



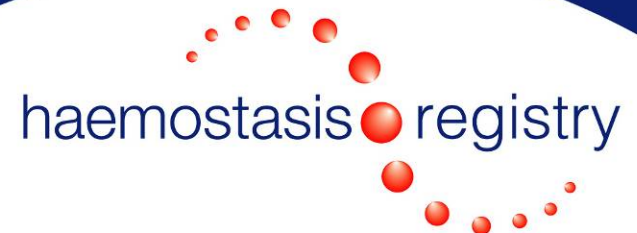
haemostasis registry



MONASH University
Medicine, Nursing and Health Sciences

Haemostasis Registry

A Register to record all off-label use of
recombinant activated Factor VII in
Australia and New Zealand



Recombinant Activated Factor VII

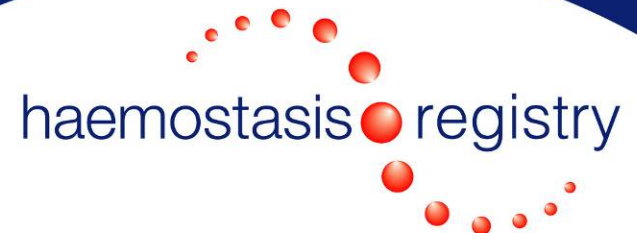
- rFVIIa, NovoSeven®, eptacog alfa
- FVIIa is a naturally occurring initiator of haemostasis
- approved by TGA for the treatment of spontaneous & surgical bleeding in patients with
 - haemophilia A or B and with antibodies to factor VIII or factor IX
 - Factor VII Deficiency,
 - Glanzmann Thrombasthenia
- Licensed in Australia since 1998

rFVIIa outside Haemophilia

Treatment of traumatic bleeding with recombinant factor VIIa

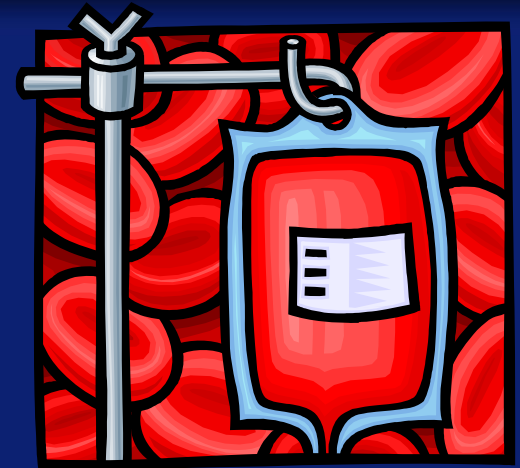
Gili Kenet, Raphael Walden, Arie Eldad, Uri Martinowitz

Surgical intervention failed to stop life-threatening bleeding caused by injury complicated by severe coagulopathy. Administration of recombinant factor VIIa immediately corrected the coagulopathy and bleeding stopped.



'Investigational Use' of rFVIIa

- Life-threatening bleeding in patients with coagulation disturbances but without coagulation inhibitors
- Mortality rates of up to 40-60 %
- Coagulation disturbances in these patients are multifactorial
- An increased risk of thrombosis is the major potential concern



Registry pre-history

- International voluntary register for off-label use set up by Novo Nordisk
- Highly biased case selection
- High level of suspicion from some clinicians
- No denominator
- Results basically unpublishable

Haemostasis Registry

- 2004 NovoNordisk Australia approaches Monash University DEPM to run Registry
- Funded through unrestricted Educational Grant
- Pilot program begins in Feb 2005 at Alfred Hospital
- Full project launched in May 2005

Aims

investigate the safety, efficacy and dosing of rFVIIa in investigational use

monitor the extent, indications for, dosages and appropriateness of use

generate information to assess cost-effectiveness and to support clinical use

publish based on analyses of local experience

provide data for physicians, hospitals and Regulatory Authorities

Governance

Steering Committee – meets twice annually

- 2 haematology experts
- 2 company representatives
- 2 registry experts (DEPM)
- Project Manager
- Database Manager

Staff

- Chief Investigator
- Project Manager - Full time
- Administrative Assistant
 - 1 x 0.6
 - 1 x 0.3
- Database Management
- Statistical Advice



How does the Registry work?

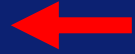
Hospital Contacts Registry to indicate interest



Complete Registry Set-Up Questionnaire



Ethics Approval



Approval to collect de-identified data without patient consent



Begin Data Collection

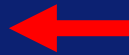


How does the Registry work?

Patient Treated with rFVIIa at hospital



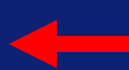
Collect Data



Patients identified through pharmacy or blood bank records



Submit Data



Data entry via web based system
ASP.NET 2.0 + SQL Server



Data Verification



Reimbursement

Web Data Entry

[Skip to content](#) | [Change text size](#)



MONASH University
Medicine, Nursing and Health Sciences



HAEMOSTASIS REGISTRY

Logged in as **lphillips SUPERUSER**

[New Case](#) [Patient](#) [Case Description](#) [rFVIIa Administration](#) [Laboratory Test Result](#) [Replacement Therapy](#) [Other Therapies](#) [Adverse Events](#) [Outcome](#) [Supplementary](#) [Reports & Documents](#) [Logout](#)

Select Patient

ALF - 0001



Changing Login Details

[Change Password](#)
[Change Email Address](#)
[Change Security Question](#)

Haemostasis Registry WEB DATA ENTRY HOME PAGE

This site is intended for data entry by Data collectors in participating Australian and New Zealand Hospitals.

For more information on the Haemostasis Registry Click on our logo ->

Contact Us:

Web Access	Data Manager	M Pruksawongsin	03 9903 0167
	Information Systems Manager	Andrew Hannaford	03 9903 0001
Project Information	Project Manager	Dr Louise Phillips	03 9903 0551

The Haemostasis Registry is based:
Dept of Epidemiology & Preventive Medicine

Central & Eastern Clinical School
Faculty of Medicine,
Nursing & Health Sciences
Monash University

Postal address:
DEPM, Monash University
Alfred Hospital
Melbourne VIC 3004

Delivery address: 3rd floor
Burnet Building (side entrance)
89 Commercial Rd Melb 3004



Supplementary Data

- Obstetric
- Cardiac Surgery
- Trauma
- Intracranial Haemorrhage

Hospital: **Alfred Hospital (VIC)** Registry No: **0039** Age: **35** Sex: **Female** Admission Date: **12/02/2007 15:30**

Obstetric

Parity Gravidity
 Weeks Gestation Onset of Labour
 Pregnancy Type Delivery Type
 Caesarian Type

Pregnancy and Delivery Details

Inter-Uterine Foetal Death

Uterine Atony

Uterine Rupture

Placenta Accreta/Percreta

Placental Abruptio

Pre-eclampsia

Other

Details

Specific agents used

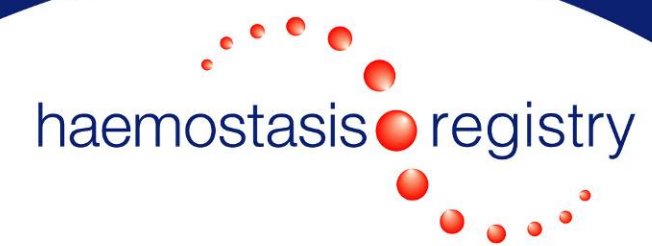
	Date time of uses	Dose (mg)
<input type="checkbox"/> Oxytocin	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Syntocinon	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Ergometrine	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Syntometrine	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Misoprostol	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Carboprost (Hemabate)	<input type="text"/>	<input type="text"/>
<input type="checkbox"/> Other <input type="text"/>	<input type="text"/>	<input type="text"/>

Other Attempts to Stop Bleeding

	Attempt date time
<input type="checkbox"/> Uterine Artery Embolisation	<input type="text"/>
<input type="checkbox"/> Uterine Artery Ligation	<input type="text"/>
<input type="checkbox"/> Internal Iliac Artery Ligation	<input type="text"/>
<input type="checkbox"/> B Lynch Suture	<input type="text"/>
<input type="checkbox"/> Hysterectomy	<input type="text"/>
<input type="checkbox"/> Other <input type="text"/>	<input type="text"/>

Attempt Details

[Save and next](#) [Cancel](#) Last Update:



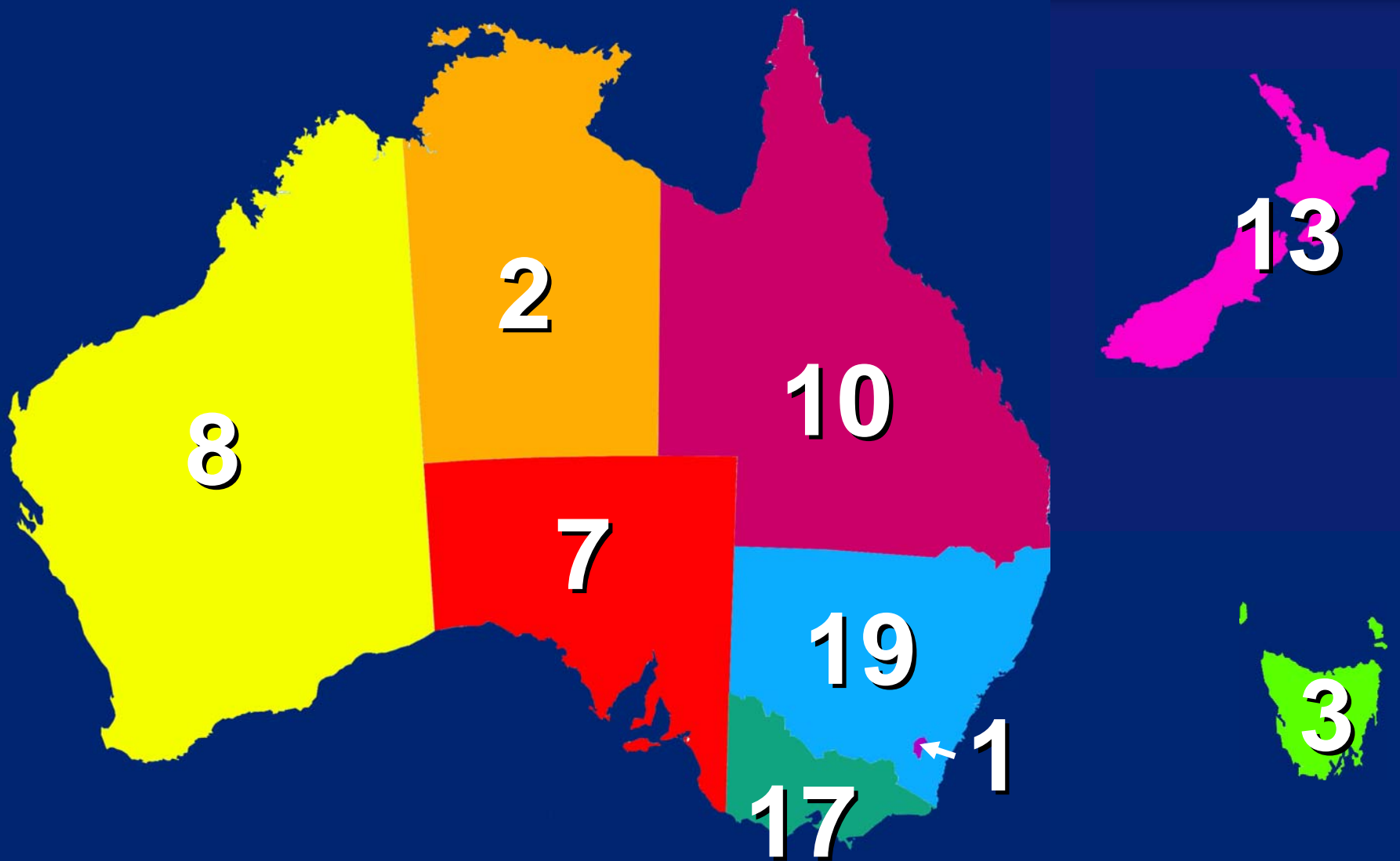
Data Verification

- Validation on Entry
 - Required Fields
 - Value Ranges
 - Enabling/disabling of dependent fields
 - Warning Messages for Unknown or extreme values
- Validation on Saving
 - Messages for Required Fields and Value Ranges
 - Date Ranges
 - Consistency Checks
- Final Manual Verification

Haemostasis Registry

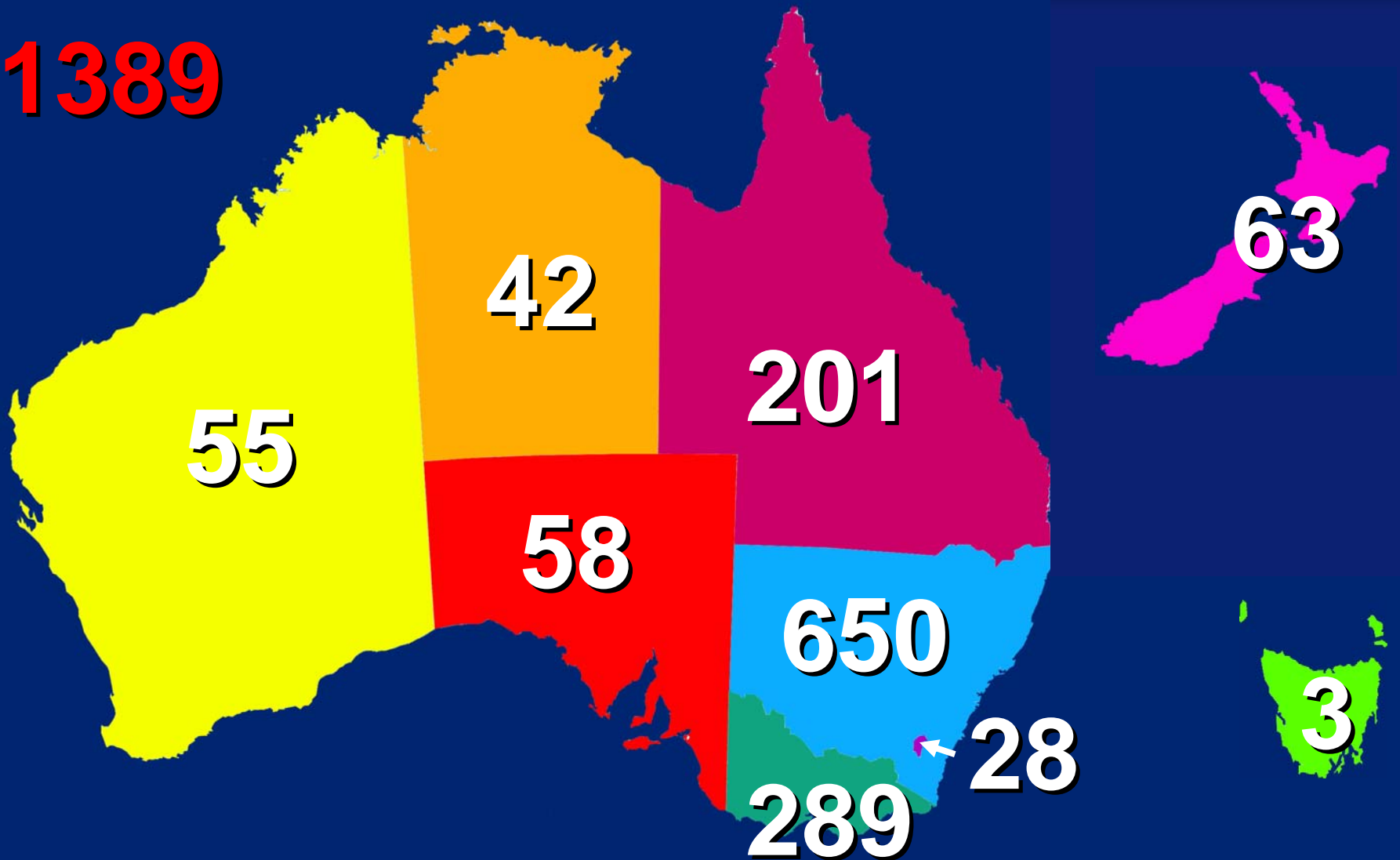
- Originally envisaged to include 5-6 hospitals
- Participating Hospitals >70
- Includes all States and Territories of Australia and New Zealand
- Public, private, large and small hospitals
- Hospitals commit to provide all cases of rFVIIa use for critical bleeding in their hospital

Participating Hospitals



Cases Submitted

1389



63

42

201

55

58

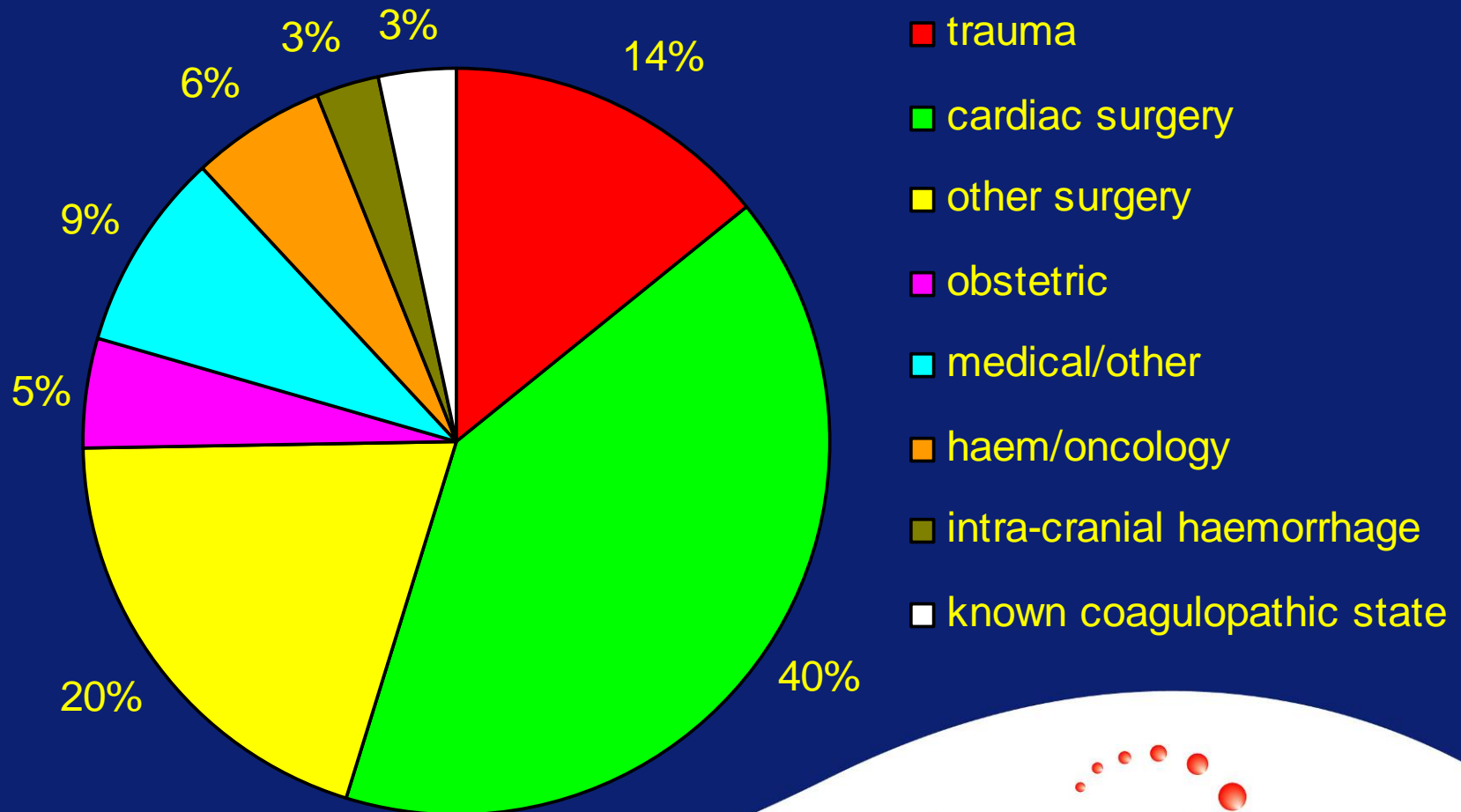
650

28

289

3

Cases by Presentation



Hospital Name

Date

purchased directly from Novo Nordisk* <small>*please check purchase records for this figure</small>	<input type="text"/>	mg
received from other hospitals	<input type="text"/>	mg
TOTAL RECEIVED	<input type="text"/>	mg

cases reported to date	<input type="text"/>	mg
cases yet to be reported	<input type="text"/>	mg
sent to other hospitals	<input type="text"/>	mg
other _____	<input type="text"/>	mg
stock on hand	<input type="text"/>	mg
TOTAL USED	<input type="text"/>	mg

I certify that the above information is correct to the best of my knowledge
 _____(sign) Date ____/____/____

Audit – Part I

- Reconcile amount purchased with cases reported
- Ensures compliance with “all cases” policy

Audit – Part IIa

Prince of Wales Hospital, Sydney

- Data collected by 2 (sometimes 3) people independently
- Matched and compared
- Numerical fields – high reproducibility
- Text fields – essence similar but depend somewhat on understanding

Audit – Part IIb

- Randomly Selected
- Hospitals with >20 cases, 5% of cases
- Hospitals with <20 cases grouped and 5% of total randomly selected
- Data re-collected by Registry Staff directly from case notes

Collaboration with ASCTS

Cardiac Surgery

HR only collects 'cases', not controls

Looking at ASCTS to provide comparison

1. Baseline data
2. Matched Case/Control series

1. Baseline data

	HR	ASCTS
Stroke	6.28 4.87	2.48 N.S.
PE	0.57 0.44	0.23 N.S.
MI	2.09 1.10	0.73 N.S.

2. Matched Case/Control Series

525 HR Cases ~ 14,000 ASCTS cases

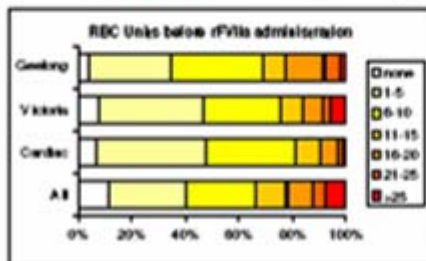
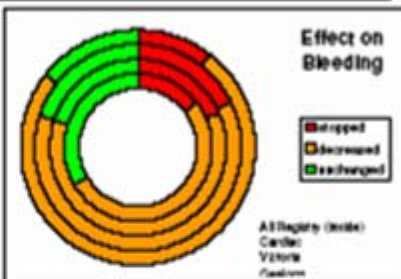
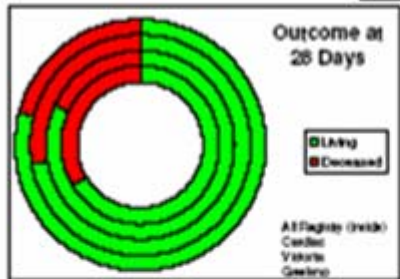
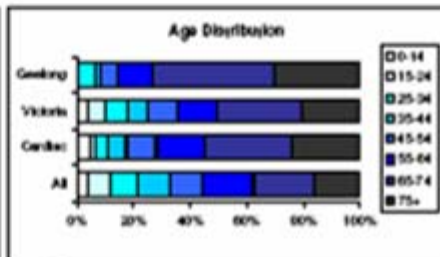
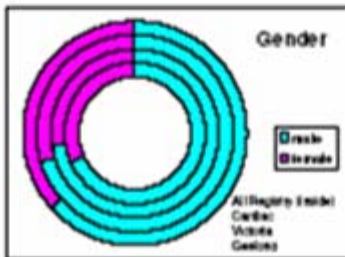
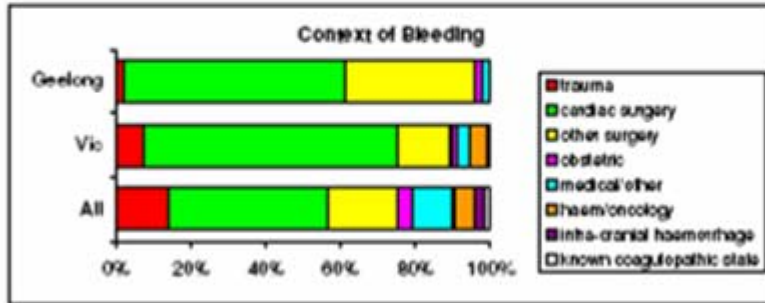
Matching for procedure type, gender,
urgency and ± 5 years of age

HR cases match with 0 and 2698 ASCTS
cases

Hospital Data Report - April 2007

Geelong Hospital

Hospital	Number of Patients	Median Dose (mg)	Median Dose (µg per kg)
Geelong Hospital	49	6.00	88.0
Victoria	245	6.15	92.3
All Cardiac Cases	467	6.00	90.0
All Registry	1129	6.00	89.6



Adverse Events

	Geelong	Vic	Card
Confirmed Linked	0	0	0
Probably Linked	1	2	2
Possibly Linked	8	16	25
Sub Total	9	18	27
Percent	18%	7%	6%
Unlikely to be Linked	10	43	95
Not Linked	11	59	115
Sub Total	21	102	240

Communication

Hospital Data Report

Twice annually
+
Annual progress report

Communication with Stakeholders

Annual Investigator Meeting



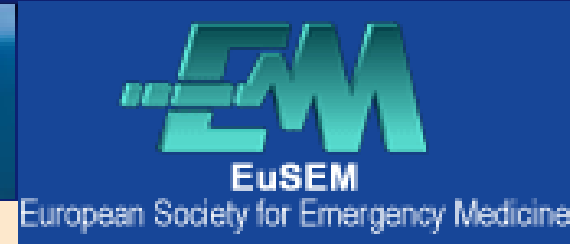
Conferences

Initial emphasis
on recruitment
and meeting
people

Now based on
communication
of results



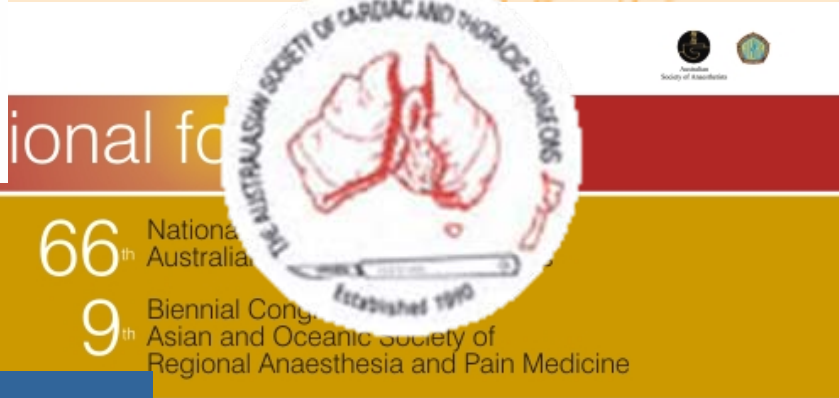
Conferences



the Date September
wood California Renaissance



ANZCA/IAS
3 - 7 May 2008
Sydney Convention & Exhibition Centre
Anaesthesia: Science, Art & Life





The use of recombinant activated factor VII in trauma patients: Experience from the Australian and New Zealand haemostasis registry

Peter Cameron^{a,*}, Louise Phillips^b, Zsolt Balogh^c, Anthony Joseph^d, Andrew Pearce^e, Michael Parr^f, Gary Jankelowitz^g

^a Department of Epidemiology and Preventive Medicine, Monash University and Alfred Hospital Emergency and Trauma Centre, Melbourne, Australia

^b Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

Recombinant Activated Factor VII in critical bleeding: experience from the Australian and New Zealand Haemostasis Register

J Isbister, L Phillips, S Dunkley, G Jankelowitz, J McNeil, P Cameron

Internal Medicine Journal (in press)

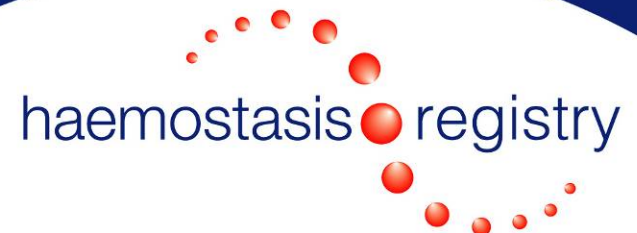
Publications

Recombinant Activated Factor VII in cardiac surgery: experience from the Australian and New Zealand

Haemostasis Register

Dunkley S, Phillips L, McCall P, Brereton J, Lindeman R, Jankelowitz G, Cameron P

Annals of Thoracic Surgery
(in press)



Strengths and Limitations

- Largest numbers of cases in all therapeutic areas in the world
- **Collecting data on entire population**
- High level of interest from local investigators
- Lack of Controls
- Missing data – especially lab results
- Some sub-groups have small numbers

Future Directions

- Obstetric publication
- Liver subcommittee
- More matching with other databases, eg trauma?
- More hospitals, more data



haemostasis registry



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