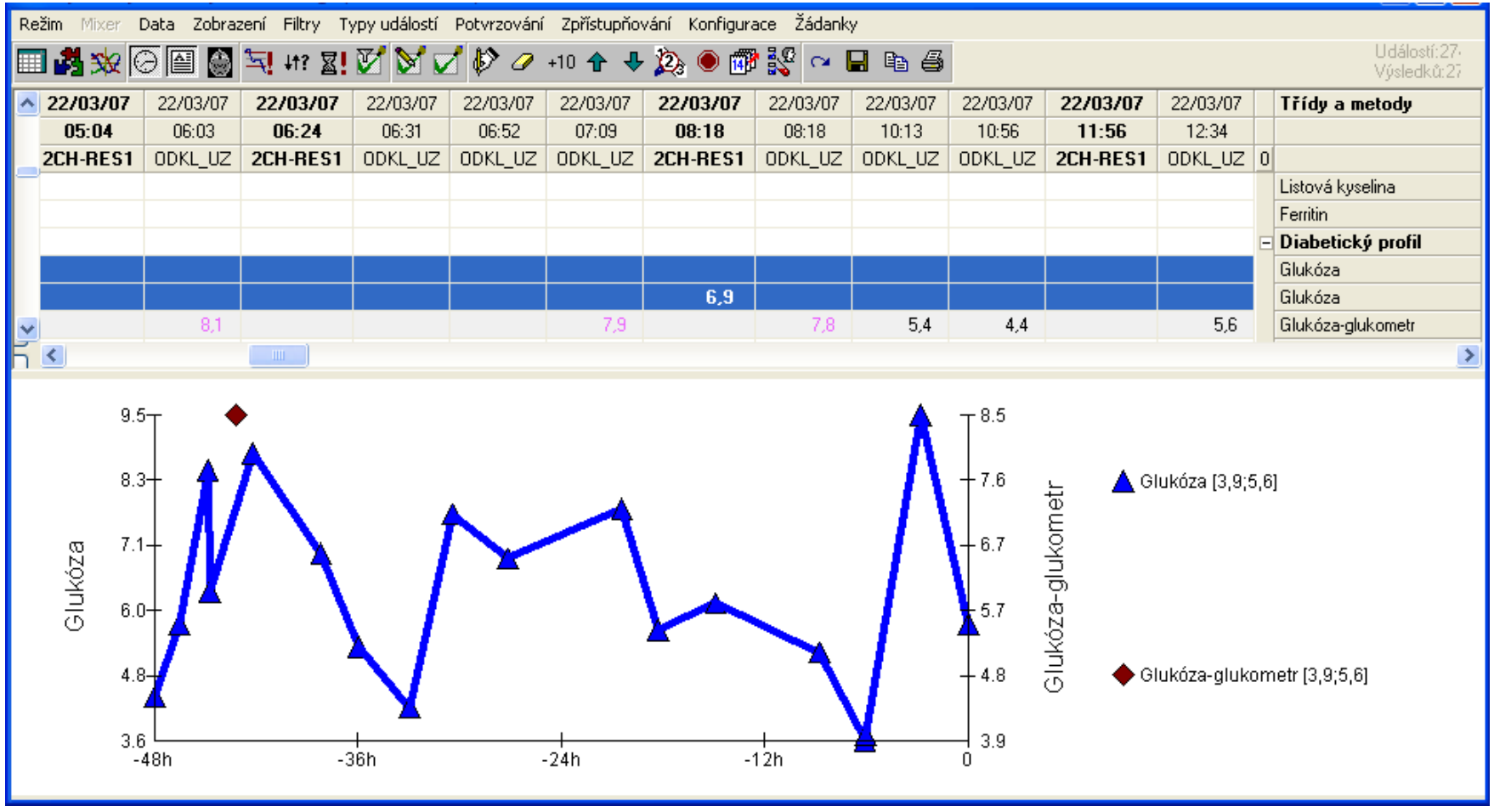
Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*



173 of all 288 episodes (60.1%) were confirmed by a laboratory measurement, 112 (38.9%) were unconfirmed bedside readings, and 3 (1.0%) were of unknown confirmation status.


Režim
Mixer
Data
Zobrazení
Filtry
Typy událostí
Potvrzování
Zpřístupňování
Konfigurace
Žádanky
Událostí:27
Výsledků:27
Třídy a metody
Listová kyselina
Ferritin
Diabetický profil
Glukóza
Glukóza
Glukóza-glukometr
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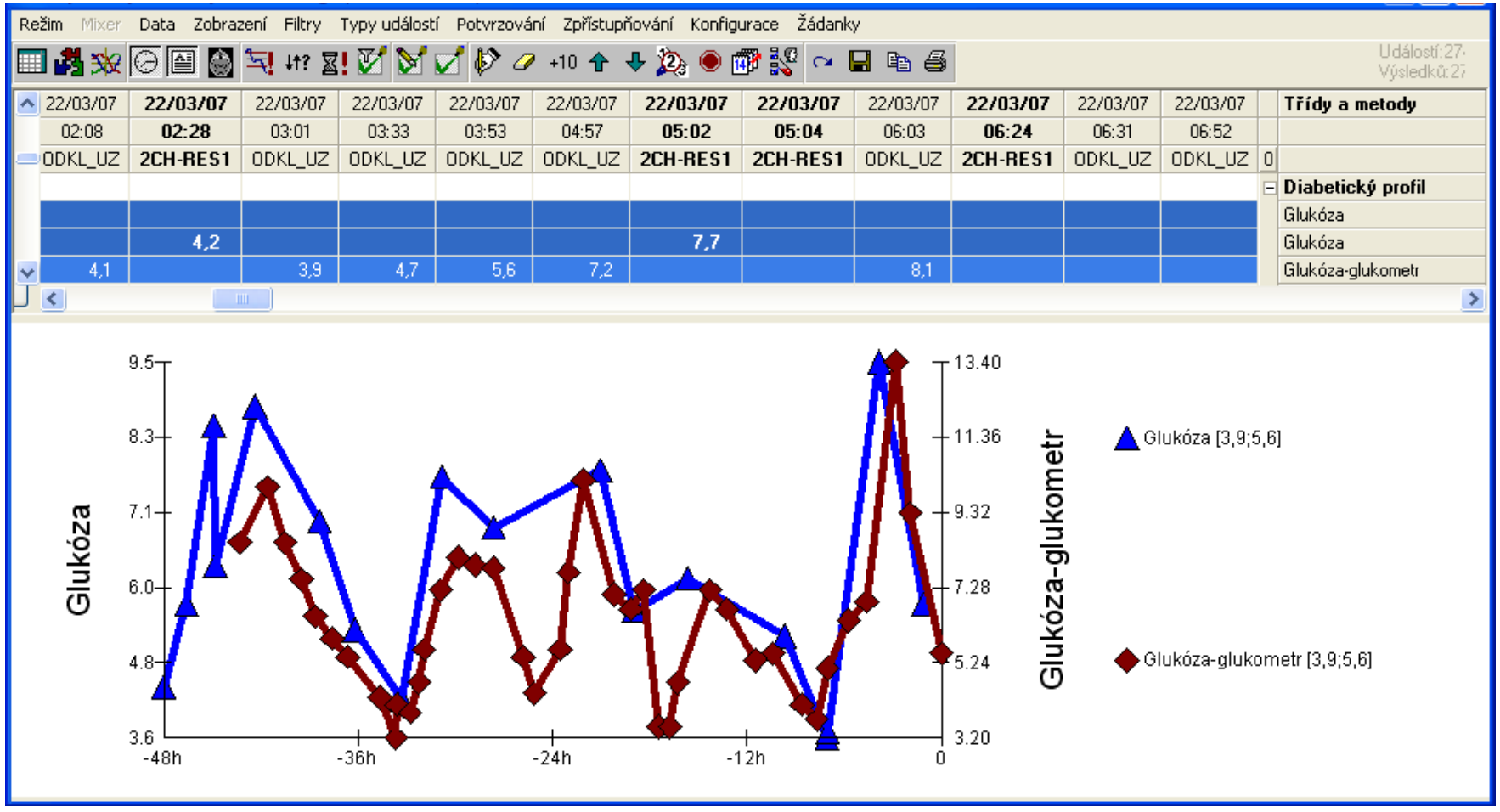
Glukóza-glukometr
Glukóza [3,9;5,6]
Glukóza-glukometr [3,9;5,6]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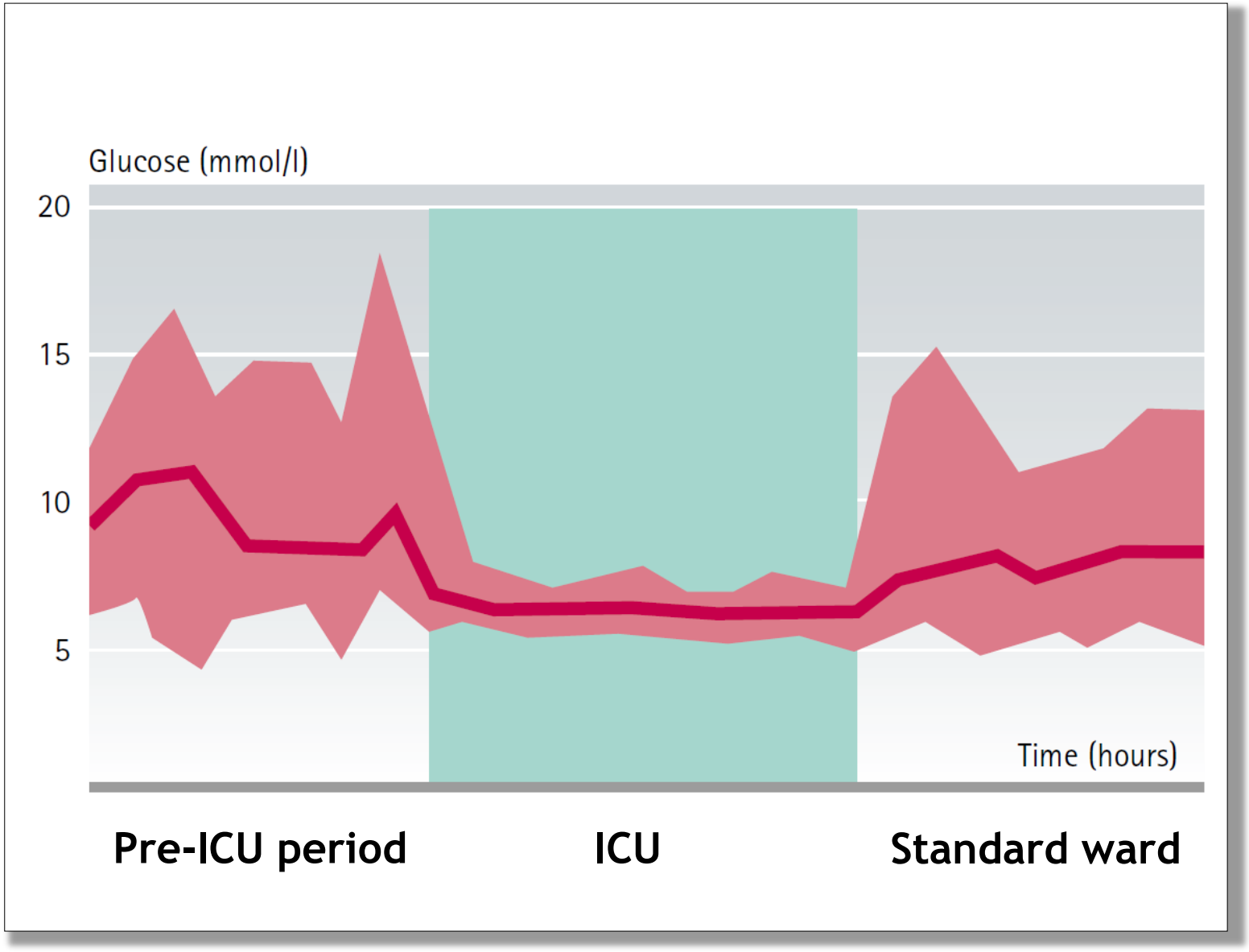
Glukóza
Glukóza-glukometr
Glukóza [3,9;5,6]
Glukóza-glukometr [3,9;5,6]
-48h
-36h
-24h
-12h
0


Glucose (mmol/l)
20
15
10
5
Time (hours)
Pre-ICU period
ICU
Standard ward

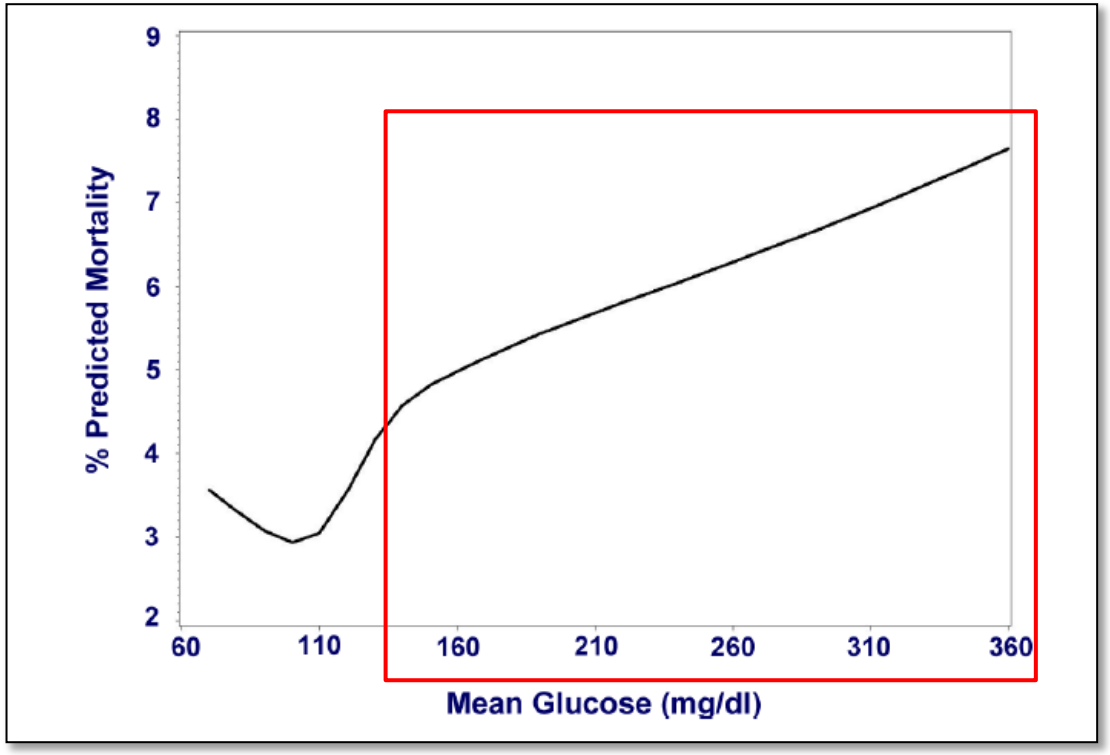
98 000 pacientů

Table 5. Relative risk of hospital mortality by categories of dysglycemia (n = 98,011)

	Unadjusted RR Hospital Mortality (95% CI)	Adjusted[a] RR Hospital Mortality (95% CI)	Glucocorticoid Adjusted[b] RR Hospital Mortality (95% CI)
Maximum average daily glucose, mg/dL			
<80	1.45 (0.95–2.24)	1.40 (0.90–2.18)	0.99 (0.49–2.03)
80–110	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
110–150	1.62 (1.50–1.76)	1.13 (1.04–1.58)	1.12 (1.01–1.24)
150–180	3.20 (2.94–3.48)	1.43 (1.30–1.58)	1.38 (1.22–1.55)
180–240	4.71 (4.33–5.12)	1.63 (1.47–1.81)	1.51 (1.33–1.72)
240–300	6.01 (5.43–6.65)	1.76 (1.55–1.99)	1.57 (1.34–1.84)
>300	7.05 (6.23–7.98)	1.89 (1.62–2.19)	1.78 (1.48–2.15)

[a]Adjusted for age, sex, race, operative admission diagnosis, history of diabetes, Acute Physiology and Chronic Health Evaluation IV score, admission glucose, admission temperature, number of glucose values per patient day, highest temperature, white blood cell count, serum sodium, and serum creatinin throughout the intensive care unit (ICU) stay, duration of mechanical ventilation, year of ICU admission, and ICU-acquired acute renal injury, respiratory failure and sepsis. [b]Adjusted for glucocorticoids in addition to primary model (n = 69,598). [c]Thresholds for percentiles of glucose variability (coefficient of variation) were 20th percentile = 0.10; 40th percentile = 0.15; 60th percentile = 0.19; 80th percentile = 0.25; and 100th percentile = 1.67.

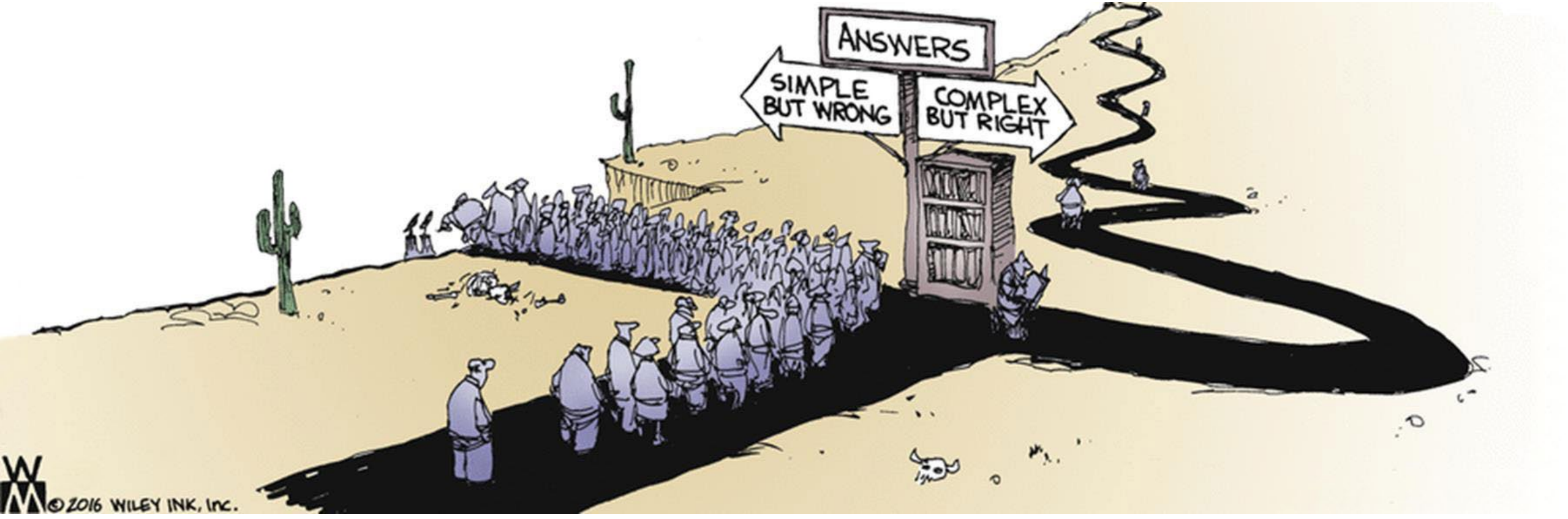
Badawi et al. Crit Care Med 2012; 40:3180–3188



Hyperglycemia is associated with increased mortality in ICU patients, independent of severity of illness. Mortality risk increases with mean glucose across the entire cohort (n = 259,040) starting at mild hyperglycemia ($p < 0.0001$). A) Odds ratios for mortality after adjustment for severity of illness are represented as point estimates with 95% confidence intervals for each mean glucose category; exclusion of unity represents a significant association. B) Cubic splines depict this relationship using mean glucose as a continuous variable.

259 000 pacientů

Falciglia M et al. *Crit Care Med.* 2009; 37(12):3001-9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