Major bleeding and transfusion: does age matter?

14 June 2017 South Central Regional Transfusion Day

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Outline

- Demographics
- Physiological changes with ageing
- Major bleeding and coagulation in older people
- Challenges of safe and appropriate transfusion in older people
- How might this affect our transfusion practice?

Over 70% of UK population growth in the next 20 years will be in the over 60 age group

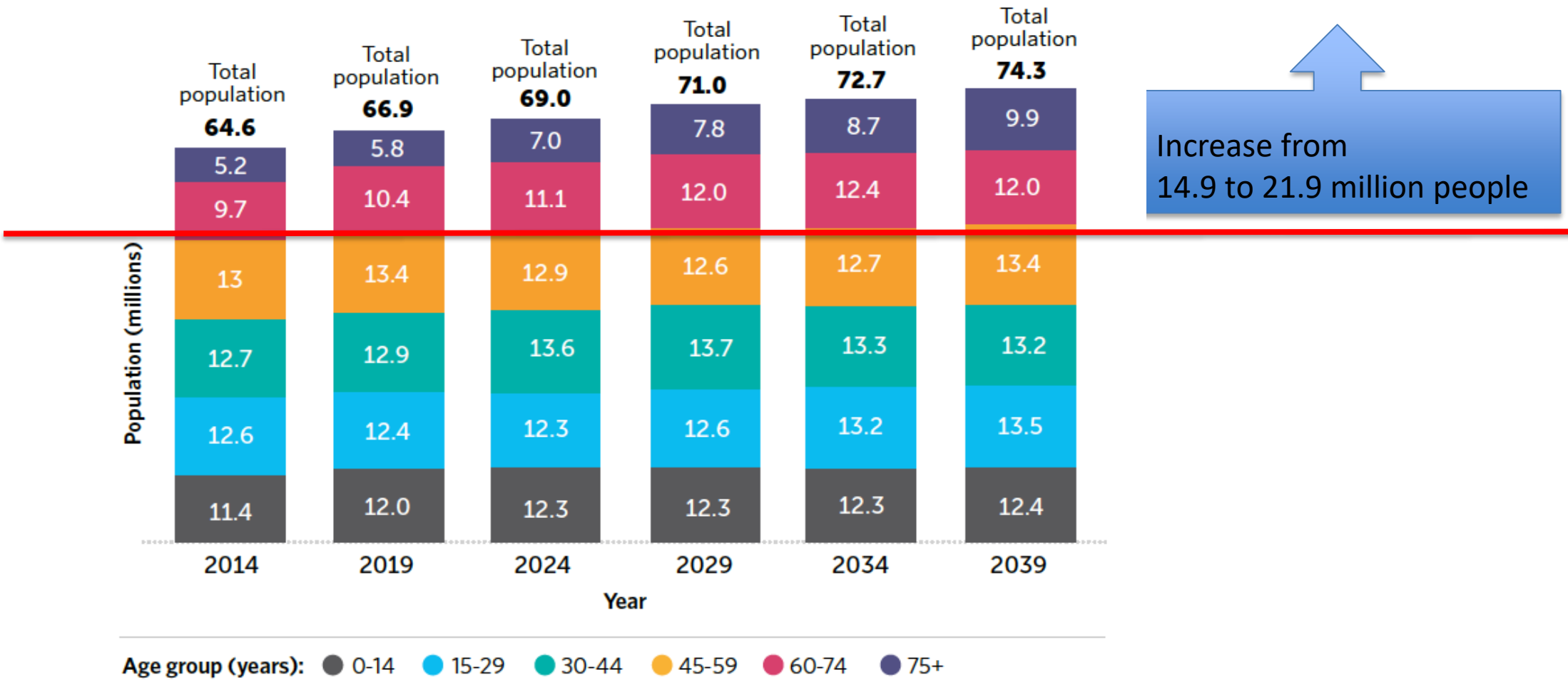
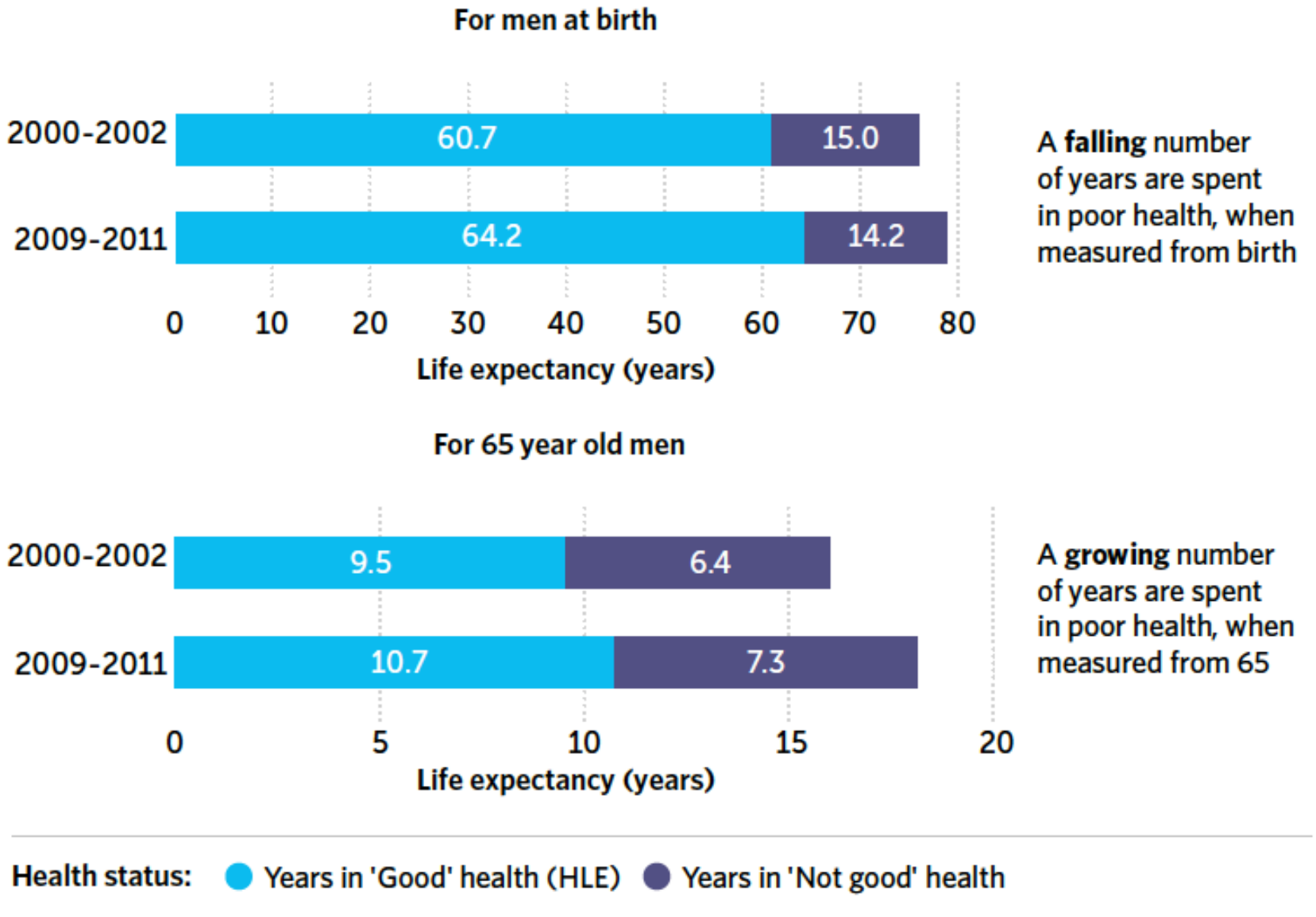


Figure 1.1: Population estimates and projections, based on ONS principal population projections, 2014[3].

Future of an ageing population, Government Office for Science, pub 2016

People aged >65 are spending more time in ‘ill-health’



Coagulation and ageing

Normal haemostasis

- Primary haemostasis
  - Activation and aggregation of platelets
- Secondary haemostasis
  - Clotting factors and formation of fibrin clot
- Fibrinolysis (breakdown of clot)

Key changes with ageing

- Platelets more active
- Fibrinogen levels rise
- Factor VIII, VWF rise
- Fibrinolysis markers – some increase

Overall: more prothrombotic

- Other factors – anaemia, drugs

Mari D, Ogliari G, Castaldi D, Vitale G, Bollini EM, Lio D. Hemostasis and ageing. *Immunity & Ageing : I & A*. 2008;5:12.
Sepúlveda C, Palomo I, Fuentes E. Primary and secondary haemostasis changes related to aging. Mech Ageing Dev. 2015;150:46-54

Age matters: host response

- Host
  - Physiological changes
  - Comorbidities
  - Frailty
  - Medication

Response to acute blood loss, form stable clot

Response to treatment (MHP)

Age matters: incidence of major bleeding

Leading causes of major haemorrhage
Surgical/cardiothoracic
Trauma
Gastrointestinal
Obstetric

Clinical features of UGI bleeding in elderly vs younger patients

Similarities

- Presenting manifestations of bleeding: haematemesis (50%); melaena (30%); haematemesis and melaena (20%)
- Peptic ulcer disease most common cause

Differences (in elderly patients)

- Fewer antecedent symptoms (abdominal pain, dyspepsia, heartburn)
- Aspirin and NSAID use
- Presence of comorbid conditions
- Higher rates of hospitalisation
- Higher rates of rebleeding
- Higher mortality rate

Yachimski PS and Friedman LS *et al*. (2008) Gastrointestinal bleeding in the elderly *Nat Clin Pract Gastroenterol Hepatol* **5:** 80–93 doi:10.1038/ncpgasthep1034

Peptic ulcer re-bleeding and mortality by patient age

Table 3 Peptic ulcer rebleeding and mortality by patient age.

Study	Endoscopic therapy	Age (years)	Number of patients	Rebleeding (%)	Mortality (%)
Choudari *et al.* (1995)[28,a]	Injection or heater probe	≤60	102	13	3
		61–74	116	20	6
		≥75	108	17	5
Chow *et al.* (1998)[30,b]	Injection and/or heater probe	<60	833	11.9	0.4
		60–79	706	17.7	5.9
		≥80	205	25.4	11.2
Yamaguchi *et al.* (2003)[10,a]	Hemostatic clip and/or injection	<80	417	5	0.5
		≥80	42	10	2

[a]All patients received endoscopic therapy. [b]Not all patients received endoscopic therapy.

Yachimski PS and Friedman LS *et al*. (2008) Gastrointestinal bleeding in the elderly
Nat Clin Pract Gastroenterol Hepatol **5:** 80–93 doi:10.1038/ncpgasthep1034

Aspirin and bleeding

Observational study from Italy 2003-2008

- Overall incidence rate of total haemorrhagic events:
  - Aspirin use 5.58 (95% CI, 5.39-5.77) per 1000 person-years
  - No Aspirin 3.60 (95% CI, 3.48-3.72) per 1000 person-years
  - Use of aspirin was associated with an excess risk of gastrointestinal (IRR, 1.55; 95% CI, 1.46-1.65) and intracranial (IRR, 1.54; 95% CI, 1.43-1.67) bleeding.

De Berardis et al. JAMA. 2012;307(21):2286-2294

Platelet transfusions and intracranial bleeding

Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial

Hypothesis: platelet transfusion reduces the risk of death and dependence compared with standard care

M Irem Baharoglu et al. Lancet. 2016 Jun 25;387(10038):2605-13

Results: baseline characteristics

	Platelet transfusion group (n=97)	Standard care group (n=93)
Mean age (years)	74·2 (49–94)	73·5 (40–92)
Men	55 (57%)	57 (61%)
Women	42 (43%)	36 (39%)
Vascular comorbidities		
Ischaemic stroke or TIA	38/94 (40%)	40 (43%)
ICH	4 (4%)	5/92 (5%)
Hypertension	68/94 (72%)	67/92 (73%)
Diabetes mellitus	15 (15%)	17/90 (19%)
Hypercholesterolaemia	46/94 (49%)	40/84 (48%)
Ischaemic heart disease	23/96 (24%)	22/90 (24%)
Peripheral arterial disease	16 (16%)	4/91 (4%)
Coagulation disorder	1/96 (1%)	2/91 (2%)
Antiplatelet therapy pre-ICH*		
COX inhibitor alone	71 (73%)	78 (84%)
COX inhibitor and dipyridamole	18 (19%)	13 (14%)
ADP inhibitor alone	4 (4%)	1 (1%)
COX inhibitor and ADP inhibitor	3 (3%)	1 (1%)
None	1 (1%)	0
Statin therapy pre-ICH	54/96 (56%)	48/92 (52%)
Median GCS score	14 (13–15)	15 (13–15)
Median NIHSS score	12 (7–19)	13 (7–17)
Mean platelet count (×10⁹/L)	229 (120–622)	241 (91–461)
Country of inclusion*		
Netherlands (27 centres)	63 (65%)	57 (61%)
France (9 centres)	19 (20%)	20 (22%)
UK (5 centres)	15 (15%)	16 (17%)
ICH location		
Supratentorial deep	62/96 (65%)	70/92 (76%)
Supratentorial lobar	32/96 (33%)	22/92 (24%)
Infratentorial	2/96 (2%)	0
Median ICH volume (mL)	13·1 (5·4–42·4)	8·0 (4·4–25·8)
Intraventricular extension	12/95 (13%)	20/92 (22%)
Median total ICH Score†	1 (0–2)	1 (0–1)
Age >80 years	28 (29%)	34 (37%)
GCS score		
5–12	19 (20%)	11 (12%)
3–4	1 (1%)	0
ICH volume >30 mL	32 (34%)	19 (21%)
Intraventricular extension	12 (13%)	20 (22%)
Infratentorial ICH location	2 (2%)	0

Table 1: Baseline characteristics of the intention-to-treat population

Results: Outcomes

Table 2: Secondary outcomes in the intention-to-treat population

	Platelet transfusion group (n=97)	Standard care group (n=93)	Odds ratio (95%CI)	p value
Alive at 3 months (survival)	66 (68%)	72 (77%)	0·62 (0·33–1·19)	0·15
mRS score 4–6 at 3 months	70 (72%)	52 (56%)	2·04 (1·12–3·74)	0·0195
mRS score 3–6 at 3 months	86 (89%)	76 (82%)	1·75 (0·77–3·97)	0·18
Median ICH growth at 24 h (mL)*	2·01 (0·32–9·34)	1·16 (0·03–4·42)	..	0·81

Data are n (%) or median (IQR). mRS=modified Rankin Scale. ICH=intracerebral haemorrhage. *n=80 in platelet transfusion group and 73 in standard care group.

Platelet transfusion seems inferior to standard care

No high level evidence to support platelet transfusion in intracranial haemorrhage

The changing face of major trauma

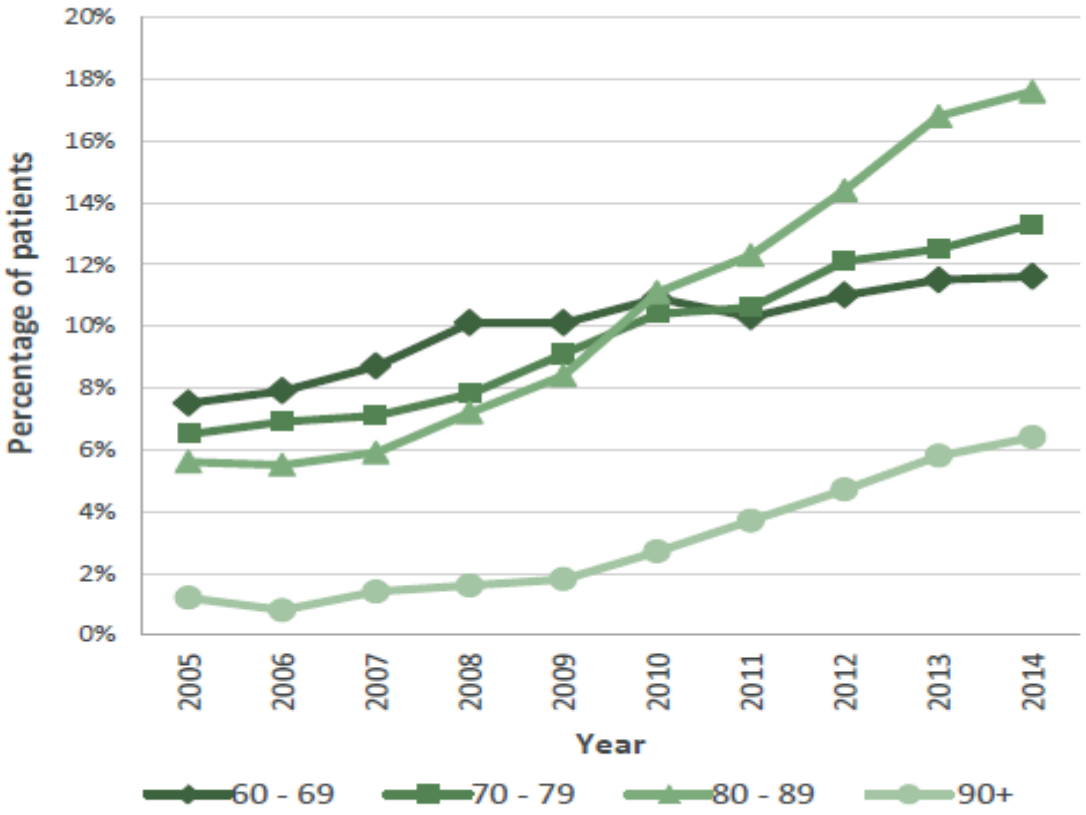


Figure 3a: Severely injured patients since 2005

- Age group >60 now accounts for >50% of severely injured patients
- Incremental change exceeds what would be projected for ageing population

TARN. Major Trauma In Older People - 2017 Report

TARN

THE TRAUMA AUDIT & RESEARCH NETWORK

England & Wales

MAJOR TRAUMA IN OLDER PEOPLE

2017

Uncontrolled bleeding is one of the leading causes of early death after trauma.

Original article

The changing face of major trauma in the UK

OPEN ACCESS

A Kehoe,[1,2] J E Smith,[1,2,3] A Edwards,[4] D Yates,[4] F Lecky[4,5]

[1]Emergency Department, Derriford Hospital, Plymouth, UK

ABSTRACT

Aim Major trauma (MT) has traditionally been viewed as a disease of young men caused by high-energy

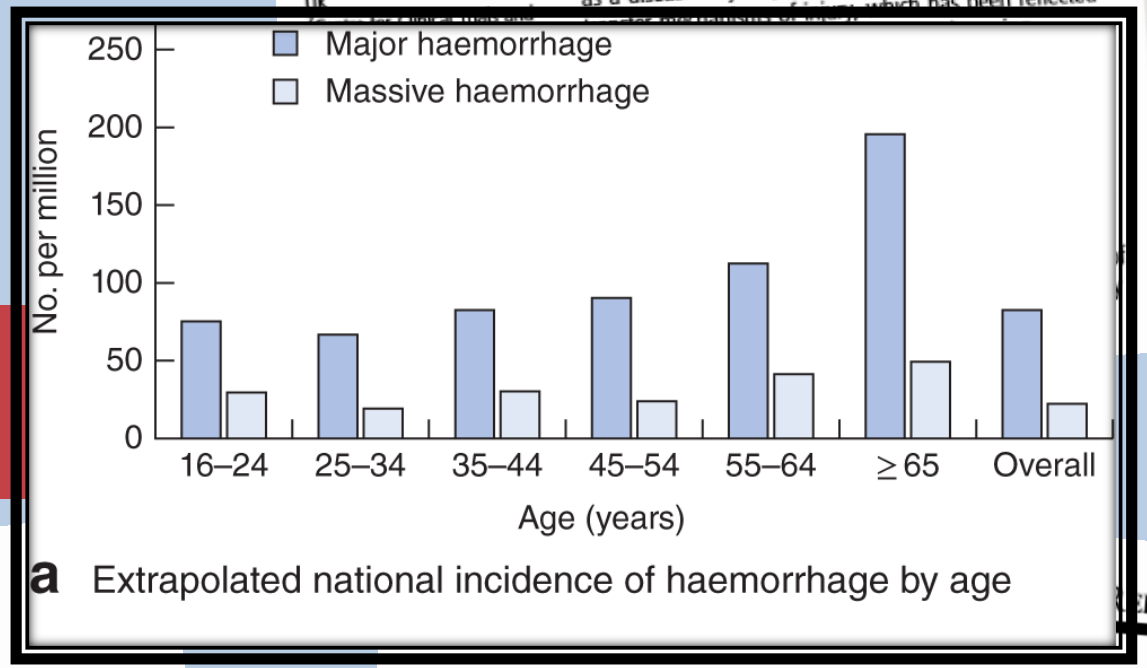
Key messages

What is already known on this subject?

- Major trauma is traditionally considered to be a problem of young men.
- With ageing populations, it is predicted that in the future the elderly will comprise an increasingly significant proportion of the major trauma workload.

What might this study add?

- The future is here already—in the UK, the average age of major trauma cases on the Trauma Audit Research Network database in 2013 was nearly 60 years.



a Extrapolated national incidence of haemorrhage by age

BJS

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Original article

Mortality from trauma haemorrhage and opportunities for improvement in transfusion practice

S. J. Stanworth, R. Davenport, N. Curry, F. Seeney, S. Eaglestone, A. Edwards, K. Martin, S. Allard, M. Woodford, F. E. Lecky, K. Brohi

First published: 3 February 2016 Full publication history

DOI: 10.1002/bjs.10052 View/save citation

EPORT

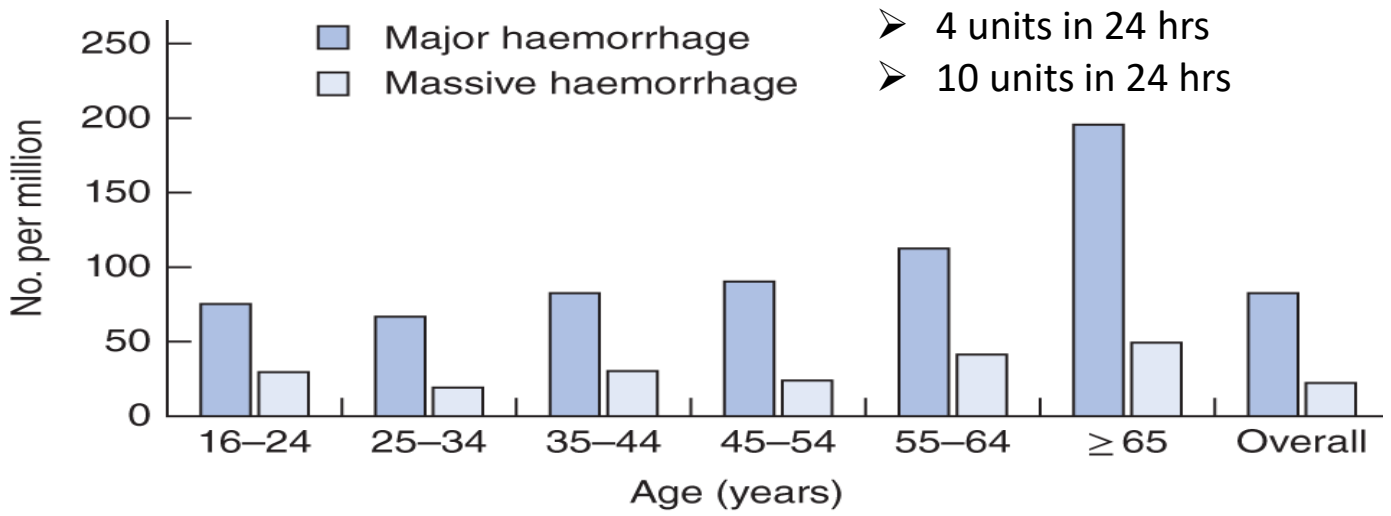
A position paper: The convergence of aging and injury and the need for a Geriatric Trauma Coalition (GeriTraC)

Zara Cooper, MD, MSc, Cathy A. Maxwell, PhD, RN, Samir M. Fakhry, MD, Bellal Joseph, MD, Nancy Lundebjberg, MPA, Peter Burke, MD, *and* Robert Baracco, MD

Increased bleeding in older patients

NIHR prospective study in collaboration with Trauma Audit Research Network:

- Increased likelihood of major or massive haemorrhage and death in patients aged > 65

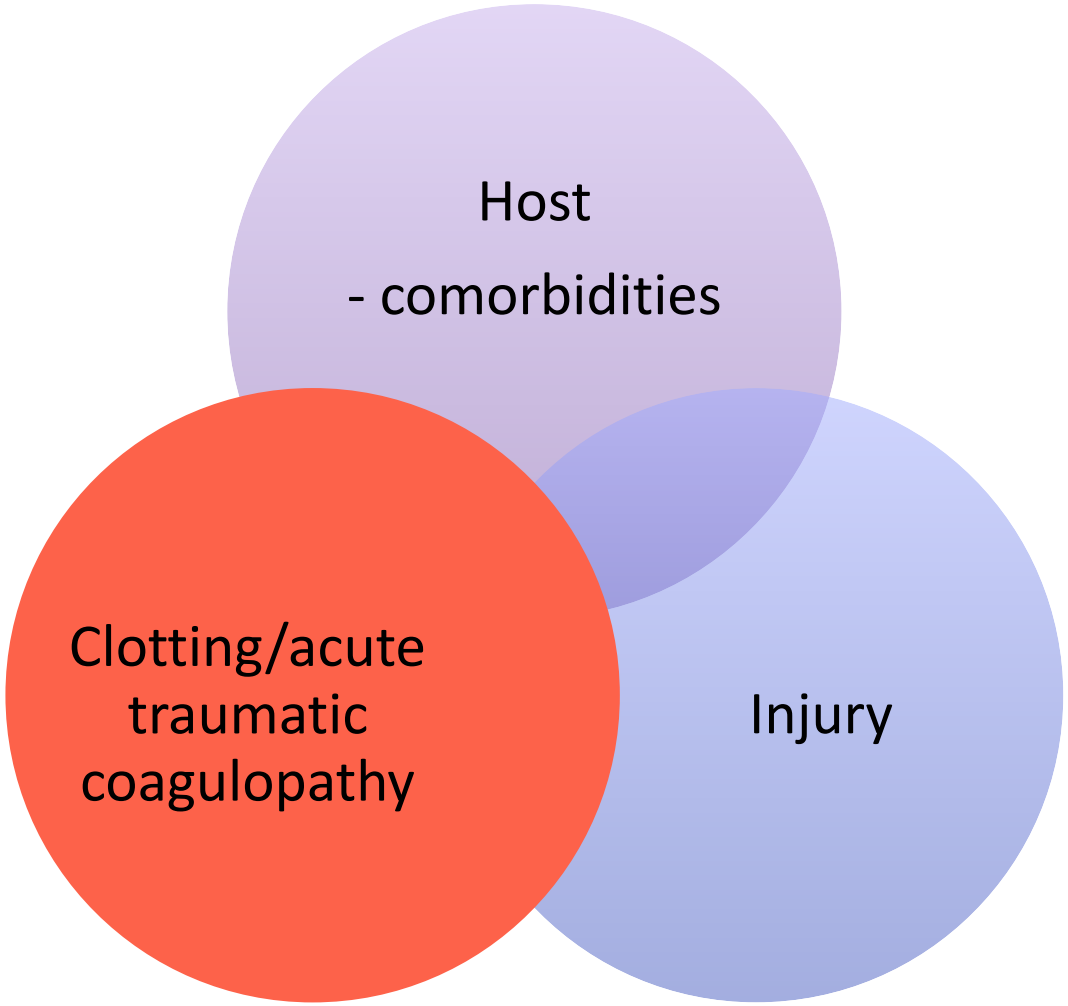


- 4 units in 24 hrs
- 10 units in 24 hrs

Extrapolated national incidence of haemorrhage by age

Stanworth SJ et al. Continuing High Mortality from Trauma Haemorrhage and Opportunities for Improvement in Transfusion Practice: An Observational Study in England and Wales. *Br J Surg*. 2016;103(4):357-65 British Journal of Surgery. 2016;103(4):357-365

Factors affecting traumatic bleeding



Factor	Younger	Older
Comorbidities	Fewer comorbidities	Heart disease Atrial fibrillation Hypertension
Acute traumatic coagulopathy	Breakdown of clot Low fibrinogen Platelet dysfunction	?
Injury mechanism	Road traffic accident Falls	Falls from <2m

Vital signs

- Undertriage
- Occult hypoperfusion
  - 39% of geriatric patients with an SBP greater than 90 mm Hg had occult hypoperfusion evidenced by abnormal base deficit or lactate.

Martin JT et al. Am Surg. 2010 Jan;76(1):65-9.

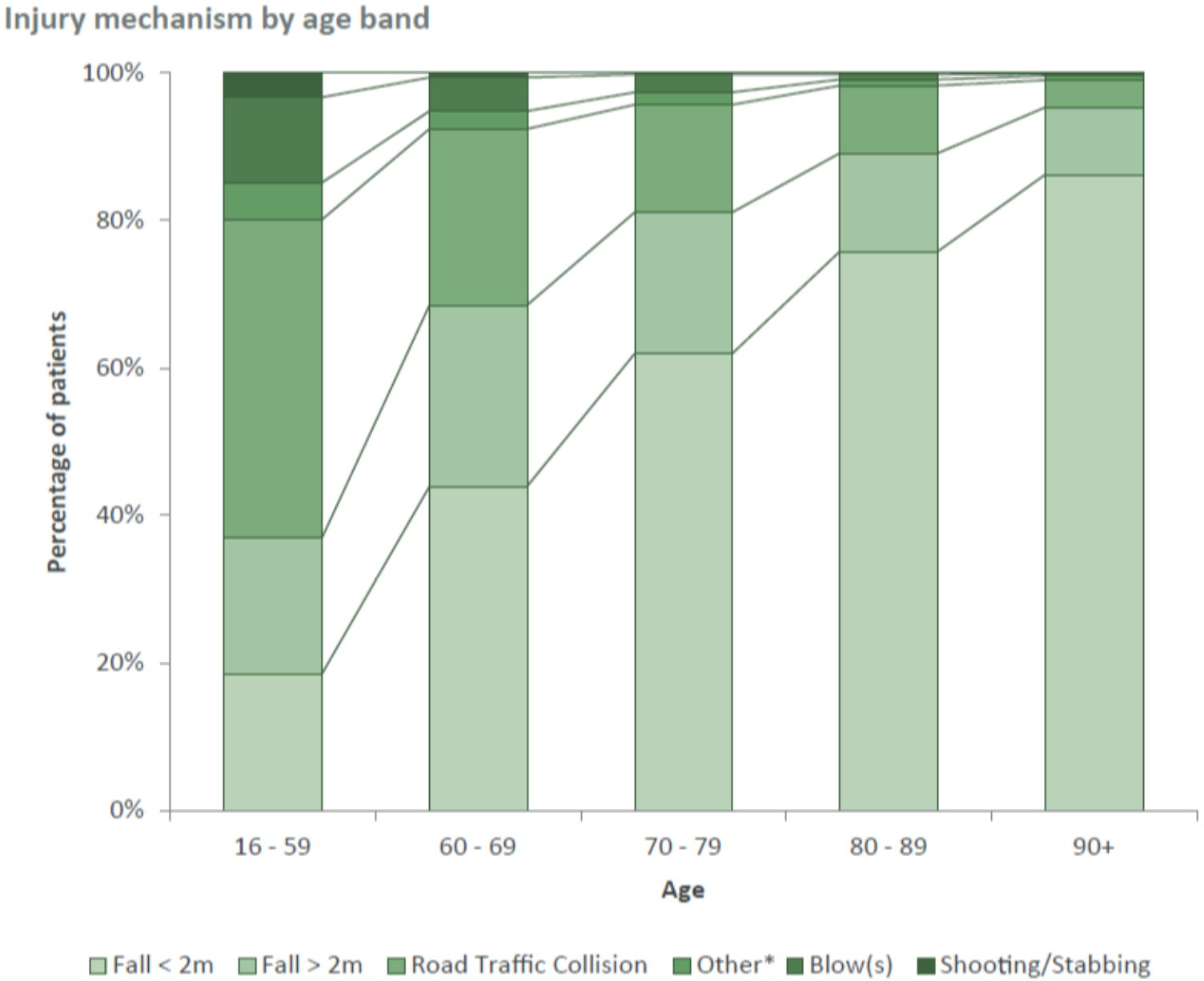


Figure 5: Mechanism of Injury of ISS> 15 patients by age (Appendix 2, Table 5)

TARN. Major Trauma In Older People - 2017 Report

Patient safety 2030 report

- Overall patients are older with more complex needs and an increasing number of comorbidities.

- ‘In particular, polypharmacy – the use of multiple prescription medications – is an important safety challenge for patients with multimorbidities. Due to the presence of multiple conditions, multimorbid patients are often prescribed a wide range of medications. Even when guidelines are followed for each individual disease, there is a chance that the combination of drugs will lead to interactions and adverse reactions, particularly given that guidelines are mostly focused on individual diseases.’

Yu et al. http://www.imperial.ac.uk/media/imperial-college/institute-of-global-health-innovation/centre-for-health-policy/Patient-Safety-2030-Report-VFinal.pdf

89 cases of TACO in 2015 SHOT report

Demographic	Number of reports
Deaths	7
Major morbidity	34
Age	6 days to 97 years (median 73 years)
Top three clinical specialties	Acute medicine (15), general medicine (13), haematology (12)
Bleeding patients	21 (indication code R1 – acute blood loss)
Non-bleeding patients	60 (other indication codes)
Unknown bleeding status	8 (no indication code given)
Single unit of red cells transfused	14

Challenges

- Recognition of bleeding: changes in physiology and vital signs
- Comorbidities
- Anticoagulation and anti-platelets
- Adverse complications e.g. TACO
- Limited evidence based management

Case

- A 75 year old lady is found on the floor at home having tripped on a rug and fallen onto the side of her coffee table.
- History from paramedics: C/o pain in her left side
- O/E Slightly pale, HR 88, BP 106/72, RR 24, Sats 94% OA, GCS 15/15

- She arrives in A+E

- How might you manage this patient?
- Is there any further information that you would like?

The future?

- Likely to be looking after an older, more frail population with comorbidities, at risk of major bleeding

- What can we do?
  - Prevention
  - Vigilance
  - Training
  - Research, evidence-based treatment

Unanswered questions

- Predictors of bleeding
- Component therapy: ratio driven?
- Coagulopathy in the older person
- Management of patients on antiplatelets
- Risk of thrombosis

Age is an issue of mind over matter. If you don't mind, it doesn't matter.

~ Mark Twain