

Čo nás naučili štúdie CRASH



Štefan Trenkler

1. klinika AIM UNLP a UPJŠ LF Košice



- Nemám potenciálny konflikt záujmov

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



NIHR | National Institute
for Health Research

1999 - 2019



Medical
Research
Council



Corticosteroid Randomisation
After Significant Head Injury



Clinical Randomisation of an Antifibrinolytic
in Significant Haemorrhage



Clinical Randomisation of an
Antifibrinolytic in Significant Head Injury

Improving health
worldwide

**Výskum ... Vzdelávanie ... Globálne zdravie
Etos spolupráce ... Translácia výskumu**

... research,
... studies and continuing
education in public and global health.

LSHTM has an international presence and collaborative ethos. It is uniquely placed to help shape health policy and translate research findings into tangible impact.



- 1999 - 2004
- RCT: metylprednizolón verus placebo
- Preukázať 2% rozdiel v mortalite
- Recruit thousands (20 000) - Keep it simple
- Protokol publikovaný v Lancet – transparentnosť
- Zaradení:
 - dospelí, trauma mozgu, GCS \leq 14; do 8 hodín
- Jednotná dávka: MP 2 g bolus
 - + 48 hod infúzia 0,4 g/hod
- Výsledok: úmrtie / prepustenie / 2 týždne + 6 mesiacov
- Komplikácie: krvácanie z GIT, infekcia

Ako na to

- Financované Medical Research Council
- Desiatky centier na celom svete; lekári + sestry
- Dobrovoľníctvo, nadšenie, komunita
- 24 /7 call centrum; web stránka
- Národný / nemocničný koordinátor
- Spätná väzba (stretnutia, buletín...)
- Jednoduchosť
 - žiadne testy navyše
 - tri protokoly po 1 strane
 - zaradenie / 2 týždne / 6 mesiacov

Potentially Eligible
Head injured patients (judged to be 16 years or older) within 8 hours of injury who are not fully conscious (any abnormality on the Glasgow Coma Scale)

Research article

The CRASH trial protocol (Corticosteroid randomisation after significant head injury) [74459797]

The CRASH trial management group, on behalf of the CRASH trial collaborators

Address: CRASH Co-ordinating Centre, FREEPOST LON 14211, London, WC1B 3BR, UK
E-mail: crash@lshtm.ac.uk

Published: 11 June 2001
BMC Emergency Medicine 2001, 1:1

Received: 16 March 2001
Accepted: 11 June 2001

Doctor is **reasonably certain** that steroids are *indicated*.
Ineligible -give steroids and don't randomise

Doctor is **reasonably certain** that steroids are *contra-indicated*.
Ineligible -don't give steroids and don't randomise

Doctor is **substantially uncertain** as to the appropriateness of steroids in this patient

TELEPHONE FOR RANDOMISATION

STERIODPLACEBO



PATIENT ENTRY

INFORMATION REQUIRED FOR PAPER RANDOMISATION

Entry Date: / / Entry Time: :

[1] Country _____

[2] Name of hospital where patient entered _____
or give your hospital code

[3] Name of caller _____

[4] Patient sex: Male Female

[5] Do you know patient's name? Yes No — if No, go to [8]

[6] Family name: _____ [7] Given name(s): _____

[8] Patient Hospital Identification Number (if name unknown): _____

[9] Do you know patient's date of birth? Yes No — if No, go to [11]

[10] Date of birth: / / — or, if not known: [11] Approximate age: _____

[12] Estimated number of hours since injury: _____

Current Glasgow Coma Scale: three questions will be asked — one or more replies must indicate an abnormality (if unable to assess, e.g. due to intubation, give most recent GCS)

[13] Eye opening:	[14] Motor response:	[15] Verbal response:
Spontaneous 4	Obeys commands 6	Orientated 5
To sound 3	Localising 5	Confused speech 4
To pain 2	Normal flexion 4	Words 3
None 1	Abnormal flexion 3	Sounds 2
	Extending 2	None 1
	None 1	

[16] This GCS is: 1 Current 2 Most recent

Pupil reactivity

[17] Left 1 Yes 2 No 3 Unable to assess

[18] Right 1 Yes 2 No 3 Unable to assess

Treatment Pack used: Box:

Now fax this form to: +44 20 7299 4663

This form need not be kept as source documentation

CRASH EARLY OUTCOME FORM
Complete at **discharge, death in hospital, or 14 days after injury** whichever occurs first
Please **PRINT** clearly and answer **EVERY** question

Attach treatment pack label here

1. Hospital name _____

2. Patient details or attach a label with these details (for 6-month follow-up)

Family name: _____ Patient identification no. (if appropriate) _____
Given name(s): _____ NHS number (if appropriate) _____
Sex: M F Date of Birth: / / (day/month/year)
Address: _____
Postcode: _____ Telephone: _____

3. Cause of injury: Road traffic accident Fall > 2 metres Other: _____

4. Outcome (please complete questions a,b,c and d)

a. Death in hospital Transferred to other acute care hospital Discharged to rehabilitation centre or nursing home Discharged home Still in this hospital now

b. Date of death, transfer or discharge: / /
If transferred give consultant name/department, _____ and name of hospital _____

c. _____

d. Tick **one box** that best describes the patient's **head injury-related symptoms now** (i.e. at 14 days or prior discharge):
 No symptoms Minor symptoms Some restriction in lifestyle but independent Dependent, but not requiring constant attention Fully dependent, requiring attention day and night Dead

5. Management and complications (please tick **ONE** box on **EACH** line)

<input type="checkbox"/> Admitted to Intensive Care Unit If Yes, please write number of days in ICU _____	<input type="checkbox"/> Obliteration of the 3rd ventricle or basal cisterns	<input type="checkbox"/> One or more p haemorrhages the brain
<input type="checkbox"/> Seizure	<input type="checkbox"/> Midline shift >5mm	<input type="checkbox"/> Cortical contus > 1cm in diam
<input type="checkbox"/> Haematemesis or melaena requiring transfusion	<input type="checkbox"/> Intracranial haematoma - evacuated	<input type="checkbox"/> Subarachnoid
<input type="checkbox"/> Wound infection with pus	<input type="checkbox"/> Intracranial haematoma - non-evacuated	<input type="checkbox"/> Normal scan
<input type="checkbox"/> Pneumonia treated with antibiotics	<input type="checkbox"/> Neurosurgical operation	
<input type="checkbox"/> Other treatment with antibiotics	<input type="checkbox"/> Major extracranial injury	

6. Head CT scan Yes No No go to _____
Date of first head CT scan: / / Time (24 hr clock) _____
Result: (please tick all that apply)

7. Trial treatment a) Loading dose: Yes No b) Hours of maintenance dose: _____ hou

Sections 8 and 9 are only required if the patient is alive

8. Reliable contact (Next of kin or friend)
Name: _____ Address: _____
Post code: _____ Tel: _____

9. Family doctor
Name: _____ Address: _____
Post code: _____ Tel: _____

10. Person completing form (please PRINT):
Name: _____ Position: _____ Date: / /

MOISTEN EDGES AND SEAL TOGETHER

MOISTEN EDGES AND SEAL TOGETHER

Keep it simple

INTERNATIONAL STUDY OF RECOVERY AFTER HEAD INJURY

These questions are about changes in your lifestyle since your injury. They can be answered by you, a relative or friend, or by you both together. If you have any questions about this form, please contact Senior Nurse Nijm Ritchie on 020 7299 4742. Please answer each question below by ticking one box: which is true for you.

Your answers will help us improve the care of people following a head injury.

Please say who filled out this form:
 Patient alone Relative, friend or carer alone Patient and relative, friend or carer together

1. At present, where do you live most of the time?
 In own home In hospital In residential care

2. As a result of your injury, do you now need help in the home?
 No Yes. I need some help in the home, but not every day. Yes. I need help in the home every day. I need help in the home, but not because of the injury.

3. As a result of your injury, do you now need help to shop?
 No Yes. I need some help, but I can go to the local shops on my own. Yes. I need help to shop even locally, or cannot shop at all. I need help to shop, but not because of the injury.

4. As a result of your injury, do you now need help to travel?
 No Yes. I need some help, but can travel locally on my own (e.g. by arranging a taxi). Yes. I need help to travel even locally, or I cannot travel at all. I need help to travel, but not because of the injury.

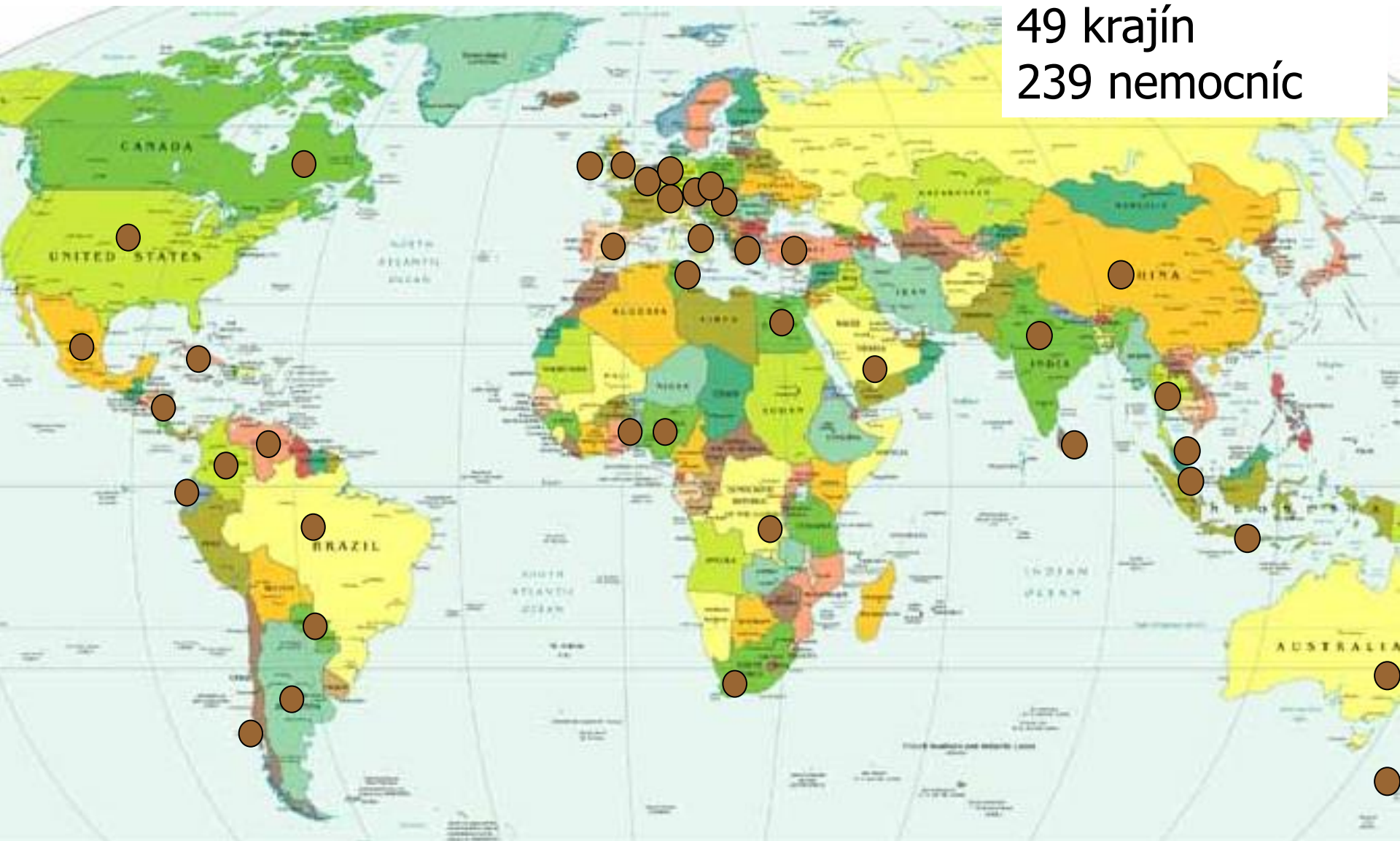
5. As a result of your injury, has there been a change in your ability to work? (or to study if you were a student; or to look after your family)
 No Yes. I still work, but at a reduced level (e.g. a change from full-time to part-time, or a change in level of responsibility). Yes. I am unable to work at present. My ability to work is restricted, but not because of the injury, or I have retired.

6. As a result of your injury, has there been a change in your ability to take part in social and leisure activities outside home?
 No Yes. I take part a bit less, but at least half as often. Yes. I take part much less, or do not take part at all. My ability to take part is restricted for some other reason, not because of the injury.

7. As a result of your injury, are there now problems in how you get on with friends or relatives?
 No Yes. There are occasional problems (less than once a week). Yes. There are frequent or constant problems. There are problems for some other reason, not because of the injury.

When complete fold form as indicated, stick together and post to: CRASH Co-ordinating Centre, FREEPOST, LON14211, London WC1N 1BR OR FAX +44 (0)20 72

1999 - 2004
10 008 pacientov
49 krajín
239 nemocníc



Masaryk Hospital
24/04/2000

Hospital
Kralovske
Vinohrady
25/05/2002

Charles University
Hospital
15/03/2002

Hospital Pribram
26/02/2000



Univerzita Karlova
Neurochirurgicka
Klinika
02/10/2000

University Hospital
Hradec Kralove
16/06/2001

**Research
Institute for
Special
Surgery and
Trauma**

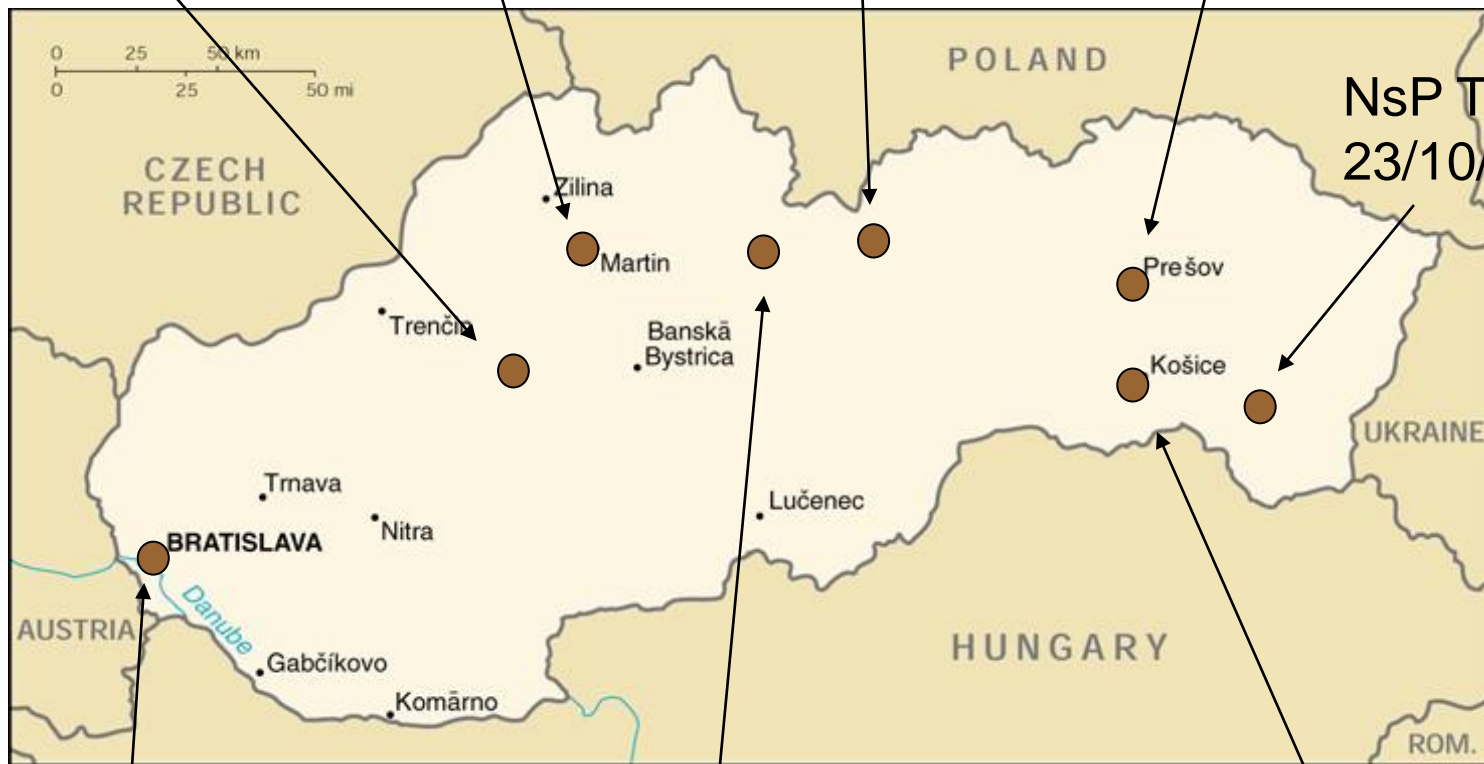
started on
16/04/1999

NsP Bojnice
14/03/2002

FNsP Martin
18/07/2002

NsP Poprad
28/01/2002

**Reimann
Hospital**
started
18/08/1999



NsP Trebisov
23/10/2002

NsP Ruzinov
25/07/2002

NsP Liptovský
Mikuláš
12/11/2002

FNsP Kosice
16/04/2002

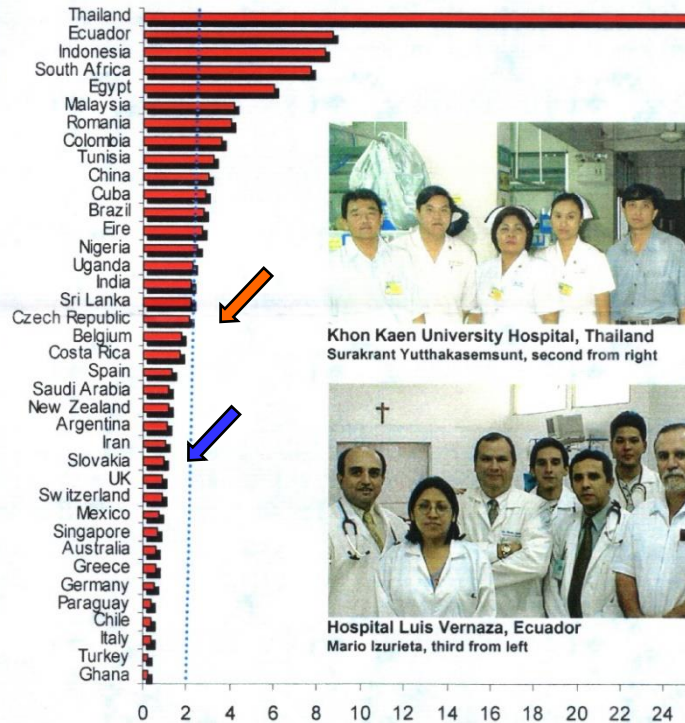
1 140 pacientov
11,4 %

Slovakia (179)—Reiman Hospital (71): Štefan Trenkler NC, Matuš Humenansky, Tatiana Stajančová; NsP Poprad (39): Ivan Schwendt, Anton Laincz; Nemocnica Bojnice (25): Zeman Julius, Stano Maros; FNsP Kosice (12): Jozef Firment; NsP Trebisov (11): Maria Cifraničova; Faculty Hospital in Martin (10): Beata Sániová; NsP Ruzinov (4): Karol Kalig; NsP Nové Zámky (3): Soňa Medekova; NsP Liptovsky Mikulas (2): Radovan Wiszt; NsP F D Roosevelt (1); NsP Zilina (1): Ivan Mačuga.

Czech Republic (961)—Research Institute for Special Surgery and Trauma (852): Petr Svoboda NC, Ilona Kantorová, Jiří Ochmann, Peter Scheer, Ladislav Kozumplík, Jitka Maršová; Masaryk Hospital (41): Karel Edelmann; Charles University Hospital, Plzen (35): Ivan Chytra, Roman Bosman; University Hospital Hradec Kralove (15): Hana Andrejsová; Hospital Kralovske Vinohrady (9): Jan Pacht; Hospital Pribram (7): Jan Bürger; Univerzity Karlovy Neurochirurgicka Klinika (2): Filip Kramar.

Bulletin CRASH 2003

Average monthly recruitment rate



Khon Kaen University Hospital, Thailand
Surakrant Yutthakasemsunt, second from right



Hospital Luis Vernaza, Ecuador
Mario Izurieta, third from left

Mentions – Thank you all!

New ethics approvals

Wang Maode and Guo Shiwen, Xi'an Jiaotong University 1st Hospital, China
 Wei Shi and Liu Chongxiao, Xi'an Jiaotong University 2nd Hospital, China ★
 Roberto Gomez Piñedo, Hospital Timothy Britton (first patient), Colombia ★
 Edgar Luna, Hospital Departamental de Pasto, Colombia
 Jesus Quiñones, Hospital San Andrés (first patient), Colombia ★
 Gladys Rivas-Caniño, Hospital Miguel Enriquez, Cuba
 Roberto Santos, Hospital Regional del IESS "Dr. Teodoro Maldonado Carbo", Ecuador
 Mario Piños Gavilanes, Hospital Alcivar, Ecuador
 Jaime Velasquez Tapia, Hospital Naval, Ecuador
 Tamara Gogichaishvili, Republican Hospital, Georgia
 Wu Hoong Chhang, North Bengal Neuro Research Centre, India
 A Satish, Abhaya Hospital, India
 Ehsan Sherafat Kazemzadeh, Social Security Hospital (first patient) and ★
 Fatemeh Zahra Hospital, Iran
 Vittorio Vitalone, S Filippo Neri, Italy
 Edward O Komolafe, Obafemi Awolowo University Teaching Hospitals (10 patients) Nigeria ★
 Jose Edmundo Mezquita, Complejo Hospitalario M. A. Guerrero, Panama ★
 David Foley, Queen Mary's Hospital, United Kingdom
 Branco Djurovic, Klinicki Centar Srbije, Yugoslavia

10 pts

Walter Videtta, Hospital Dr Ramón Carillo, Argentina

Ivan Chytra, Charles University Hospital, Plzen, Czech Republic

50 pts

Ignacio Gonzalez and Miguel Fernando Arango, Hospital General de Medellin, Colombia

Alvaro Ardila Otero, Hospital Universitario San Jorge, Colombia

Nyoman Golden, Sanglah General Hospital, Indonesia

Stefan Trenkler, Reimann Hospital, Slovakia

Surakrant Yutthakasemsunt, Khon Kaen Regional Hospital, Thailand – 50 pts in the first seven weeks

200 pts

Bennie Hartzenberg, Tygerberg Academic Hospital, South Africa

1st patient

Marcos Iraola Ferrer, Hospital Universitario "Dr Gustavo Aldereguia Lima", Cuba
 Mario A Domínguez Perera, Hospital Universitario "Arnaldo Milán Castro", Cuba
 Antonios Karavelis, University General Hospital of Larissa, Greece
 K S Maheshwari, Maheshwari Orthopaedic Hospital, India
 Manas Panigrahi, Nizam's Institute of Medical Sciences, India
 Adam Danil and Remus Iliescu, Sfantum Pantelimon Hospital, Romania
 Charles Seah, Changi General Hospital, Singapore
 Maria Cifranicova, NsP Trebisov, Slovakia
 Radovan Wiszt, NsP Liptovsky Mikulas, Slovakia
 Alfonso Muñoz López, Hospital Carlos Haya, Spain
 Titus Odedun, Ormskirk And District General Hospital, United Kingdom

Effect of intravenous corticosteroids on death within 14 days in 10008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial



CRASH trial collaborators*

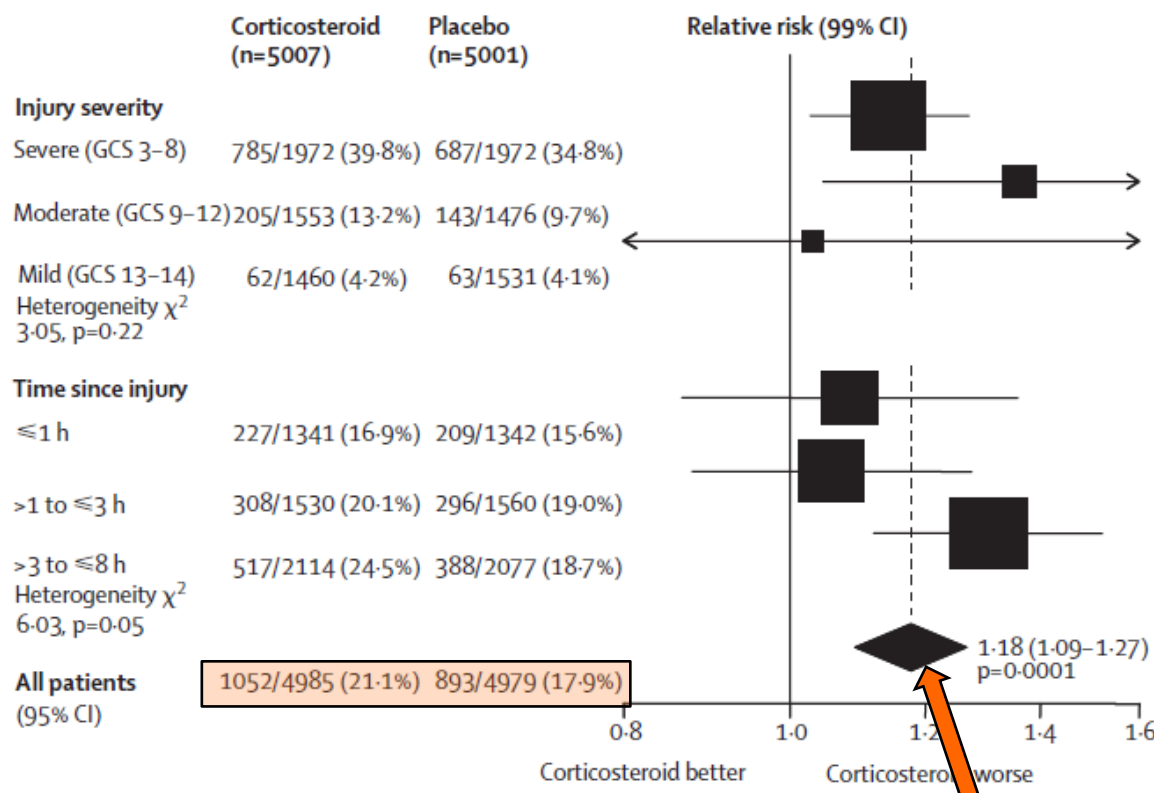
Lancet 2004; 364: 1321-28

See [Comment](#) page 1291

*Listed at end of report

Summary

Počet pacientov: 10 008
 Predčasné ukončenie
 Výsledné údaje: 99 %
 Mortalita: 21,1 / 17,9 %
MP: úmrtie ↑ 3,2 %
 Nie: GCS, čas

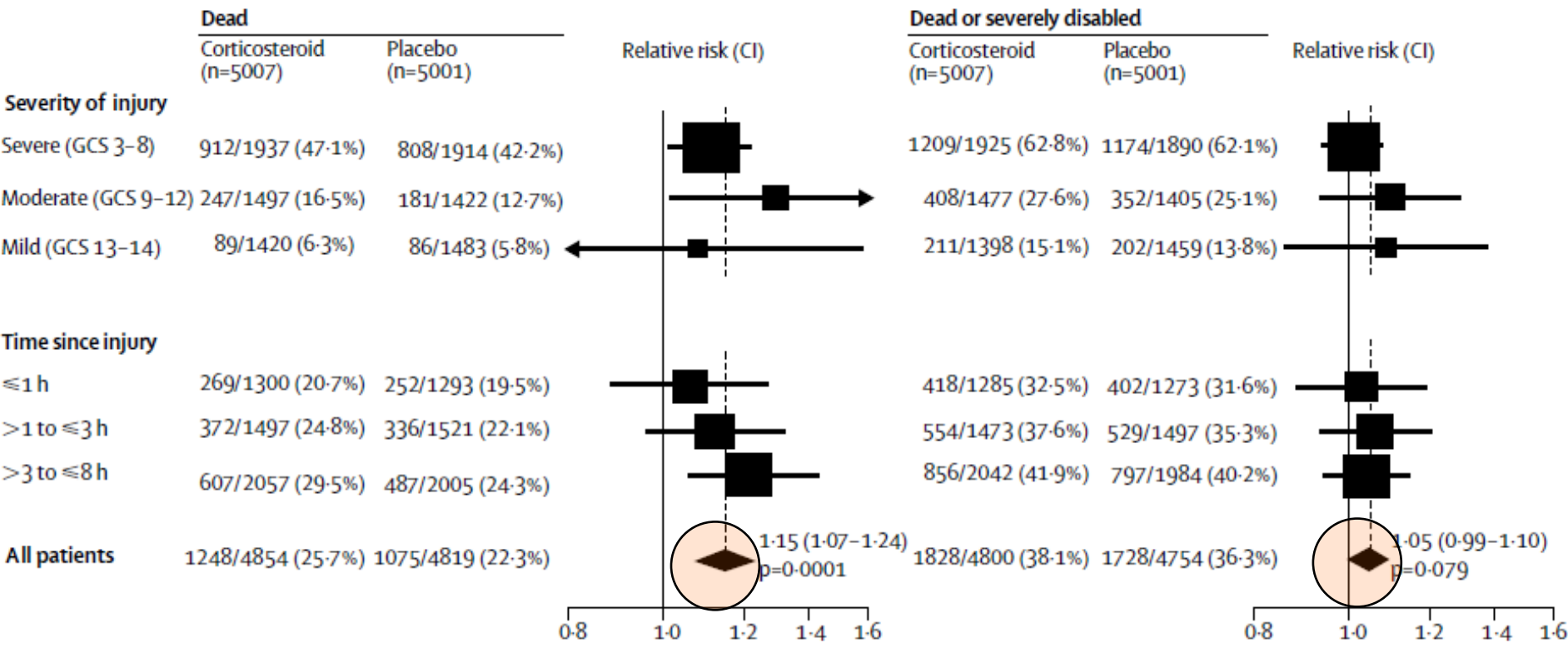


Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury—outcomes at 6 months



CRASH trial collaborators*

MRC CRASH is a randomised controlled trial (ISRCTN74459797) of the effect of corticosteroids on death and *Lancet* 2005; 365: 1957-59



Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury—outcomes at 6 months



*CRASH trial collaborators**

MRC CRASH is a randomised controlled trial (ISRCTN74459797) of the effect of corticosteroids on death and disability after head injury. We randomly allocated 10 008 adults with head injury and a Glasgow Coma Scale score of 14 or less, within 8 h of injury, to a 48-h infusion of corticosteroid (methylprednisolone) or placebo. Data at 6 months were obtained for 9673 (96·7%) patients. The risk of death was higher in the corticosteroid group than in the placebo group (1248 [25·7%] vs 1075 [22·3%] deaths; relative risk 1·15, 95% CI 1·07–1·24; $p=0\cdot0001$), as was the risk of death or severe disability (1828 [38·1%] vs 1728 [36·3%] dead or severely disabled; 1·05, 0·99–1·10; $p=0\cdot079$). There was no evidence that the effect of corticosteroids differed by injury severity or time since injury. These results lend support to our earlier conclusion that corticosteroids should not be used routinely in the treatment of head injury.

Published online

May 26, 2005

DOI:10.1016/S0140-6736(05)66552-X

*See end of paper.

Correspondence to: CRASH Trials Co-ordinating Centre, London School of Hygiene and Tropical Medicine, Keppel St, London WC1E 7HT, UK
crash@lshtm.ac.uk

Guidelines for the Management of Severe Traumatic Brain Injury

4th Edition 2016

RECOMMENDATIONS

Level I

- The use of steroids is not recommended for improving outcome or reducing ICP. In patients with severe TBI, high-dose methylprednisolone was associated with increased mortality and is contraindicated.

Changes from Prior Edition

The body of evidence was updated to include the 6-month outcomes of the CRASH trial.¹⁴

There were no changes to the recommendations for this topic.



Slovenská spoločnosť urgentnej medicíny a medicíny katastrof

Prednemocničná neodkladná starostlivosť o pacientov s neurotraumou

Odporúčaný postup SSUMaMK

Členovia komisie: MUDr. Monika Paulíková (predseda), MUDr. Štefan Trenkler, PhD., MUDr. Katarína Brštiaková, MUDr. Miloslav Hanula, PhD., MUDr. Kamil Koleják, PhD.

Posúdili: doc. MUDr. Viliam Dobiáš, CSc., MUDr. Táňa Bulíková, PhD., MUDr. Štefan Svitok.

Schválil výbor SSUMaMK ku dňu 9.1.2015.

Príloha 1. Indikátory kvality

1. Dýchacie cesty priechodné
2. Krčná chrbtica správne fixovaná
3. ETI v sedácii a relaxácii (rapid sequence induction)
4. SpO₂ > 90 %; ETCO₂ monitorované, udržiavané v rozmedzí 35 - 40 mmHg
5. TK monitorovaný, TKs > 110 mmHg (cievny prístup, infúzia, noradrenalín)
6. GCS opakovane vyhodnotené a zapísané
7. Neboli použité kortikosteroidy
8. Neurologický stav dokumentovaný
9. Glykémia vyšetrená
10. Dokumentácia úplná
11. Transportovaný/á do traumacentra
12. Čas do odovzdania v zdravotníckom zariadení do 60 minút.



Slovenská spoločnosť urgentnej medicíny a medicíny katastrof

Prednemocničná neodkladná starostlivosť o pacientov s neurotraumou

Odporúčaný postup SSUMaMK

2013 Odporúčanie pre nepodávanie MP u pacientov so spinálnou traumou prednemocnične

Posúdili: doc. MUDr. Viliam Dobiáš, CSc., MUDr. Táňa

Schválil výbor SSUMaMK ku dňu 9.1.2015.



Štefan Trenkler, PhD.,
eják, PhD.

Dr. Štefan Svitok.

Príloha 1. Indikátory kvality

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Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients

MRC CRASH Trial Collaborators

Head injury prognosis



These prognostic models may be used as an aid to estimate mortality at 14 days and death and severe disability at six months in patients with traumatic brain injury (TBI). The predictions are based on the average outcome in adult patients with Glasgow coma score (GCS) of 14 or less, within 8 hours of injury, and can only support - not replace - clinical judgment. Although individual names of countries can be selected in the models, the estimates are based on two alternative sets of models (high income countries or low & middle income countries).

Country

Age, years

Glasgow coma score

Pupils react to light

Major extra-cranial injury?

CT scan available?

Prediction

Risk of 14 day mortality (95% CI) -

Risk of unfavourable outcome at 6 months -

Reset

Reference:
The MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008 doi:10.1136/bmj.39461.643438.25 2007;

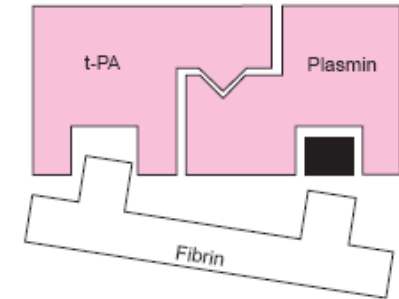
CRASH₂

Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



- 2005 - 2010
- Keep it simple, recruit many (20 000)
- RCT: kys. tranexánová vz. placebo; multicentrická
- Zaradení:
 - dospelí s traumatickým krvácaním/potenciálom, do 8 hodín
- Jednotná dávka:
 - TXA 1 g/10 minút i.v. + TXA 1 g/8 hod inf.
- Výsledok: úmrtie do 4 týždňov
- Trombembolické komplikácie
- Žiadne testy, jednoduché protokoly



CRASH₂

Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage

20,211 patients randomised
99.6% follow-up
40 countries – 274 hospitals



Congratulations to all our collaborators around the world!



El Salvador
 Sri Lanka
 Albania

Top 20 countries

2005 - 2010
20 211 pacientov
40 krajín
274 nemocníc



Výsledky

Kolumbie	2 940	Austrálie	17
Kuba	575	Belgie	51
Ekvádor	1 198	Kanada	2
Egypt	2 234	Česká rep.	17
Gruzie	1 783	Itálie	57
Indie	4 768	Japonsko	9
Indonézie	706	Slovensko	38
Nigérie	2 053	Španělsko	23
Thajsko	903	UK	135
	17 160		349

20 211 pacientů z 274 nemocnic ve 40 zemích (ovšem >98% z rozvojových zemí)



55 pacientov
0,27 %

Appendix 1 CRASH-2 trial organisation

Slovakia (38)—FNsP Ružinov: Aktham Yaghi; NsP Poprad: Anton Laincz;
NsP JA Reiman Hospital: Stefan Trenkler; Faculty Hospital F D Roosevelt:
Jozef Valky.

Czech Republic (17)—Research Institute for Special
Surgery and Trauma: Petr Svoboda.

Celková mortalita

Tranexamic acid allocated Placebo allocated

Risk ratio (99% CI)

Time from injury (h)

≤1	509/3747 (13.6%)	581/3704 (15.7%)
>1-≤3	463/3037 (15.2%)	528/2996 (17.6%)
>3	491/3272 (15.0%)	502/3362 (14.9%)

$\chi^2=4.411$; $p=0.11$

Systolic blood pressure (mm Hg)

≥90	702/6878 (10.2%)	736/6761 (10.9%)
76-89	280/1609 (17.5%)	313/1689 (18.5%)
≤75	478/1562 (30.6%)	562/1599 (35.1%)

$\chi^2=1.345$; $p=0.51$

GCS

Severe (3-8)	796/1789 (44.5%)	860/1830 (47.0%)
Moderate (9-12)	219/1349 (16.2%)	249/1344 (18.5%)
Mild (13-15)	447/6915 (6.5%)	502/6877 (7.3%)

$\chi^2=1.387$; $p=0.50$

Injury type

Blunt	1134/6788 (16.7%)	1233/6817 (18.1%)
Penetrating	329/3272 (10.1%)	380/3250 (11.7%)

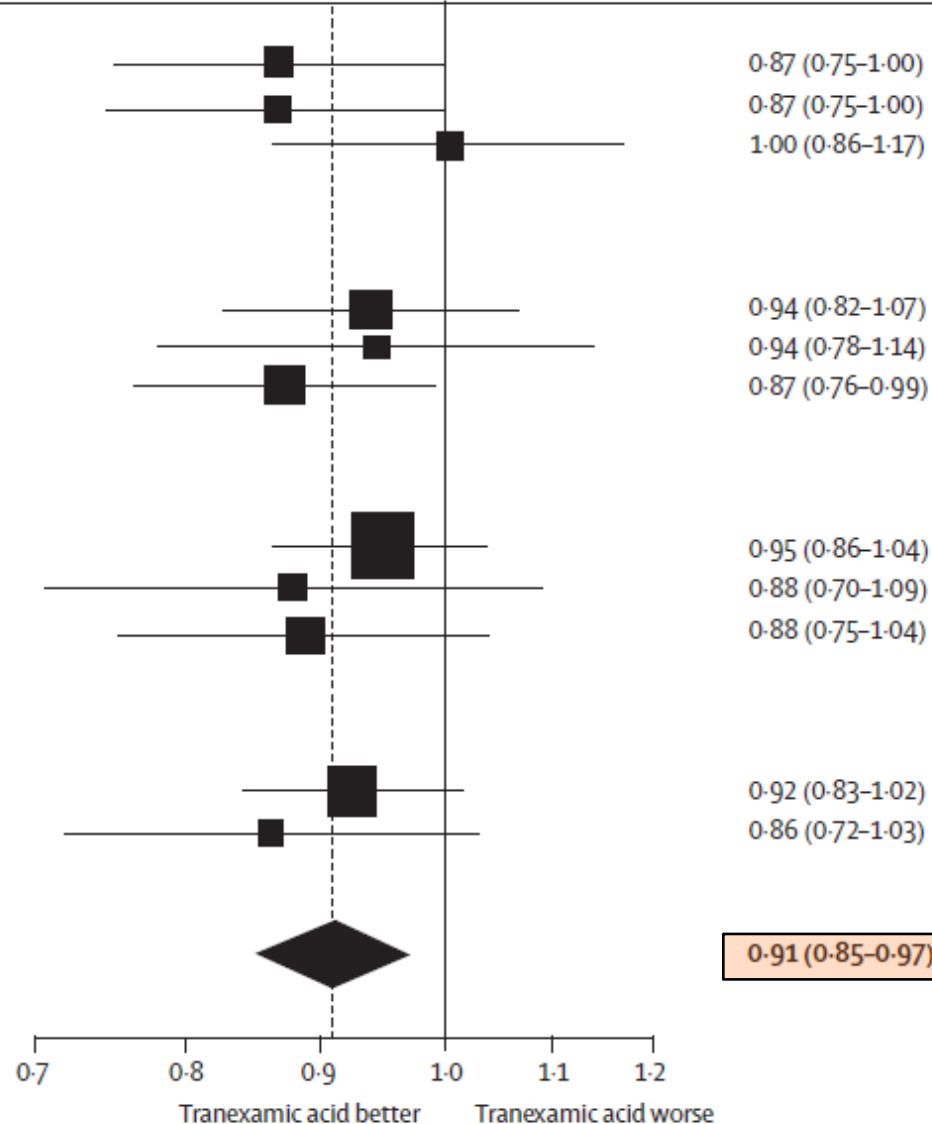
$\chi^2=0.791$; $p=0.37$

All patients

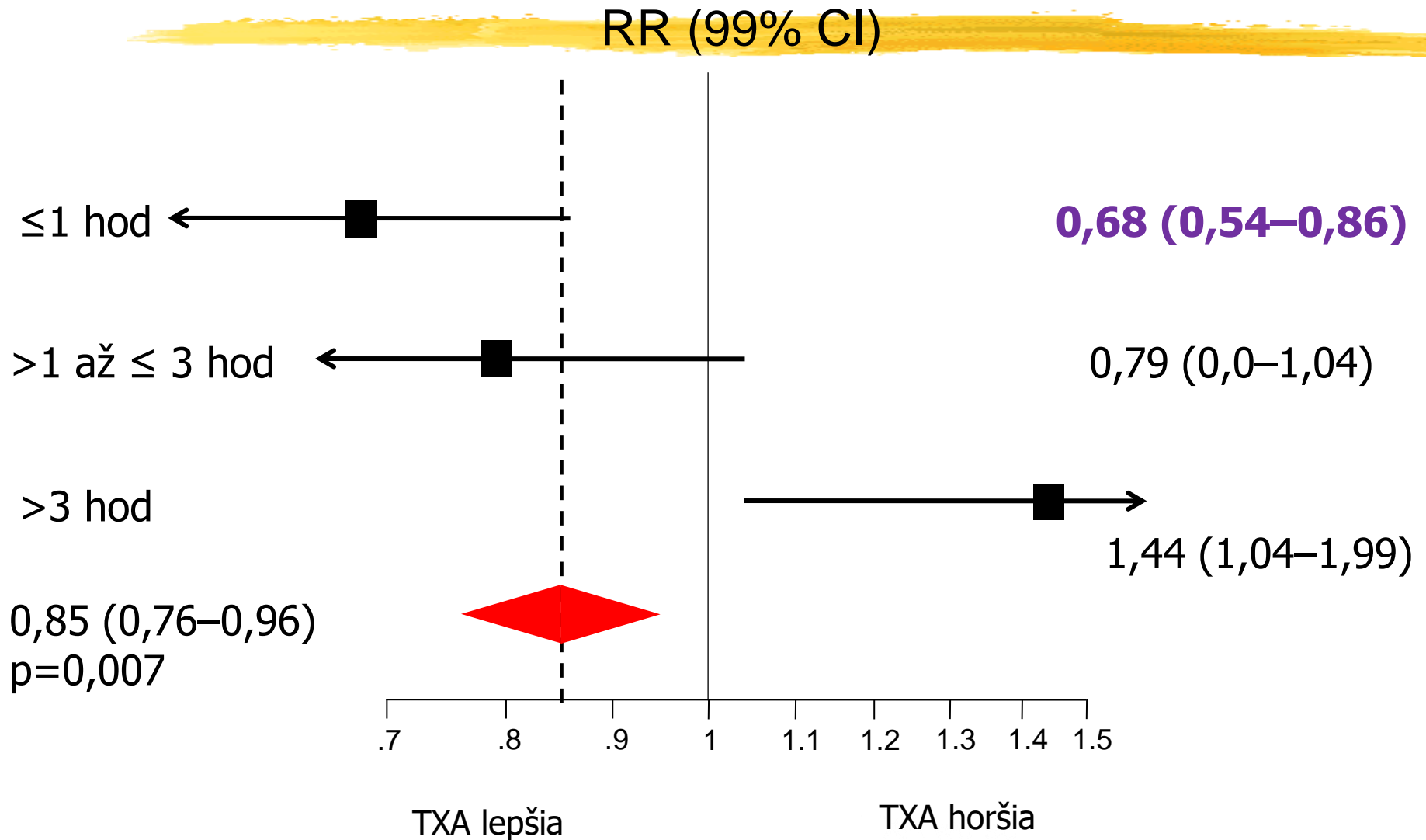
1463/10060 (14.5%)	1613/10067 (16.0%)
--------------------	--------------------

Two-sided $p=0.0035$

Rozdiel 1,5 %



CRASH-2: mortalita pre krvácanie




RESEARCH

Open Access

The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition



Donat R. Spahn¹, Bertil Bouillon², Vladimir Cerny^{3,4,5,6}, Jacques Duranteau⁷, Daniela Filipescu⁸, Beverley J. Hunt⁹, Radko Komadina¹⁰, Marc Maegele¹¹, Giuseppe Nardi¹², Louis Riddez¹³, Charles-Marc Samama¹⁴, Jean-Louis Vincent¹⁵ and Rolf Rossaint^{16*} 



TXA

1. Krvácanie/riziko
2. Čo najskôr/do 3 hod
3. 1 g bolus + 1 g počas 8 hod
4. Protokol, prednemocnične
5. Aj bez vyšetrení (TEG, ROTEM)

V. Initial management of bleeding and coagulopathy *Antifibrinolytic agents*

Recommendation 22 We recommend that TXA be administered to the trauma patient who is bleeding or at risk of significant haemorrhage as soon as possible and within 3 h after injury at a loading dose of 1 g infused over 10 min, followed by an i.v. infusion of 1 g over 8 h. (Grade 1A)

We recommend that protocols for the management of bleeding patients consider administration of the first dose of TXA en route to the hospital. (Grade 1C)

We recommend that the administration of TXA not await results from a viscoelastic assessment. (Grade 1B)

INTENZIVNÍ MEDICÍNA

PŮVODNÍ PRÁCE

Vplyv kyseliny tranexámovej na mortalitu, cievne okluzívne príhody a transfúzie krvi u pacientov s veľkým poúrazovým krvácaním (CRASH-2) – randomizovaná, placebom kontrolovaná štúdia*

Trenkler Štefan¹, Laincz Anton², Valky Jozef³, Yaghi Ajtham⁴, Svoboda Petr⁵ (za spolupracovníky CRASH-2 studie^{})**

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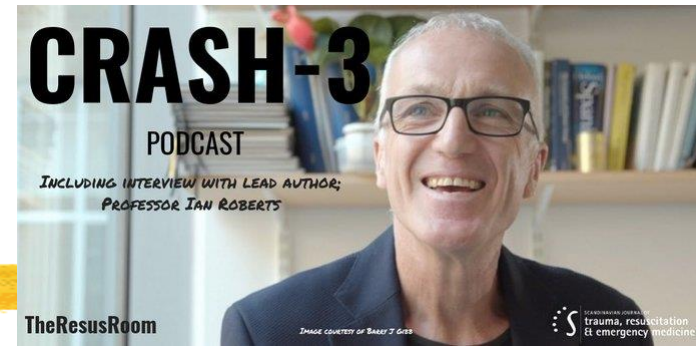
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⁴Klinika anestéziológie a intenzívnej medicíny, Univerzitná nemocnica Bratislava, Nemocnica Ružinov

⁵Úrazová nemocnice v Brně

^{**}Další účastníci sú uvedení na konci článku

Implementácia



- Ian Roberts – implementácia: zapojiť umenie, emócie
- Video TranMan
- Hudba: skladba pre zbor „Doctor, give me TXA, save my life...“
- Knihy: Komiks
- WWW stránka
- Twitter
 - how CRASH 2 got it wrong/wright
- „FOAM“ (free access Meducation)
- Kampaň „Trauma promise“
- BBC, ABC, Holby City, WikEM ...
- „Klima, morálna povinnosť, sociálna spravodlivosť“



Oh my docta! Save my life today! For my car crash bleedin give

Barking and Dagenham Community Choir

<https://www.youtube.com/watch?v=aGYG19krCa0>

Komiks





That's not a peer-reviewed number, but it's in the ballpark. That's pretty exciting for something that's arguably safer than normal saline—and almost as cheap.

It may be time to start thinking of TXA as **“aspirin” for trauma.**

M.Bivens

CRASH-2 Study of Tranexamic Acid to Treat Bleeding in Trauma Patients: A Controversy Fueled by Science and Social Media

Sophia Binz,¹ Jonathon McCollester,² Scott Thomas,³ Joseph Miller,¹ Timothy Pohlman,⁴ Dan Waxman,⁵ Faisal Shariff,^{3,6} Rebecca Tracy,³ and Mark Walsh^{3,7}

- Subjektívne zaradenie
- Pokles mortality iba o 1,5 %
- Žiadny rozdiel v transfúziách
- Iba polovica dostala transfúziu, málo pacientov s hypotenziou
- Mechanizmus účinku?
- Žiadne laboratórne vyšetrenia
- 99% výsledky?
- Málo nežiaducich účinkov (0,4 % DVT, 0,7 % TE)
- Rozvojové krajiny



- 2012 – 2019
- RCT: TXA verzus placebo
- Zaradení:
 - dospelí s izolovanou traumou mozgu; do 8 hodín
 - GCS \leq 12, krvácanie na CT
- Jednotná dávka: TXA 1 g/10 min + 1 g/8 hodín
- Výsledok: úmrtie / prepustenie / 28 dní
 - invalidizácia, kŕče, DVT/PE, komplikácie
- Jednoduchý protokol





HOME

ABOUT THE TRIAL

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Search

10157 patients randomised
(last updated **13/10/2017**)



Time since injury

Read Post →



BREAKING NEWS

Read Post →

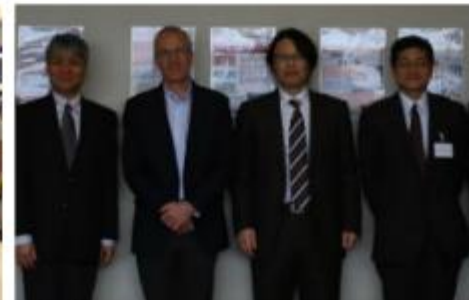


Time is Brain poem

Read Post →

TIME
IS
BRAIN

Randomise and
treat urgently



Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial



The CRASH-3 trial collaborators*




Summary

Background Tranexamic acid reduces surgical bleeding and decreases mortality in patients with traumatic extracranial bleeding. Intracranial bleeding is common after traumatic brain injury (TBI) and can cause brain herniation and death. We aimed to assess the effects of tranexamic acid in patients with TBI.

Published Online
October 14, 2019
[https://doi.org/10.1016/S0140-6736\(19\)32233-0](https://doi.org/10.1016/S0140-6736(19)32233-0)

- 2012 - 2019
- 12 737 pacientov
29 krajín
175 nemocníc
- **SK, CZ = 0**

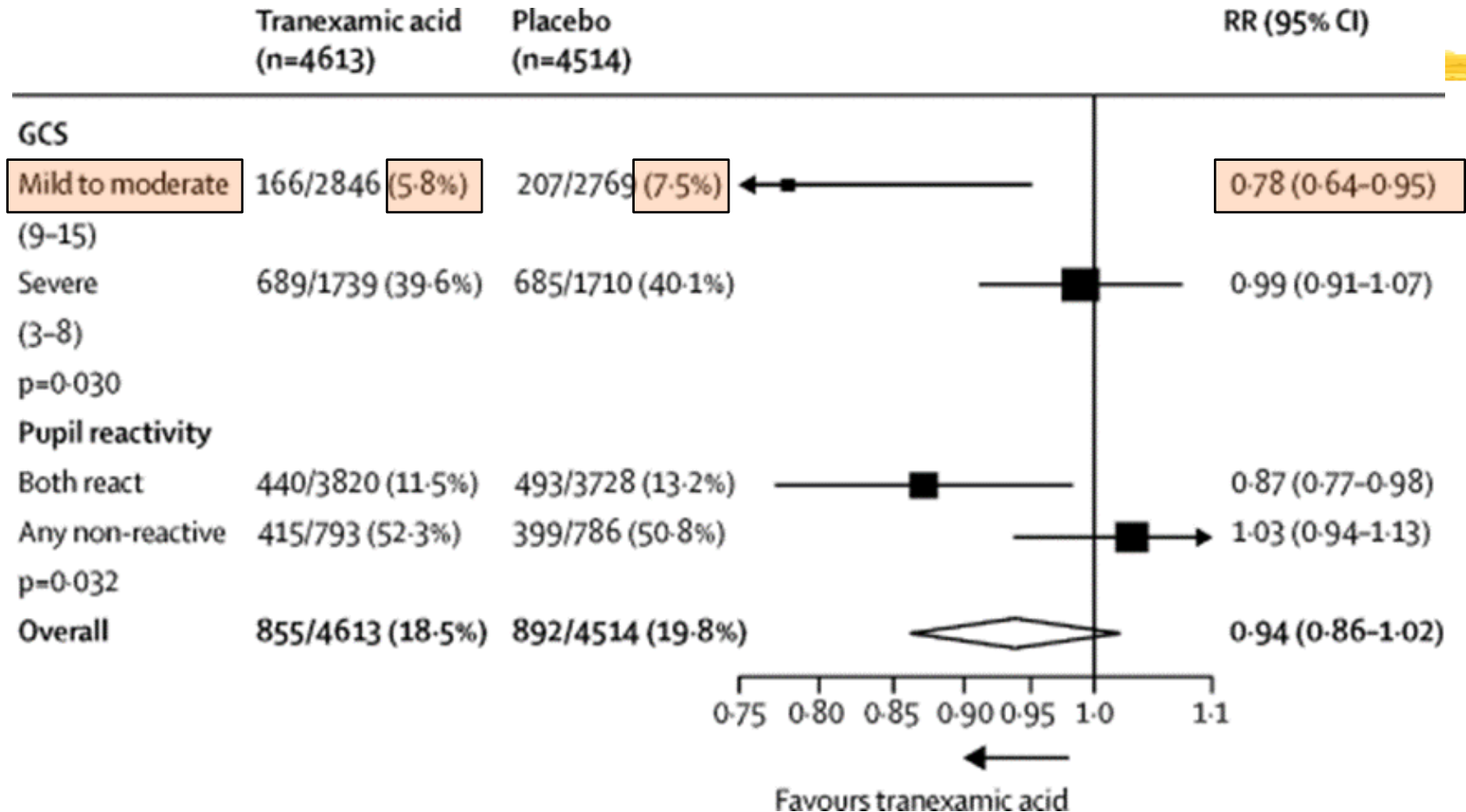
14.10.2019



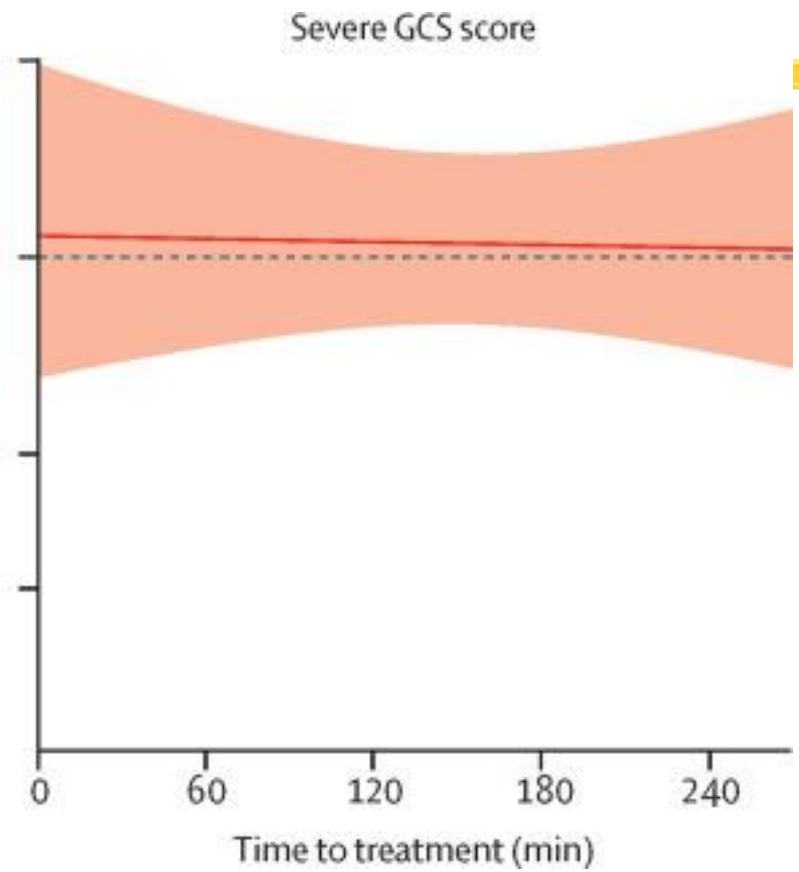
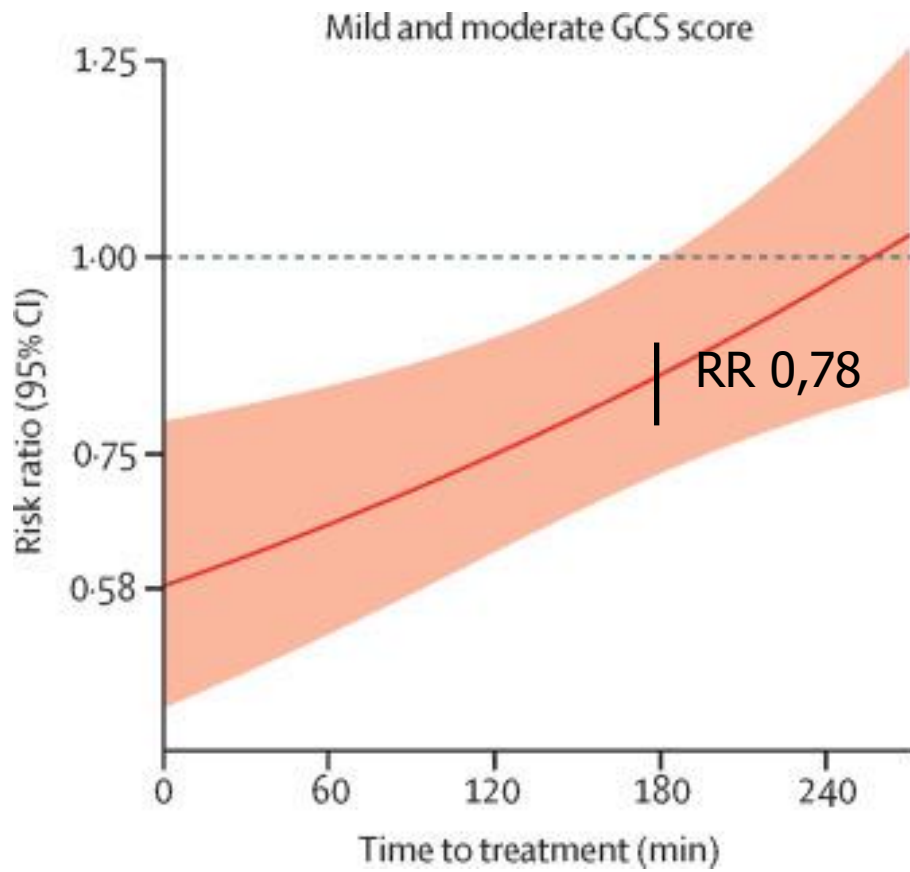
The CRASH-3 Trial
399 zhladnutí • 15. 10. 2019

2 0 ZDIELAŤ ULOŽIŤ ...

CRASH 3 mortalita pri podaní do 3 hodín



Celková mortalita nezmenená



Závery

- Celková mortalita znížená nesignifikantne
- Signifikantný prínos:
 - GCS 9 - 12
 - podanie do 3 hod
5,8 % vz. 7,5 %, RR 0,78 (0,64 - 0,95)
NNT = 55
- Podanie je bezpečné
 - bez rozdielu DVT/PE
 - invalidizácia rovnaká
- Implementovať

Research in context

Evidence before this study

Evidence from the CRASH-2 trial that administration of tranexamic acid within 3 h of injury in patients with traumatic

events or seizures. Combining the results of all available randomised trials shows a reduction in head injury-related death in patients treated with tranexamic acid. Early administration of tranexamic acid should be considered in patients with traumatic brain injury.

Our search were
we found two small randomised trials of tranexamic acid in traumatic brain injury with a total of

510 patients. Meta-analysis of the two trials showed a statistically significant reduction in death with tranexamic acid.

However, given the small size of the trials, we considered this evidence to be hypothesis generating, requiring confirmation in larger randomised trials.

Added value of this study

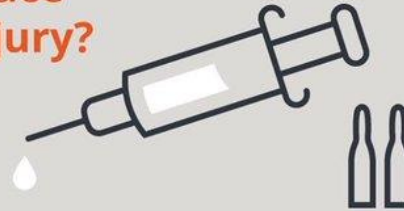
Our study found that the risk of death from head injury was reduced in patients treated with tranexamic acid, particularly

when patients

randomised
acid in 967 patients with
traumatic brain injury. The dose of tranexamic acid was the same as in the CRASH-3 trial and patients with a GCS score of 3 and those with unreactive pupils at baseline were also excluded. When the two trials were pooled, we found a reduction in head injury-related death with tranexamic acid and no evidence of an increased risk in vascular occlusive events or seizures. Combining the results of all available randomised trials shows a reduction in head injury-related death in patients treated with tranexamic acid. Early administration of tranexamic acid should be considered in patients with traumatic brain injury.

Can tranexamic acid (TXA) reduce death from traumatic brain injury?

TXA is a drug that prevents bleeding by stopping blood clots from breaking down



CRASH 3 Trial



12,737
Patients



29
Countries



175
Hospitals

Results



TXA could save **1 in 5** people who would have died following a mild or moderate head injury

Time is vital - TXA is more effective the earlier it is given

Every **20 minute delay** leads to a **10%** reduction in effectiveness

TXA is **safe to give**, there's no evidence of side effects and no increase in disability



Štúdie CRASH 1, 2, 3

- Tri štúdie zmenili medicínsku prax
 - zmeny v odporúčaníach
 - TXA: WHO esenciálny liek
 - London School of Hygiene – profesionáli
(Ian Roberts, David Yates, Hallema Shakur)
 - Financovanie cez Medical Research Council
 - Lacné lieky
 - Pri menších účinkoch je potrebný veľký súbor
 - Celosvetová spolupráca, rozvojové krajiny,
vrátane CZ a SK
- 49 / 239 / 10 008
40 / 274 / 20 211
29 / 175 / 12 737



Štúdie CRASH 1, 2, 3



- Spolupráca lekár + sestra
- Pocit dobre vykonanej práce
- Vysoká dohľadanosť
- Transparentne publikovaný protokol (Lancet, peer review)
- Intention-to-treat
- Kvalita štúdie?
- Publikácia v Lancet (IF 59) 2004, 2010, 2019, open access
- Autormi sú všetci zúčastnení
- Dôraz na implementáciu, disemináciu
- Republikácia v národnom jazyku

Štúdie CRASH 1, 2, 3

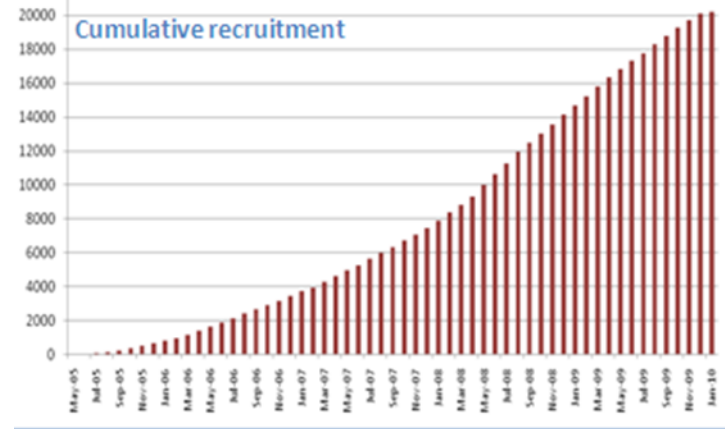
- Big international study
- Keep it simple, recruit thousands
- No extra work, no extra changes in practice
- No extra tests



Štúdie CRASH 1, 2, 3

- Big international study
- Keep it simple, recruit thousands
- No extra work, no extra tests
- No extra tests

Zapájat' sa!



Ďakujem za pozornosť



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