Bloodberedskap i kris och krig

Agneta Wikman, överläkare, professor, Klinisk immunologi och transfusionsmedicin, Karolinska Universitetssjukhuset och Karolinska Institutet och Transfusions specialist Försvarsmakten, Sverige

SWEDISH ARMED FORCES

Karolinska Institutet

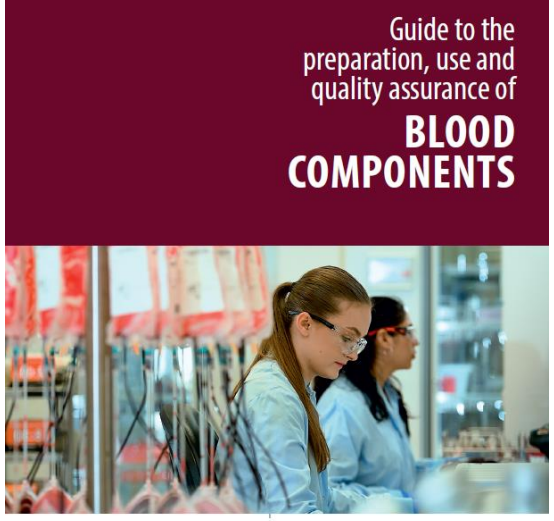
KAROLINSKA UNIVERSITETSSJUKHUSET

Disclosure

50% anställning Försvarsmakten, 50% Region Stockholm

Bakgrund och utmaningar

- Transfusionsmedicin i våra regioner producerar blodkomponenter för att täcka normalbehov – med låg kassation
- Blodkomponenter har förvaringstid på 7 dagar (trombocyter) -42 dagar (erytrocyter)
- Försvarsmakten är beroende av civil blodförsörjning
- Blod kan begäras till konfliktområden inom NATO alliansen
- NATO efterfrågar helblod eller helblodsekvivalenter (erytrocyter/plasma/trombocyter)
- Interoperabilitet mellan NATO länder krävs i men det är skillnader i lagar och regelverk som styr blod
- **Lokala, regionala, nationella, nordiska och NATO beredskapsplaner krävs**



EU Directive 2002/98/EG
2004/33/EG: Technical requirements
2005/61/EG :Traceability and noncormancies
2005/62/EG :Quality systems in Blood Establishments

National interpretation and translation ⟹ Regulations differ between the nations

SoHO Substances of Human Origin regulations approved, under translation in EU nations and planned implementation before 2027. *Article 63-67 deals with emergencies.*

US: FDA/AABB regulations

Canada: Health Canada regulations

NATO Blood Panel: Agreement on minimal requirements

Article 63 National SoHO emergency plans in collaboration with authorities
Nationella SoHO-beredskapsplaner

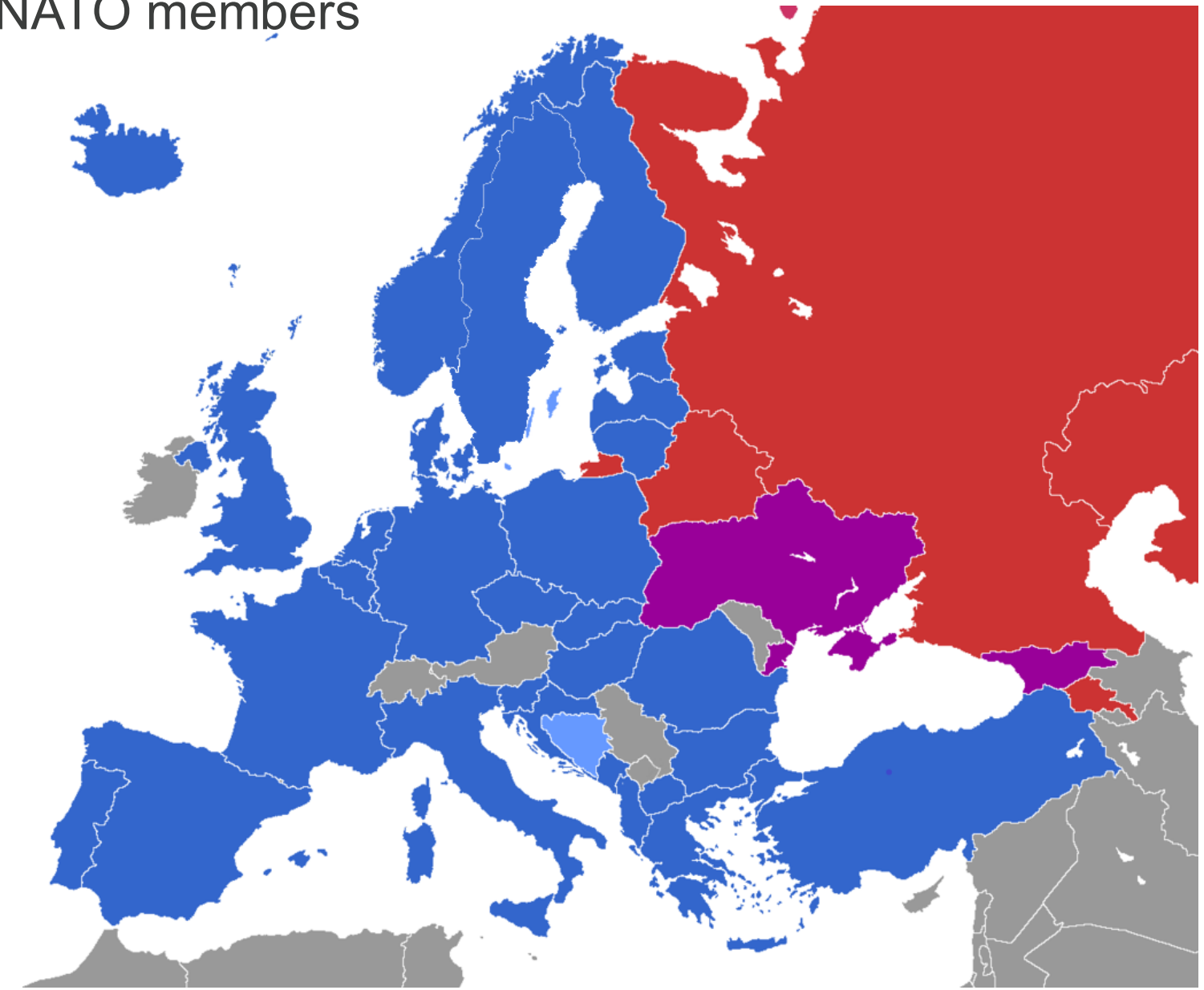
Article 64 Supply alerts for critical SoHO
Varningar avseende bristande tillgång på kritiska humanmaterial

Article 65 Derogation from the obligations to authorise SoHO preparations in health emergency situations
Undantag från skyldigheterna att bevilja tillstånd för SoHO-preparat vid en hälsokris

Article 66 Emergency derogations in man-made or natural disasters
Nödundantag i samband med katastrofer orsakade av människor eller naturkatastrofer
(e.g. non-leukocyte depleted blood, O RhD pos red cells/WB as emergency blood, virustesting….)

Article 67 SoHO entity emergency plans
Beredskapsplaner för SoHO-enheter

NATO members



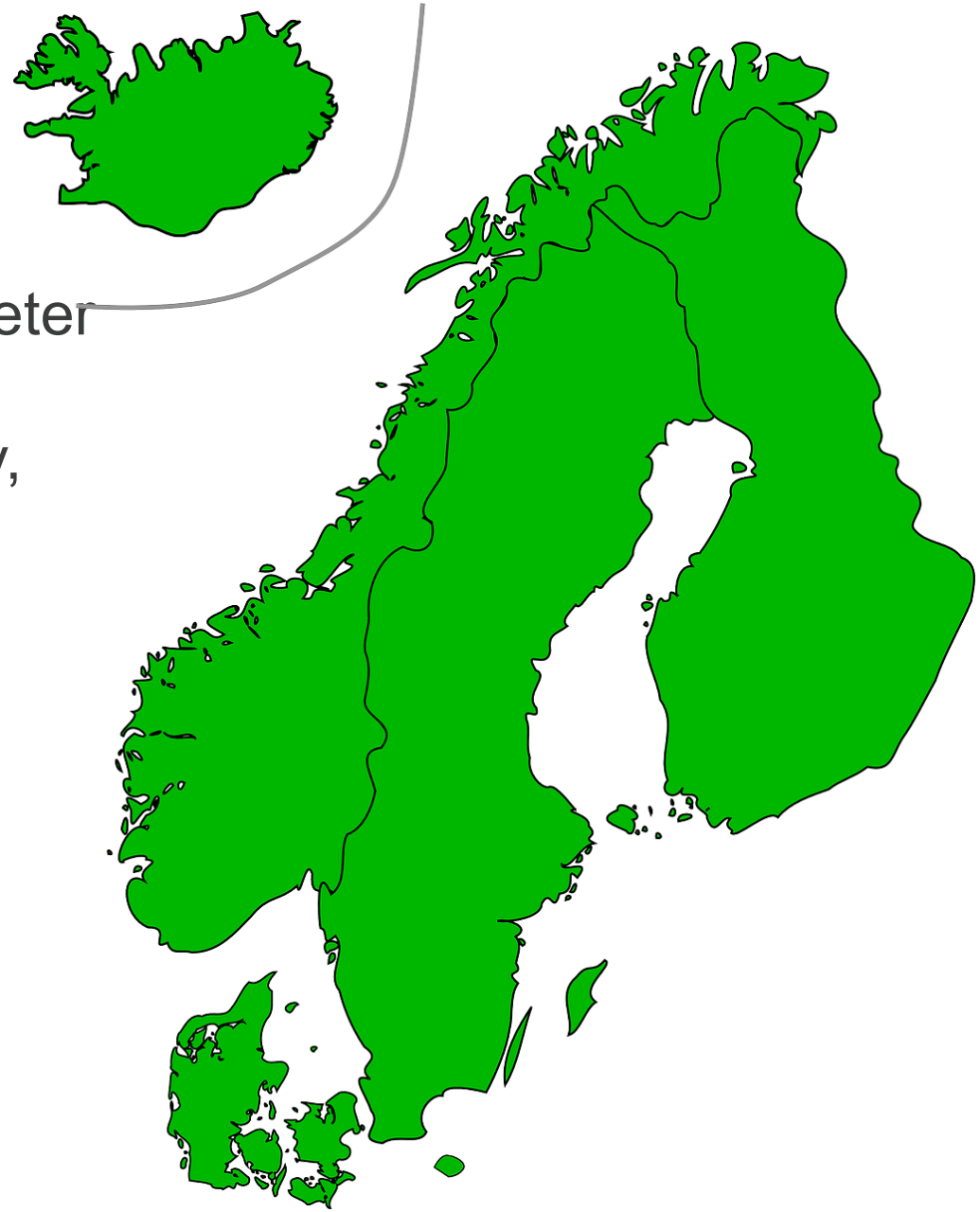
Norge, Sverige och Finland delar långa gränser och har liknande geografi med glest befolkade områden och få sjukhus i norr och mer tätbefolkat I söder.

Estland, Lettland och Litauen är nära grannar runt Östersjön

Den ryska invasionen av Ukraina 2022 har lett till ökat focus på civil och militär beredskap och nordiskt samarbete

Nordiskt samarbete

- Från 2022 har vi haft årliga möten med representation från civila, militärer och myndigheter
- Vi identifierar skillnader i regelverk, kvalitetskrav, personal, rutiner
- Rutiner som behöver harmoniseras
- Gemensamma beredskapsprojekt (t.ex. torkad plasma, logistik, kritiskt material)



Behandling vid stora blödning på sjukhus

Balanserad transfusion
4:4:1 (4 enheter erc, 4 enheter plasma,
1 enhet trc)

Fibrinogen
Tranexamsyra
Kalcium

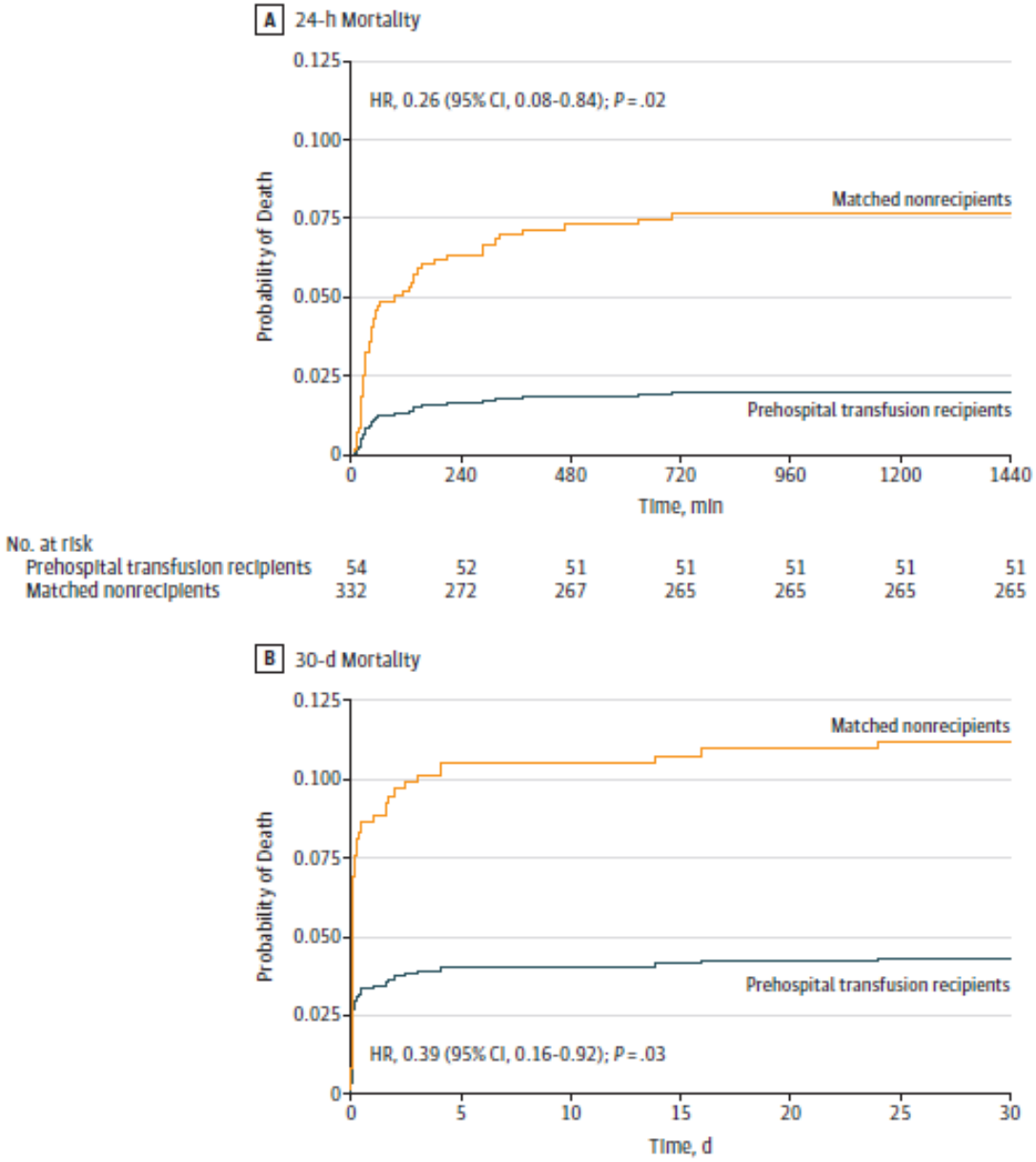
Restriktivitet med klara vätskor

Monitorering
Målstyrd behandling

Shackelford S et al, JAMA 2018

Retrospective study, matched controls
Prehospital blood transfusion within 36 min
- reduces 24 hours mortality (HR 0.26)
- reduces 30 days mortality (HR 0.39)

Figure 3. Mortality of Prehospital Transfusion Recipients vs Matched Nonrecipients



Published in final edited form as:
J Trauma Acute Care Surg. 2017 July ; 83(1): 19–24. doi:10.1097/TA.0000000000001531.

EVERY MINUTE COUNTS: TIME TO DELIVERY OF INITIAL MASSIVE TRANSFUSION COOLER AND ITS IMPACT ON MORTALITY

David E Meyer, MD, MS,
University of Texas Health Sciences Center and McGovern School of Medicine, Houston, TX

Conclusion: Every minute delay of blood increased mortality 5%

ORIGINAL STUDY 2024 Ann Surg

Whole Blood and Blood Component Resuscitation in Trauma

Interaction and Association with Mortality

Dorken-Gallastegi, Ander MD*; Spinella, Phillip C MD†; Neal, Matthew D MD†; Leeper, Christine MD†; Sperry, Jason MD MPH†; Peitzman, Andrew B MD†; Brown, Joshua B MD MSc†

Reduced 4h, 24 h and 30 d mortality in WB compared to BC

Prehospitalt helblod och blodkomponenter

- Alla ambulanshelikoptrar har blod, 5 har helblod i Sverige, resten har erc och plasma, i Norge har alla helblod, Finland har erc och plasma, en studie pågår med helblod
- Vägburen ambulans har bara klara vätskor

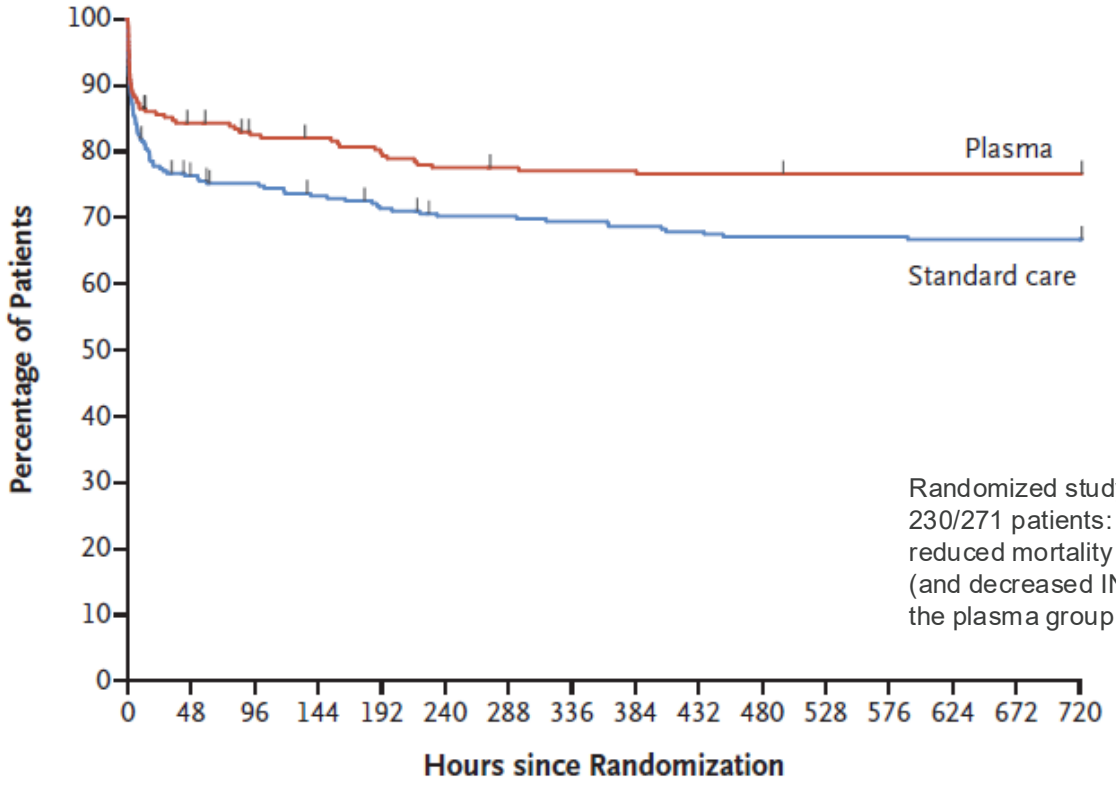
Helblod på sjukhus

- Tre universitetssjukhus i Sverige,
- Några i Norge, fler på gång att implementera helblod
- Ej implementerat i Finland på sjukhus

NEJM 2018

Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock

J.L. Sperry, F.X. Guyette, J.B. Brown, M.H. Yazer, D.J. Triulzi, B.J. Early-Young, P.W. Adams, B.J. Daley, R.S. Miller, B.G. Harbrecht, J.A. Claridge, H.A. Phelan, W.R. Witham, A.T. Putnam, T.M. Duane, L.H. Alarcon, C.W. Callaway, B.S. Zuckerbraun, M.D. Neal, M.R. Rosengart, R.M. Forsythe, T.R. Billiar, D.M. Yealy, A.B. Peitzman, and M.S. Zenati, for the PAMPer Study Group*



Randomized study
230/271 patients:
reduced mortality
(and decreased INR) in
the plasma group

"Prehospital treatment with dried plasma in patients with major bleeding– A prospective randomized controlled multicentre trial: Statistical analysis protocol" *Sandstrom et al, Acta Anaesthesiologica Scandinavica.*

Research

Pusateri et al 2019

JAMA Surgery | Original Investigation

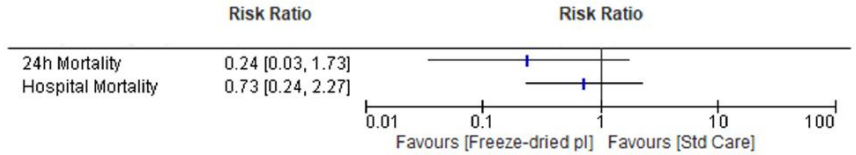
Association of Prehospital Plasma Transfusion With Survival in Trauma Patients With Hemorrhagic Shock When Transport Times Are Longer Than 20 Minutes

A Post Hoc Analysis of the PAMPer and COMBAT Clinical Trials

Acad Emerg Med. 2023;00:1–7.

Pre-hospital freeze-dried plasma for critical bleeding after trauma: A pilot randomized controlled trial

FIGURE 2 Mortality outcomes.



Skallsjö *et al.*
Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine
(2025) 33:130
https://doi.org/10.1186/s13049-025-01439-7

Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine

RESEARCH Open Access

Bleeding resuscitation in the ambulance service, an observational study of standard care in Sweden

- A large proportion had a high shock index (SI) and impaired coagulation at arrival at hospital
- a third received more than 1000 mL of clear fluids
- A high SI and a large prehospital bleed predicted worse outcome (death, massive transfusions)

Dried plasma alternatives in Europe today

Lyoplas N-w, (German Red Cross)

Freeze-dried single donor, blood group specific
(Pharmaceutical product)

French Lyophilized Plasma, FLYP (French Military Blood Institute, Centre de Transfusion Sanguine des Armees, CTSA)
Freeze-dried, pools of 11, pathogen reduced, universal
(Blood product)

Octaplas LG Powder (Octapharma) Freeze dried, pools of 630-1520, SD treated, blood group specific
(Pharmaceutical product)

FrontlineODP (Velico Medical) spray-dried, single donor, intended for local production in the Blood Banks, installation of an instrument/system, under evaluation in Europe and in USA.

Platelet to erythrocyte transfusion ratio and mortality in massively transfused trauma patients. A systematic review and meta-analysis

Rijnhout et al, J Trauma Acute Care Surg 2021

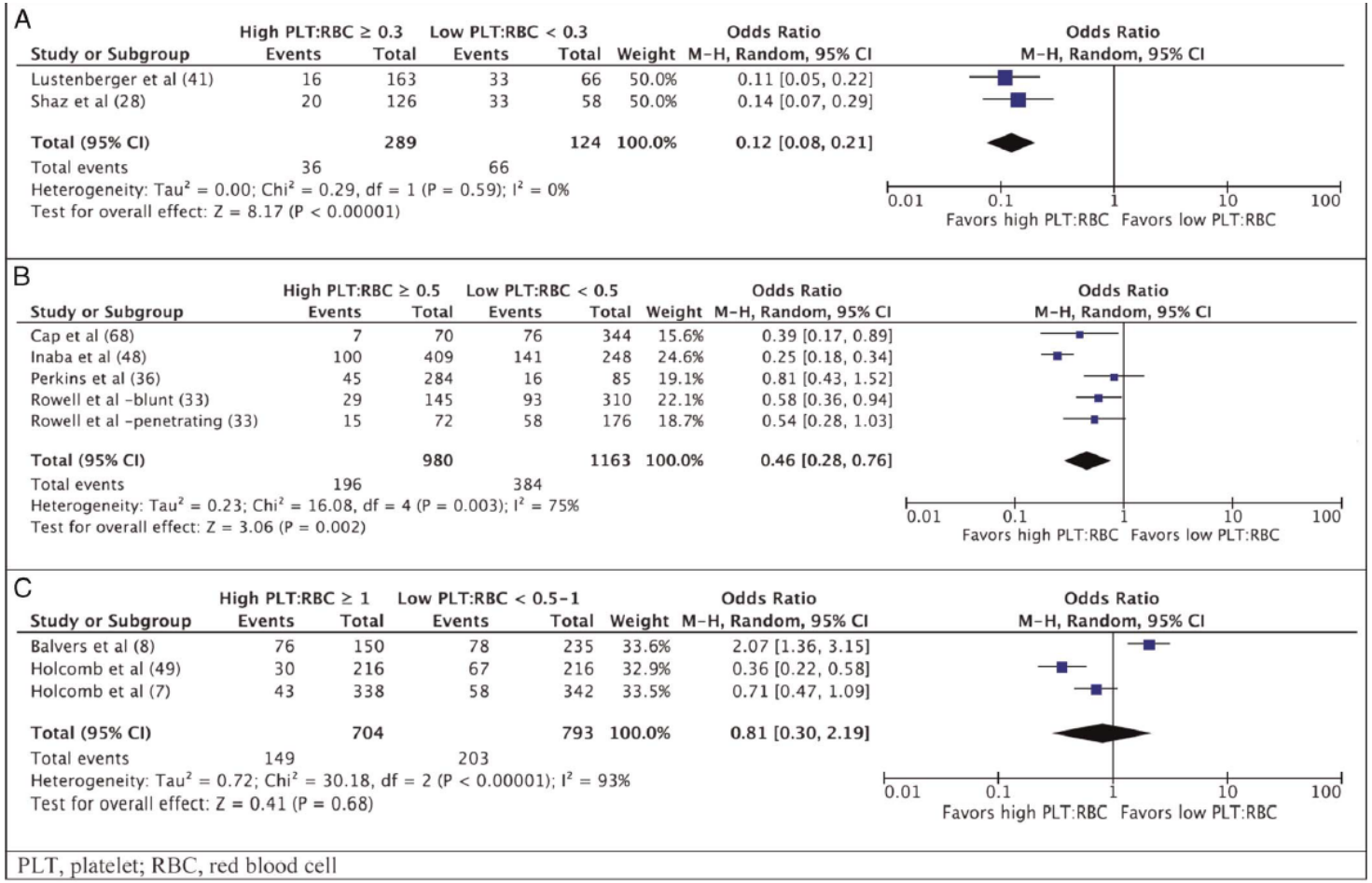


Figure 3. (*A*), 24 hours mortality in low <0.3 as compared with high ≥0.3 PLT/RBC ratio. (*B*), 24 hours mortality in low <0.5 as compared with high ≥0.5 PLT/RBC ratio. (*C*), 24 hours mortality in low 0.5 or <1 as compared with high ≥1 PLT/RBC ratio.

Do not forget the platelets: The independent impact of red blood cell to platelet ratio on mortality in massively transfused trauma patients Gallasteghi AD Trauma Acute Care Surg 2022

Gallastegi et al.

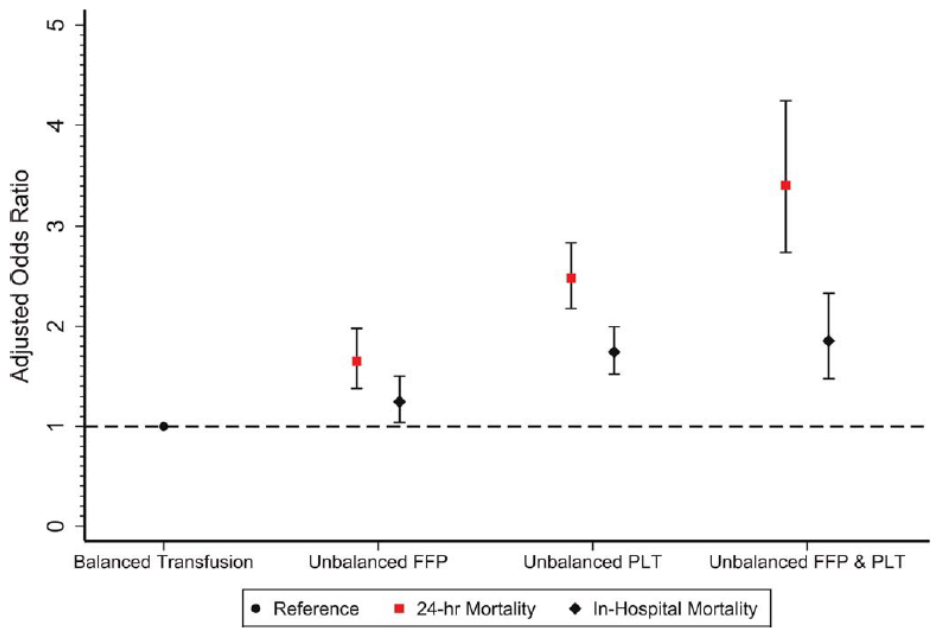


Figure 4. Risk-aORs by deviation from balanced transfusion.

Platelet transfusions improve hemostasis and survival in a substudy of the prospective, randomized PROPPR trial *Cardenas JC et al Blood Advances 2018*

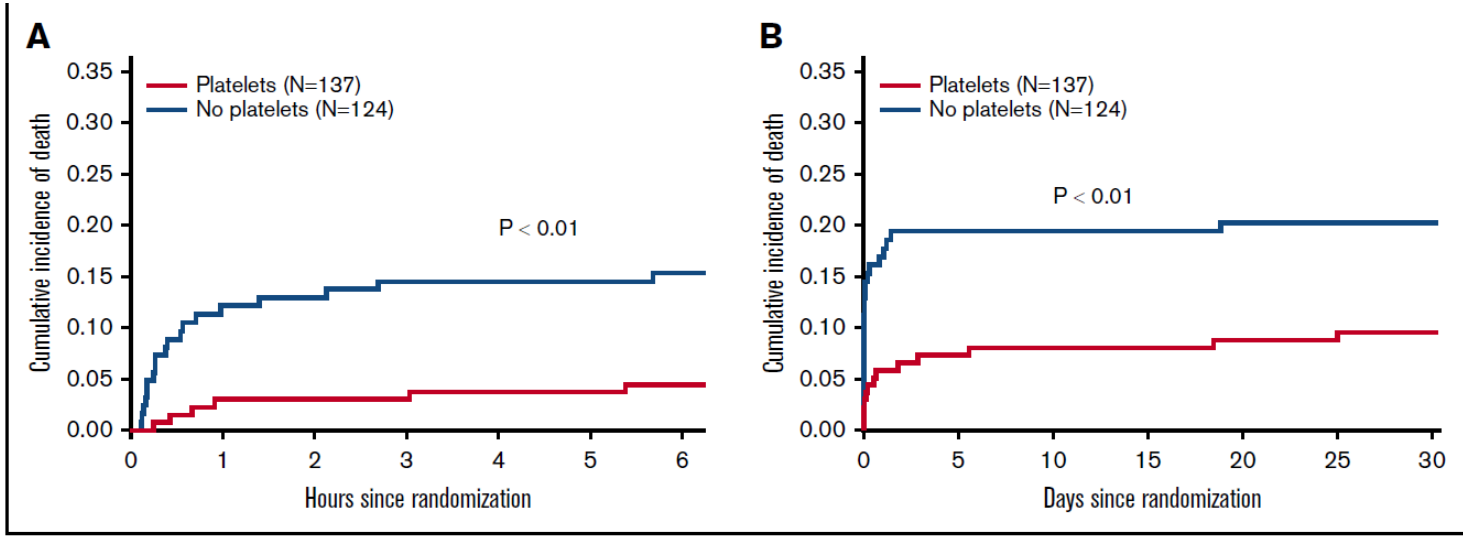


Figure 1. Kaplan-Meier curves. Curves demonstrate cumulative incidence of death during the first 6 hours (A) and 30 days (B).

Hospitals

Sverige har långa avstånd
Många små sjukhus har inga trombocyter i lager

Förvaringstid 7 dagar
ojämn efterfrågan
För många eller för få
Hög kassation- höga kostnader

Men har emellanåt blödande patienter, trauma, GI blödningar, obstsriska blödningar, perioperativa blödningar

Frontiers of Public Health 2023

Cryopreserved platelets in bleeding management in remote hospitals: A clinical feasibility study in Sweden

Agneta Wikman[1,2]*, Beatrice Diedrich[1,2], Karl Björling[3], Per-Olof Forsberg[4], Anna-Maria Harstad[5], Ragnar Henningsson[5], Petter Höglund[1,6], Hans Sköld[7], Lars Östman[3] and Per Sandgren[1,2]

Background:
We have many hospitals in Sweden with no platelet or 1-2 platelets in stock, despite occasionally treating major bleeding

Major Aim:
To evaluate the safety and feasibility of using cryopreserved platelets in those hospitals

Methods:
Bleeding patients to whom platelet transfusions were indicated were consecutively included in two remote hopitals

Results: 23 patients were included, 9 GI bleeding, 5 perioperative bleeding, 4 trauma bleeding. 4,9+3,3 RBC, 3,2+2,3 plasma units, 1,9+2,2, platelet units, whereof 1,5+1,1 cryopreserved

Conclusion: Cryopreserved platelets in remote hospitals are logistically feasible in the treatment of bleeding
Clinical effectiveness and safety previously shown in other studies are supported in this small feasibility study.

Cryopreserved platelets

– Have been used since the 1970ies
– Previously, mainly special indications such as HLA immunized refractory patients or rare HPA types
– Clinical and experimental studies supporting good hemostatic effect and safety
– Experiences from military healt care *(NL, Noorman et al, Czech Republique, Bohonek et al)*
– Randomized studies on going in Australia and New Zeeland *Read MC 2019, Transfusion, McGuiness S 2022 Vox Sang*
– Remote hospitals and preparedness in crisis and catastrophies *Cryopreserved platelets in bleeding management in remote hospitals: A clinical feasibility study in Sweden, Wikman et al 2023*

Add cryoprotectant (DMSO in saline) to fresh platelets

Centrifugation

Remove supernatant

Concentrated platelets (volume 10 mL)

Cryopreserved at -80°C up to 4 years

Conclusion

- stored for many years
- Prepared in 20 minutes on request
- Implemented and used in remote hospitals in Sweden and as back-up inventory in large hospitals. Used only on bleeding indication.

Reconstitute in thawed plasma at issue

Collaboration in a pilot project Norway, Sweden, Finland
Nordic Blood Preparedness Project
Initiated from Norway, Centre of Blood Preparedness, funded from the Norweigan Ministry of Health

A civilian project in the Cap of the North: Norway, Sweden and Finland
- there is a need for blood preparedness systems in all levels of health care services to reduce deaths from bleeding in areas with long patient transport times.
- emergency collection of whole blood was identified as a valuable management strategy in situations where banked blood was unavailable.
- there is a need for a Nordic collaboration and cross-country interoperability.

Working groups:
- Regulatory issues
- Clinical management
- Blood service
- Crossborder issues
- Communication/ IT-supportive systems

Received: 15 February 2022 | Revised: 2 May 2022 | Accepted: 2 May 2022
DOI: 10.1111/trf.16968

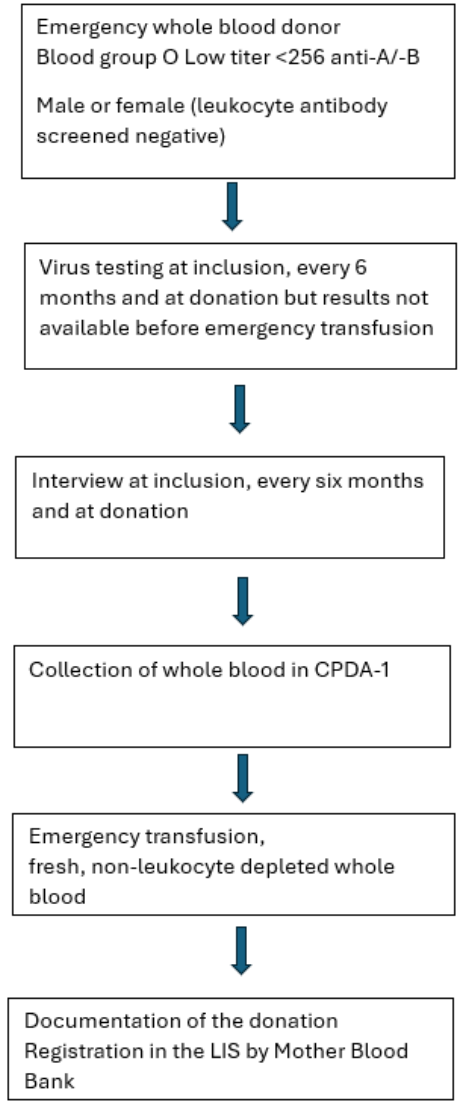
DISASTER PREPAREDNESS

TRANSFUSION

The Norwegian blood preparedness project: A whole blood program including civilian walking blood banks for early treatment of patients with life-threatening bleeding in municipal health care services, ambulance services, and rural hospitals

Torunn Oveland Apelseth[1,2,3] | Mirjana Arsenovic[4] | Geir Strandenes[1]

Fig 2 The Preplanned Walking Blood Bank in North of Norway



Försvarsmaktens Blodcentral

Tillstånd att tappa helblod, utbildar läkare och sjuksköterskor på försvarshälsor och traumatroppar

Godkända blodgivare på civil blodcentral

Blodgrupp O låg titer anti-A,-B

Bör ge blod 1 g/år på civil blodcentral (inkl. tester på ett ackrediterat lab)

Tappning inom FM Blodcentral vid risk uppdrag, akuta händelser, kompetensvidmakthållande

Testas med snabbtester vid egen tappning

Samarbete med utvalda blodcentraler-rutinerna behöver beskrivas

Katastrofplaner

- Katastrofplaner för blodverksamheten/transfusionsmedicin samordnade med sjukhuset ska finnas och uppdateras regelbundet
- Blodverksamheten/Transfusionsmedicin ska delta i i sjukhusets katastrofövningar (inte bara i en telefon kedja)
- Rutiner för säker ID-märkning och säkra blodgrupperingar!
- Akut blodtappning bör ingå i planerna vid stora katatstrofer/masskadehändelser för produktion av helblod och blodkomponenter
- Identifierade O blodgivare med låg titer anti-A och anti-B (IgM<256) som kan kallas in akut kan ge helblod som är prioriterat vid akuta stora blödningar *(How do I implement a whole blood program with low blood wastage, Backstrom et al, Transfusion 2025)*

Konklusioner

- Nära samarbete mellan Nor-Sve-Fin + Danmark är viktigt
- Prioritet
  - **blodprodukter med längre förvaringstid (torkad plasma, frysta trombocyter)**
  - **”surge plans” vid stora akuta händelser-helblod**
  - harmoniserade rutiner (märkning, spårbarhet….)
  - harmoniserade undantag SoHO art 63-67
  - deltagande i övningar (sjukhus, relevanta militära övningar)

- “Competent authority” Socialstyrelsen är ansvarig för att samordna och koordinera beredskap i regionerna
- T.ex. om vi blir tillfrågade att leverera till konfliktområden?

Acknowledgements

Torunn Apelseth Norweigan Center for Blood Preparedness, Bergen and
Jouni Lauronen, Finnish Red Cross Blood Service Helsinki

Försvarsmakten

NATO Blood Panel

Region Stockholm, speciellt tack till Ingrid Engström, Region Norrbotten, Västerbotten, Gotland, Jämtland, Örebro, Värmland m.fl.

och många andra