



haemostasis registry



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Medicine, Nursing and Health Sciences

Identifying and improving unreliable items in clinical registries through data auditing

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Haemostasis Registry

- Established to collect all cases of rFVIIa use for critical bleeding in participating hospitals throughout Australia and New Zealand
- Funded through unrestricted Education Grant from Novo Nordisk Pharmaceuticals

Haemostasis Registry

- Commenced data collection May 2005
- Includes retrospective cases back to 2000
- Concluded at the end of 2009
- Ethical approval obtained at 96 hospitals
- Included all major users of rFVIIa in Australia and New Zealand
- 3440 cases of off-label use

In an ideal world

- all data elements are epidemiologically sound
 - easily accessible
 - systematically and objectively recorded
 - use standard definitions and procedures
- all data collectors are perfect

Audit in our ideal world

- just to check that our data collectors are (still) perfect

Why bother?

Without good data

- registry analyses may generate misleading findings
- leading to poor clinical/policy decisions
- and potentially poorer patient outcomes

Audit in the real world

Because the world isn't ideal we need to check

- if our data items really are epidemiologically sound

and

- how good our data collectors are

Audit Program

Credibility of data/results relies on

- Accuracy
 - “epidemiologically sound”
 - “acceptable” level of error
- Completeness
 - missing data
 - no patient selection bias “cherry picking”

Audit Program

Aspects of audit program:

1. Data Validation Accuracy + Completeness
2. Case Accrual Completeness
3. Audit against primary sources Accuracy

Data Validation

- range & consistency checks in database
 - reduces error
- manual validation of fields
 - eg choice of Context of Bleeding
 - sufficient detail in text fields, etc
- follow up with data collectors
 - sort out problems or gain extra information
 - minimise missing data

Data Validation

Hospital: Princess Alexandra Hospital (QLD) Registry No: 0004 Age 60 Sex Male Admission Date: 03/10/2004 13:09

Case Description

Context of Bleeding

Select only one primary context and tick one or more secondary context as appropriate

Primary Context:

Secondary Context:

- | | | |
|--|---|---|
| <input type="checkbox"/> Trauma | <input type="checkbox"/> Obstetric | <input type="checkbox"/> Intra-Cranial Haemorrhage |
| <input type="checkbox"/> Cardiac Surgery | <input type="checkbox"/> Medical/Other | <input type="checkbox"/> Known Coagulopathic State |
| <input type="checkbox"/> Other Surgery | <input type="checkbox"/> Haem/Oncology | <input type="checkbox"/> Congenital Platelet Disorder |
| <input type="checkbox"/> Liver | <input type="checkbox"/> Acquired Haemophilia | |

Description of Case

For Trauma cases please include list of injuries

Overdose of oral morphine preparation and alcohol,
GCS 3/15, Cyanosed on presentation then intubated and ventilated.
Rhabdomyolysis, acute renal failure with acidosis and hyperkalaemia
Pressure areas with compartment syndrome to left deltoid, left forearm, right forearm,
left buttock and left thigh.
Surgery for fasciotomies for compartment release on day 1 of admission.
Large amount of blood loss from wounds - developed coagulopathy.
Massive transfusion of blood products over 48-72 hours, including rFVIIa.
Worsening clinical condition with haemodynamic compromise (inotrope dependent),
hypothermia, renal replacement therapy, atrial fibrillation, poor gas exchange with
difficult ventilation and hypoxic brain injury.

Prophylaxis:

Date/Time of Bleeding Onset:

Medical History

Case Accrual

- ideally triangulate against another source to ensure all cases collected
 - or at least to estimate proportion of cases collected
- for Haemostasis Registry:
 - pharmaceutical company records
 - issues with commercial confidentiality
 - hospital pharmacy records

Hospital Name

Date

purchased directly from Novo Nordisk* mg
*please check purchase records for this figure

received from other hospitals mg

TOTAL RECEIVED mg

cases reported to date mg

cases yet to be reported mg

sent to other hospitals mg

other _____ mg

stock on hand mg

TOTAL USED mg

I certify that the above information is correct to the best of my knowledge

_____ (sign) Date ___/___/___

Case Accrual

Audit against primary sources

Audit date selected = 15 August 2007

- total of 1345 records

Stratified sampling approach

- each hospital with ≥ 20 cases
 - random 5% of each hospital's cases
- hospitals with < 20 cases pooled
 - random 5% of pool

Audit against primary sources

- blinded note-validation approach to re-abstract data
 - ie data re-collected by trained (independent) data collector blinded to previous data collection
 - NOT ticking off against data already collected

Results

Audit data from 76 patient records

= 5.7% of registry cases at the time of audit

- 86 binary/categorical
- 80 continuous
- 18 date/time variables

Variables analysed for agreement between original data (N1) and audited data (N2)

Analysis

binary/categorical

- % agreement (+ 95% CI)
- kappa (+ 95% CI)
 - κ values <0.5 = low, $0.5 - 0.8$ = fair, >0.8 = good
- directional bias (McNemar's test of symmetry)
 - is one observer (either original or auditor) more likely to score in a particular way

Analysis

continuous variables (+ date/time variables)

- proportion of cases with perfect agreement
- mean difference (+ SD)
- 'prediction interval' = mean difference $\pm 2 \times \text{SD}$
 - estimates the likely range of error in any single case
- coefficient of variation (CV)
 - = SD of differences, expressed as a % of mean of the observed (original & audited) values
 - values above 100% suggest extremely noisy and unreliable data

Binary Variables

Variable	% Agreement [95% CI]	κ [95% CI]	Symmetry (p)
Gender (M/F)	99 [93, 100]	0.96 [0.90, 1.00]	0.317
Admitted to ICU (Y/N)	99 [93, 100]	0.85 [0.56, 1.00]	0.317
Adverse Events (Y/N)	78 [67, 86]	0.54 [0.35, 0.73]	0.808

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?

kappa

- routinely used to measure agreement between repeated data collections
 - but is problematic under some conditions
- is dependent on prevalence
 - low numbers or imbalances in categorical variables increase risk of chance agreements and therefore decrease the κ value
- no accepted alternative available
- audits of registry data need to be mindful of statistical limitations

Continuous Variables

Variable	N1	N2	N3	N4
Age (years)	75	76	75	1
Number of Doses	76	76	76	0
pH	49	36	28	29
PT Before (sec)	59	59	55	8
RBC prior to dose 1 (units)	75	75	74	2
Crystalloid prior to dose 1 (ml)	72	75	71	5
Size of Dose 1 (mcg/kg)	64	66	58	14
Time to Dose (mins)	61	63	53	18
Bleeding Onset (date/time)	62	65	56	14
Date of Dose 1 (date/time)	75	74	73	3

N1: Number of original data collections including data for this variable

N2: Number of audit data collections including data for this variable

N3: Number of cases with data for this variable from both original and audit data collections. Analysis is based on these cases.

N4: Number of cases in which either original or audit data (but not both) is missing for this variable

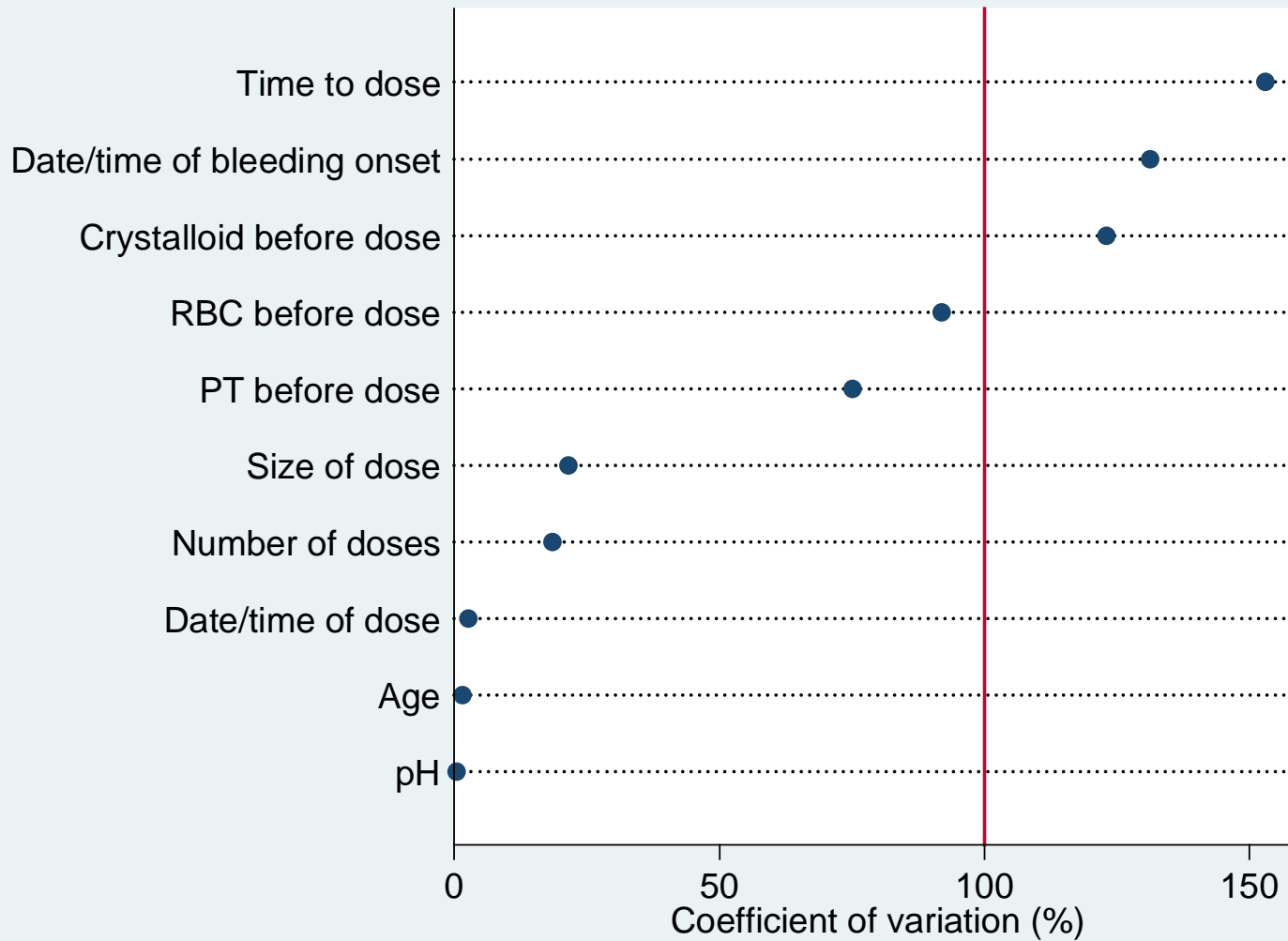
Continuous Variables

Parameter	N3	% Agreement [95% CI]	Mean (SD) of difference	95% prediction interval
Age (years)	75	88 [78, 94]	0.07 (0.79)	[-1.5, 1.6]
Number of Doses	76	95 [87, 99]	0.04 (0.30)	[-0.5, 0.6]
pH	28	68 [48, 84]	0.008 (0.04)	[-0.06, 0.08]
PT Before (sec)	55	91 [80, 97]	20.06 (172.57)	[-318.2, 358.3]
RBC prior to dose 1 (units)	74	57 [48, 68]	1.03 (10.71)	[-20, 22]
Crystalloid prior to dose 1 (ml)	71	32 [22, 45]	891.55 (3566.42)	[-6098.6, 7881.7]
Size of Dose1 (mcg/kg)	58	67 [54, 79]	2.36 (18.78)	[-34.4, 39.2]
Time to Dose (mins)	53	30 [18, 44]	549.32 (3204.28)	[-5731.1, 6829.7]
Bleeding Onset (date/time)	56	39 [27, 53]†	475.36 (3131.92)	[-5663.2, 6613.9]
Time of Dose 1 (date/time)	73	73 [61, 82]‡	9.51 (62.18)	[-112.4, 131.4]

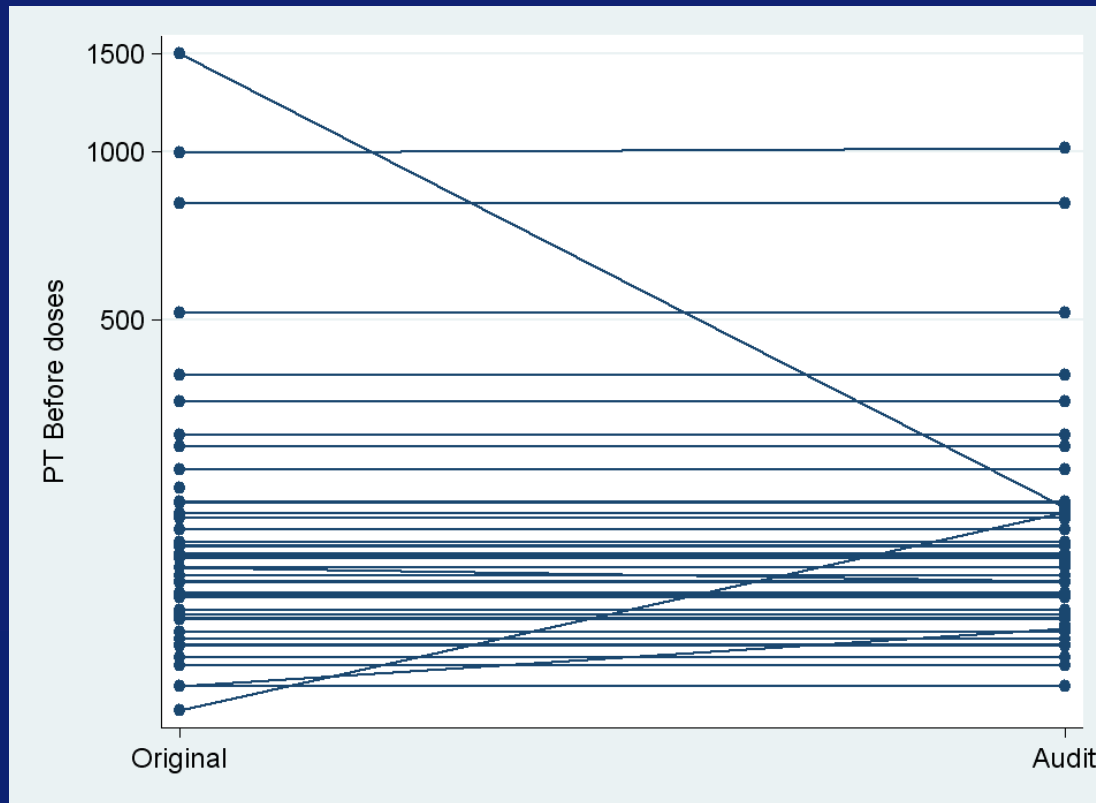
† Same day agreement 86.11%

‡ Same day agreement 100.00%

Continuous variables

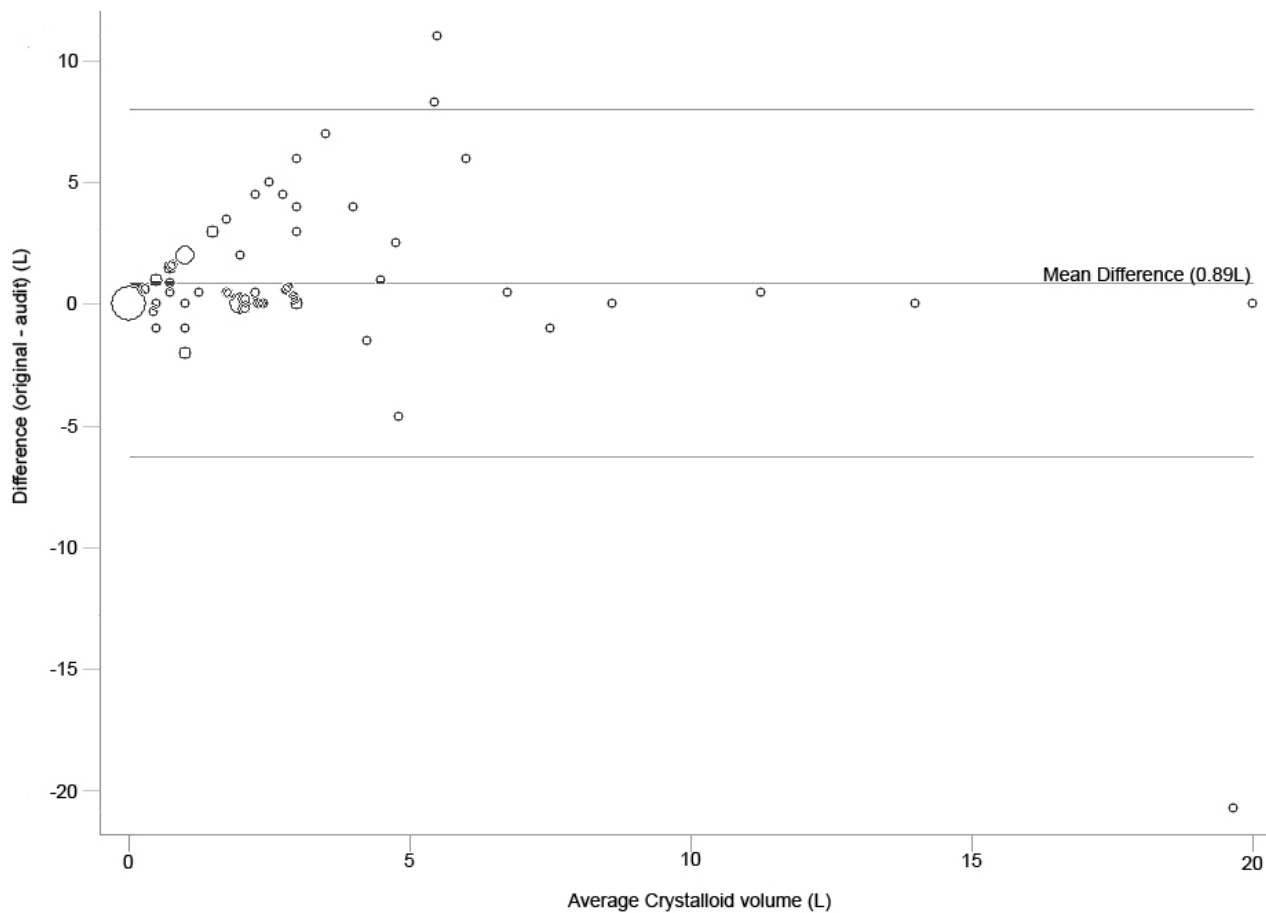


Prothrombin Time (PT)



- High agreement
- Low CV
- influenced by few highly discrepant cases

Crystalloid Volume



- higher agreement for cases with lower volumes

- greater variability at higher crystalloid volumes

Time to dose

- Worst variable
 - 30% agreement, CV 153%
- calculated variable

time to dose = time of bleeding onset – time of dose

↑
30%
CV 153

↑
39%
CV 131

↑
73%

What next?

Some variables

- are accurate and reliable
- are not accurate and reliable
 - but clinically important
 - may be able to be improved or collected in another way
- are unreliable with little opportunity for improvement

Strategies to Improve Data Quality

pH

- *Introduction of aids to systematic recording:*
- In-note reminder stickers
- missing data reduced by 18% post introduction

haemostasis registry **Use of rFVIIa (NovoSeven®)**

Dose Volume		mg
Date of Dose	/	/
Time of Dose	:	hrs
Body Temperature		°C
pH		
Place of Administration (ED, OT, Recovery, ICU, Ward)		
Effect on Bleeding (Stop, Decr, Unch, Incr)		
Blood tests taken:		
Platelets	<input type="checkbox"/> Before	<input type="checkbox"/> After
Fibrinogen	<input type="checkbox"/> Before	<input type="checkbox"/> After

Strategies to Improve Data Quality

PT Before (sec)

- *Systematise and Standardise data collection:*
- Investigating methods of automatic data extraction from electronic pathology sources where available

Strategies to Improve Data Quality

RBC prior to dose 1 (units)

- *Systematise and Standardise data collection:*
- Policy to obtain transfusion data from hospital blood bank laboratory systems

Strategies to Improve Data Quality

Crystalloid prior to dose 1 (ml)

- *Recommendation to remove data element from future CRF due to:*
- Specific data collector training unable to improve data collection.
- No standardised method available for data documentation

Strategies to Improve Data Quality

Bleeding Onset (date/time)

- *Proxies of bleeding onset being investigated:*
- admission time in trauma patients
- surgery commencement time in surgical patients

Why 5%

- little in the literature re sample size
- depends on required 'precision' usually specified by width of CI around point estimates of 'reliability eg % agreement or ICC
- precision depends on number of disagreements & number of sampled cases but not on size of registry or % of cases sampled
- *a priori* we had no idea of the precision we would find
 - (that was part of the point of doing the study)

Cost becomes important

- Cost
 - A. Design, overhead and analysis fixed cost
 - B. Data collection cost proportional to size of sample
- Ideally built in to costs of Registry
- When?
 - a once-off audit of quality and reliability of all items
 - repeat studies of some items

So...sample size

- should be chosen independently of the size of the registry (ie not a % of cases)
 - with more available information/experience from other studies we should form a better picture of numbers likely required for particular items
- adequacy of sample size evident after estimates of reliability and CIs are calculated
- inadequate sample size indicated by CIs which are wide and fail to exclude clinically relevant alternatives for the variables
- for this reason, reporting CIs for all important registry reliability parameters is critical
- P-values and traditional hypothesis-test statistics should be avoided when reporting reliability results.

Conclusion

Registry audits provide valuable information for determining

- which variables are accurate and reliable,
- which variables are clinically important but currently poorly collected, and
- which variables are unreliable with little opportunity for improvement in data accuracy



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