

The 1st Turku Traumatic Brain Injury Symposium
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Welcome



Clinical summary of the TBIcare study

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Clinical background

- Extreme heterogeneity of TBI populations
 - Nearly all study populations selected (excluding e.g. by age, earlier TBIs, psychiatric or neurologic disorders, alcohol misuse problems)
- There is a common problem about the **generalizability** of TBI research for everyday clinical work
- Reliability of the data (in retrospective data collection)
 - Combining biomarkers from the very same patients!
- Few studies have the properties required for extensive **diagnostic modeling**

Aims of the TBicare clinical data collection

- To collect **unselected consecutive adult patients attending the Emergency Department** because of a TBI
 - To collect **prospective clinical data and biomarkers**
 - To **combine extensive clinical information, blood biomarkers, and imaging data** from the same patients
 - To **evaluate the outcome reliably and comprehensively**
- To create a study sample that is ideal for **diagnostic modeling of an adult clinical TBI population**

Inclusion criteria

1. Age \geq 18 years
2. Clinical diagnosis of acute TBI
3. Indications for acute head CT according to NICE criteria

Exclusion criteria

- **Age < 18 years (< 16 UK)** at study entry
- **Blast-induced TBI** (requires separate modelling)
- **Perforating or penetrating mechanism** of TBI (- “ -)
- **Chronic subdural bleedings** (not necessary traumatic)
- **Unable to live independently** because of a brain disease (= e.g. people with dementia, Down’s syndrome, cerebral palsy etc.) or other medical cause before the injury (hard to assess TBI-related outcome)
- TBI or suspected TBI **not needing cranial CT imaging** (excludes the mildest TBIs with negligible risk for incomplete recovery)

Exclusion criteria, continued

- **More than 2 weeks from the injury** (rare, acute modelling impossible)
- **Not living in the district** (not available for outcome visit) (not an exclusion in UK)
- **Not speaking native language** (outcome evaluations impossible)
- **No consent**

Controls

Acute orthopedic non-trivial injuries.

Exclusion criteria:

- **Any signs of acute CNS involvement in the injury (including marked risk for ICU treatment)**
- **Any information of existing CNS disease or other pathologic CNS condition (including earlier TBIs)**

Controls needed for...

- **Blood sampling – trauma-related or TBI-related finding?**
- **Serial MRI interpretation – only aging-related change between two scans vs. TBI-related?**
- **Outcome evaluation – injury-related or TBI-related outcome?**

Data collection

Blood sampling for protein biomarkers, metabolomics & genomics at:

- Admission
- Days 1, 2 and 3
- Day 7

Imaging:

- CT at admission
- CT repeated when clinically indicated
- MRI (aiming ASAP, preferably within 2 weeks from the injury)
 - 3T
 - MPRAGE, DWI, DTI (64 directions), GRE, SWI, T2, FLAIR

Extensive clinical data

Data collection, outcome

Outcome visit at 6 – 12 months from injury (3 months in UK for mild TBI), including:

- **GOSE** (Glasgow Outcome Scale, extended)
- **RPSQ** (Rivermead Post-Concussion Symptom Questionnaire)
- **QOLIBRI** (quality of life questionnaire)
- **RAND-36** (health survey)
- **CANTAB** test battery
 - visual memory, executive function, working memory, planning, attention, semantic/verbal memory, decision-making, and response control
- **Clinical data** about rehabilitation, medications, late complications, other illnesses, return to work/activities
- **Blood sample** for proteomics and metabolomics
- **MRI** (identical protocol with the 1st)

Demographic summary

	Turku	Cambridge	Total (%)
TBI	200	193	393
- mild	139	93	232 (59 %)
- moderate	30	25	55 (14 %)
- severe	31	75	106 (27 %)
Controls	40	42	82

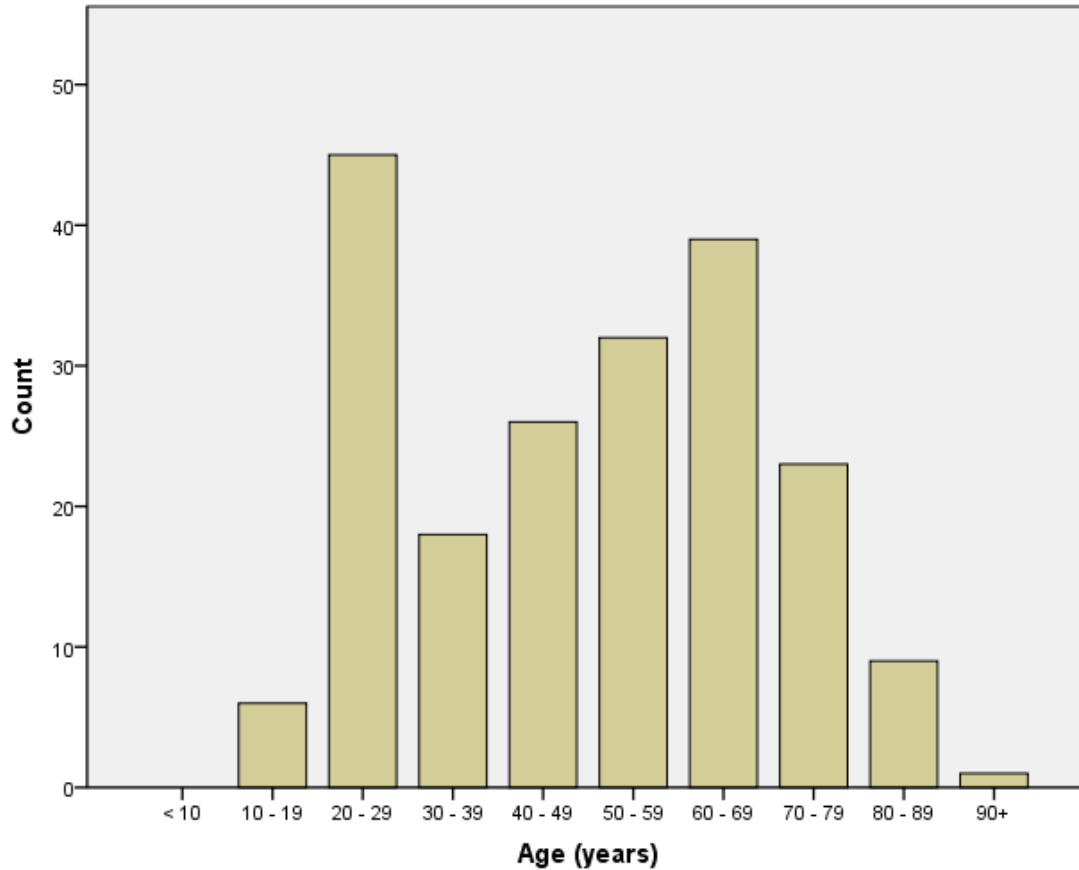
Severity based on admission Glasgow Coma Score

- GCS 14-15 = mild
- GCS 9 – 13 = moderate
- GCS 3 – 8 = severe

Mean GCS: Turku 12.6 Cambridge 10.7

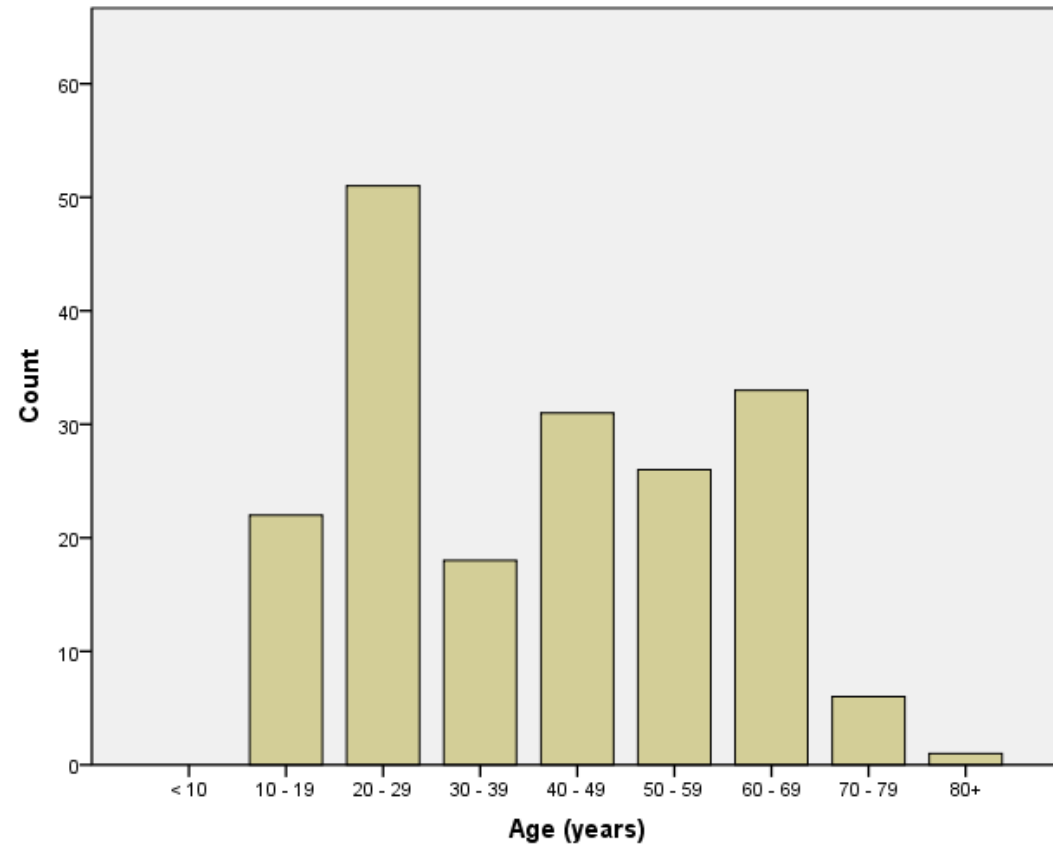
Age distributions

Turku



Mean **49.3** yrs

Cambridge



Mean **40.1** yrs

Gender distribution

	Turku	Cambridge	Total	%
Male	142 (71 %)	139 (72 %)	281	72.4
Female	58 (29 %)	49 (28 %)	107	27.6

Injury mechanisms

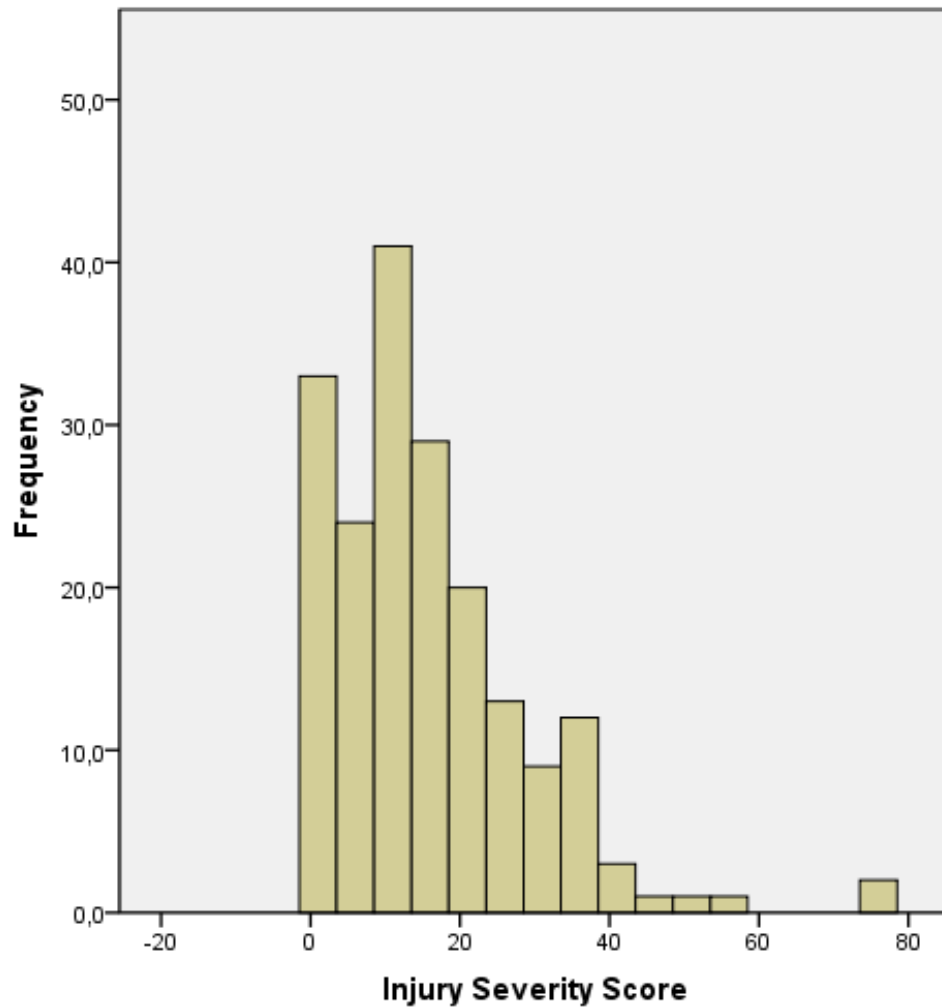
Mechanism	Turku (n)	Cambridge (n)	Total (%)
Traffic	35 (18%)	65 (34 %)	25.4
Fall from height > 1 meter (3ft)	45 (23 %)	31 (16 %)	19.3
Ground level fall	64 (32 %)	43 (22 %)	27.2
Violence	17 (9 %)	16 (8 %)	8.4
Bike accident	25 (13 %)	19 (10 %)	11.2
Object strikes the head	2	12	3.6
Other	3	2	1.2
Unknown	9	5	3.6

All falls 46.6 % (n = 184)

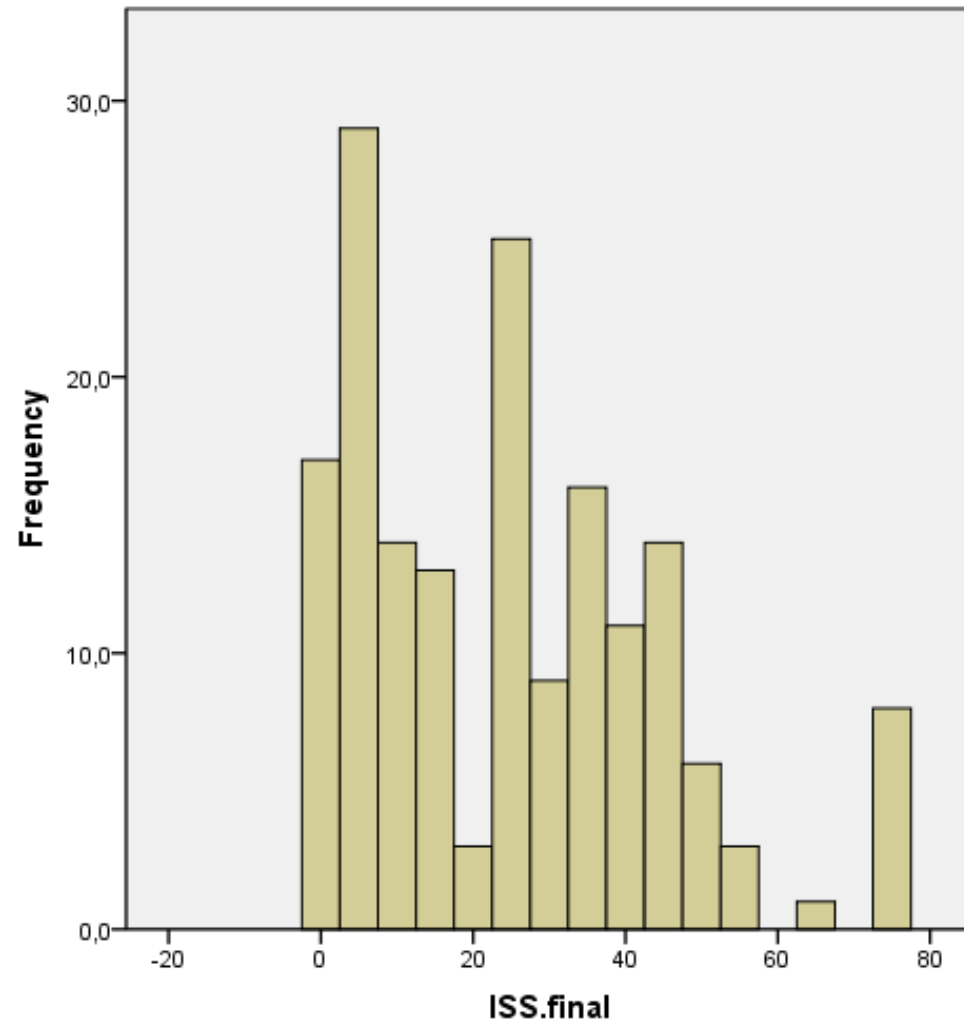
All traffic injuries 36.6 % (n = 144)

Injury severity scores

Turku - mean 15.9



Cambridge - mean 24.6



MRI and blood sampling

MRIs:

	Acute	Outcome
Turku	160	146
Cambridge	82	87

Blood sampling:

	Arrival	Day 1	Day 2	Day 3	Day 7
Turku	177	131	117	51	49
Cambridge	36	43	57	62	59

Treatment strata

	Emergency Dept.	Ward	ICU
Turku	39 (20 %)	84 (42 %)	77 (38 %)
Cambridge	34 (18 %)	49 (25 %)	110 (57 %)

Drop-outs (without any outcome data)

	Mild	Moderate	Severe	% total
Turku	10	5	2	8.5 %
Cambridge	13	0	4	8.8 %

Withdrawn:

Turku 2
Cambridge 5

Deaths

	Mild	Moderate	Severe	< 1 month	> 1 month
Turku	8	5	9	15	7
Cambridge	2	2	10	12	2
% of the class	4.3 %	12.7 %	17.9 %	75 %	25 %

Mortality

- **Turku** **11.0 %** **(one month 7.5 %)**
- **Cambridge** **7.3 %** **(one month 6.2 %)**

Deaths

All	Mean age	Male / female	Mean GCS	Mean delay (days)
Turku	63.1	17 / 5	9.9	14.3
Cambridge	46.6	12 / 2	6.9	11.6

< 1 month	Mean age	M / F	Mean GCS	Mean delay
Turku	63.2	13 / 2	8.2	9.5
Cambridge	43.4	10 / 2	6.5	8.5

Cause	Fall	Traffic	Bike	Violence	Uncertain	Hit to head
Turku	15	-	4	2	1	-
Cambridge	4	8	-	1	-	1

Mortality

- **Survival rate with severe TBI** (GCS \leq 8 at arrival)
 - Turku 22/31 = 71 % (mean age 49.5 yrs)
 - Cambridge 65/75 = 86.7 % (mean age 39.1 yrs)
- **Survival rate with GCS 3** at arrival
 - Turku 13/17 = 76.5 %
 - Cambridge 21/26 = 80.1 %

Outcome by GOS-E (percentage)

	1	2	3	4	5	6	7	8
Turku	11.0	0.0	6.6	7.8	7.8	15.0	26.3	25.1
Cambridge	7.3	0.1	16.0	9.0	5.6	14.6	12.5	31.9

Outcome by GOS-classes (percentage)

	Severe	Moderate	Good
Turku	14.4	22.8	51.4
Cambridge	25.1	20.2	44.4

GOS-E 1 = Dead, 2 = Persistent vegetative state, 3 = Lower severe disability, 4 = Upper severe disability, 5 = Lower moderate disability, 6 = Upper moderate disability, 7 = Lower good recovery, 8 = Upper good recovery

Outcome by severity (Turku data)

From the total study population

GOS	Dead	Severe	Moderate	Good
GCS				
Severe	5 %	4 %	5 %	1 %
Moderate	3 %	3 %	4 %	2 %
Mild	4 %	8 %	14 %	48 %

By severity category

GOS	Dead	Severe	Moderate	Good
GCS				
Severe	33 %	25 %	33 %	8 %
Moderate	24 %	24 %	33 %	19 %
Mild	5 %	10 %	17 %	61 %

Outcome from GCS 3

	1	2	3	4	5	6	7	8	ND
Turku	4	-	2	2	3	3	2	-	1
Cambridge	5	-	6	1	1	2	3	2	6
%	21 %		26 %		21 %		16 %		

Outcome from GCS 15

	1	2	3	4	5	6	7	8	ND
Turku	4	-	4	4	5	15	31	29	13
Cambridge	-	-	-	2	3	5	8	19	22
%	2.3 %		5.7 %		16.1 %		22.4%	27.6 %	20.1 %

Representativeness of the study population (Turku data)

Not included:	N = 429	(Study sample)
Mean age:	45.8 yrs	(49.3)^{***}
Male / female:	56 / 44 %	(71 / 29 %)***
Mean GCS	14.2	(12.6)^{***}
Causes:		
- traffic	20.5 %	(30 %)***
- fall	63.6 %	(55 %)***
- non-intentional	3.7 %	
- violence	5.1 %	(8.5 %)°
- suicide attempt	1.4 %	
- uncertain	4.2 %	

Causes for exclusion (Turku data)

Age < 18	68	(10.8 % of all)
Blast	0	
Penetrating	8	(1.2 % of all)
ADL dependency	19	
Uncertain diagnosis	67	(10.7 % of all)
Too mild	51	
> 2 weeks from injury	4	
Chronic SDH	11	
No consent	36	(5.7 % of all)
Not living in the area	57	
Foreign language	5	
No information for research team	194	(30.8 % of all)
Lack of resources	2	
Other	11	

Comparison between UK and Finland

	No consent	Not eligible*
UK	30.7 %	35 %
Finland	5.7 %	62.5 %

*cf. age and not living in the district

Clinical notes

- **Especially of mild cases, almost 1/3 during late evening and night, mostly falls**
- **In-hospital mortality low, even in severe cases (< 20 %, strongly age dependent)**
- **A significant proportion of GCS 3 will have a good outcome**
- **Large cultural differences in obtaining consent**

Clinical notes

- Of "mild" TBIs (based on GCS) only about 60 % have good outcome (< 30 % symptom free)
- Of all patients, only about $\frac{1}{4}$ - $\frac{1}{3}$ have a full recovery
- Around 20 % of patients will remain severely disabled

Caution: representativeness!

- The outcome from a moderate TBI (based on GCS) is very unpredictable

Lessons learnt

- **Secondary referral centre (Turku) receives on the average older and less severe patients (also in regard to other injuries) than a tertiary referral centre (Cambridge)**
- **Without a 24 h recruitment the TBI population will easily be skewed (towards older and more severe patients, and surprisingly with a higher percentage of males)**
- **Clinical notes and even assessments are often unreliable**

Lessons learnt

- **Clinical impressions may turn wrong in a systematic analysis**
- **Drop-outs can be minimized by active telephone contacting with the patient**
- **Outcome evaluation without a proxy informant is often unreliable especially in more severely injured subjects and requires expertise**
- **Motivating those with a mild injury and full subjective recovery to an outcome evaluation visit is often difficult**



Thanks for Jo Outtrim, Hilkka Runtti, Satu Timlin and the whole splendid TBicare team !