Is therapeutic quality influenced by choice of thromboplastin?

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Therapeutic quality

- Surrogate quality markers:
  - Cross-section of the files
    - INR's of total population at anti-coagulation clinics
    - March 31th and October 31th
    - % of patients in specific INR-range
  - Time in range
    - Estimate of time in range by linear interpolation between sequential INR-values

Dutch situation (1)

- 58 anti-coagulation clinics in the Netherlands
- 400,000 patients

- Two target-ranges
  - first range: 2.5 ≤ INR ≤ 3.5 (goal / aim)
    - therapeutic level: 2.0 ≤ INR ≤ 3.5
  - second range: 3.0 ≤ INR ≤ 4.0 (goal / aim)
    - therapeutic level: 2.5 ≤ INR ≤ 4.0

Dutch situation (2)

- Each year:
  - Statistical information from all the Dutch anti-coagulation clinics is collected centrally.
  - Summarized in annual report
- Quality is measured using “cross-section of the files method”
  - % of long-term patients in therapeutic INR-range 2.0 – 3.5
- Notable “quality-differences” between clinics (69.5% - 88.4%).
  - accepted explanation: fenprocoumon versus acenocoumarol.
  - not all discrepancies can be explained by the kind of VKA used.

Tabel 4c

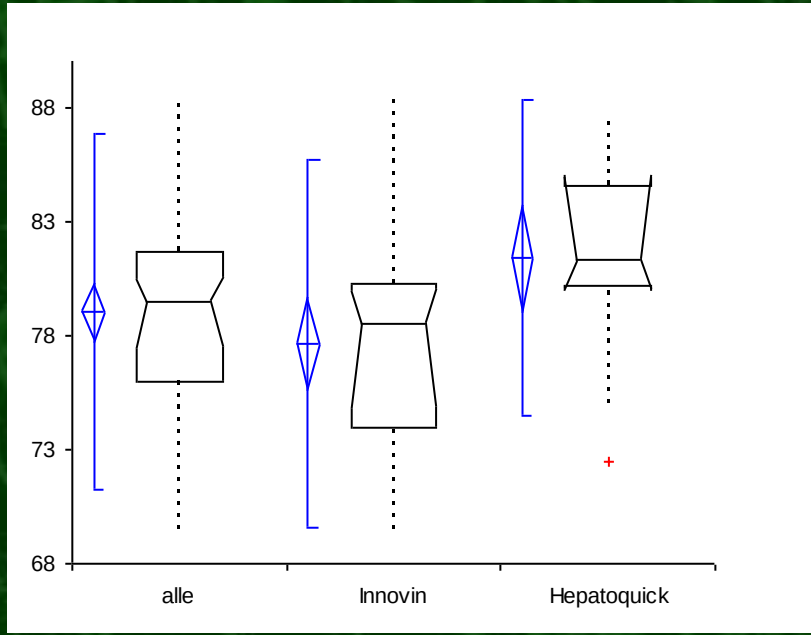
Nummer	Long-term patiënten							
	% binnen therapeutische range		% boven therapeutische range		% onder therapeutische range		% binnen streefgebied	
	1e inten.gr	2e inten.gr	1e intengr	2e inten.gr	1e inten.gr	2e inten.gr	1e inten.gr	2e inten.gr
	2.0 - 3.5 INR	2.5 - 4.0 INR	2.0 - 3.5 INR	2.5 - 4.0 INR	2.0 - 3.5 INR	2.5 - 4.0 INR	2.5 - 3.5 INR	3.0 - 4.0 INR
71	69,5	63,0	21,5	23,3	9,1	13,8	54,5	47,0
17	70,5	66,5	21,0	21,0	8,5	12,0	59,5	54,0
70	70,5	67,5	22,9	10,9	6,7	21,7	55,0	39,5
37	70,6	65,5	26,0	26,4	3,4	8,2	58,0	50,5
13	71,1	68,8	22,4	20,3	6,6	10,9	56,0	53,0
82	71,3	66,6	19,5	19,9	9,3	13,5	55,0	49,5
34	72,5	69,7	20,7	18,1	6,7	12,1	60,5	54,5
57	72,5	66,0	18,5	21,0	9,0	13,0	56,0	51,0
84	73,2	68,3	19,9	18,7	6,9	13,1	57,5	50,0
21	74,0	69,0	19,0	18,0	7,5	13,0	57,5	49,5
54	74,8	71,9	16,8	16,8	8,3	11,3	58,0	55,0
75	75,0	70,0	17,5	21,5	7,5	8,5	58,5	55,5
76	75,0	73,0	18,5	16,5	6,5	10,5	62,5	59,0
66	75,4	73,3	18,5	18,2	6,1	8,4	61,5	57,0

Does choice of thromboplastin influence quality of treatment?

Innovin versus Hepatoquick:

1st level	n	Mean	Median
all	57	79,007	79,500
Innovin	25	77,656	78,500
Hepatoquick	15	81,393	81,300

p	0,0079	(exact, double 1-tailed p)

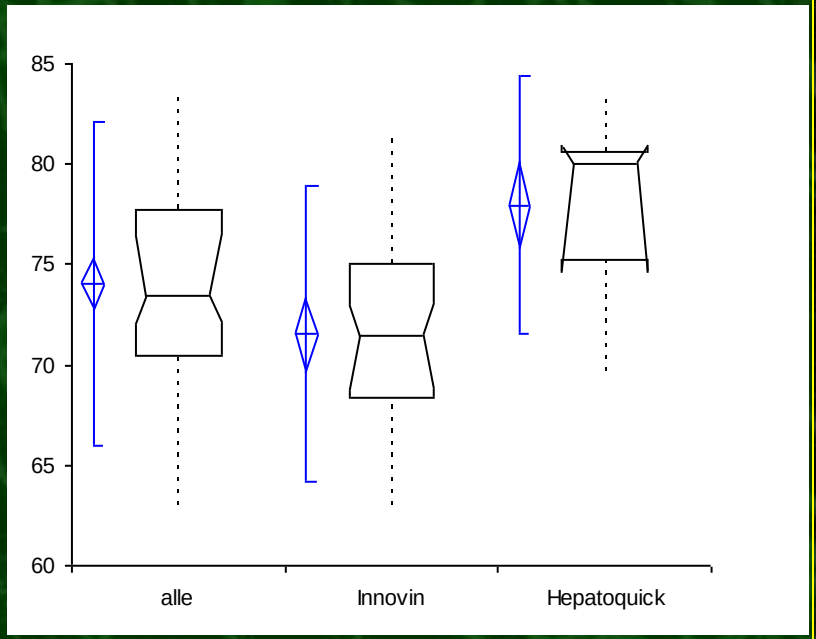


$2.0 \leq \text{INR} \leq 3.5$

Innovin versus Hepatoquick:

2nd level	n	Mean	Median
all	57	74,07	73,40
Innovin	25	71,53	71,50
Hepatoquick	15	77,95	80,00

p	0,0008	(exact, double 1-tailed p)

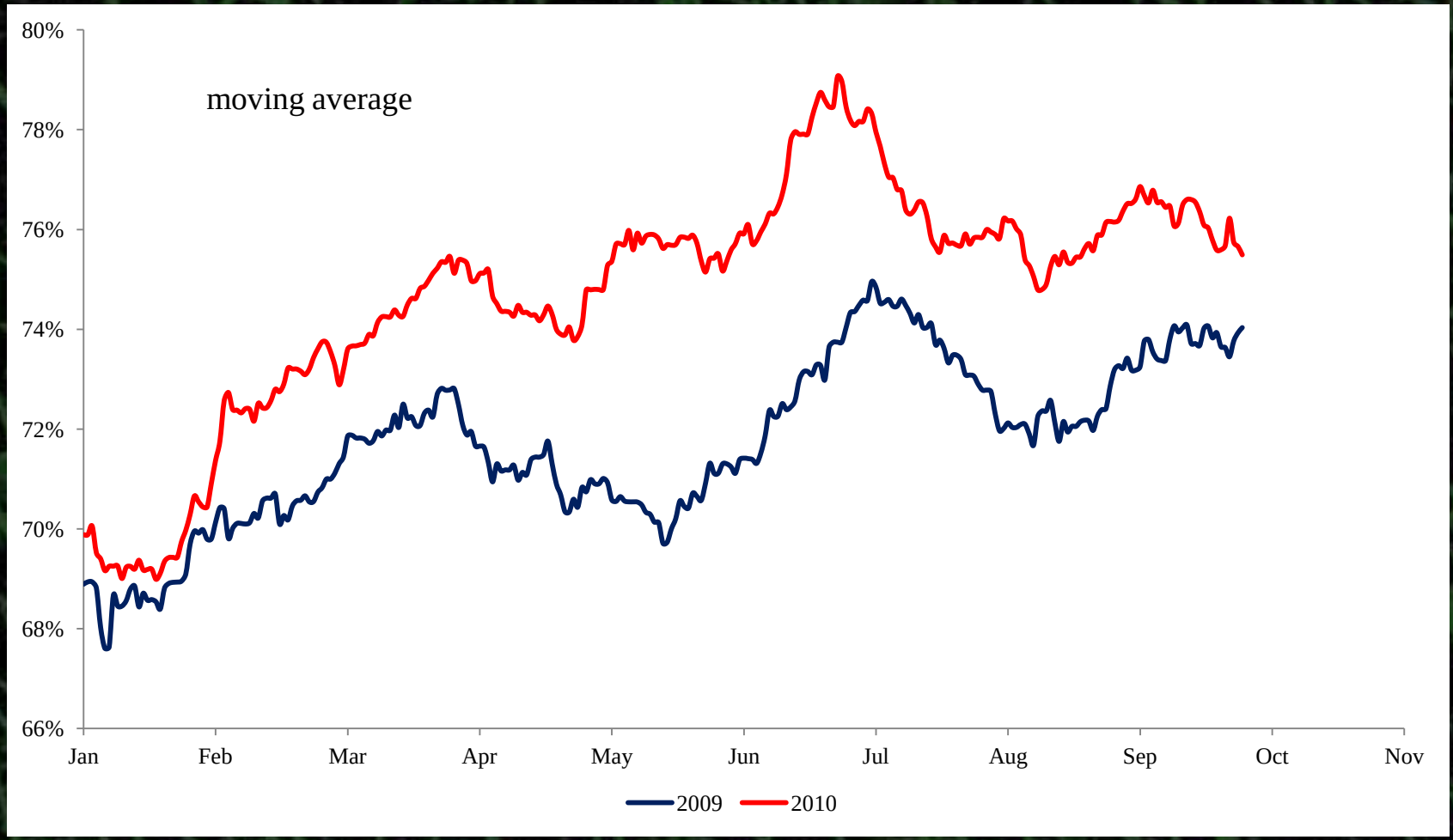


$2.5 \leq \text{INR} \leq 4.0$

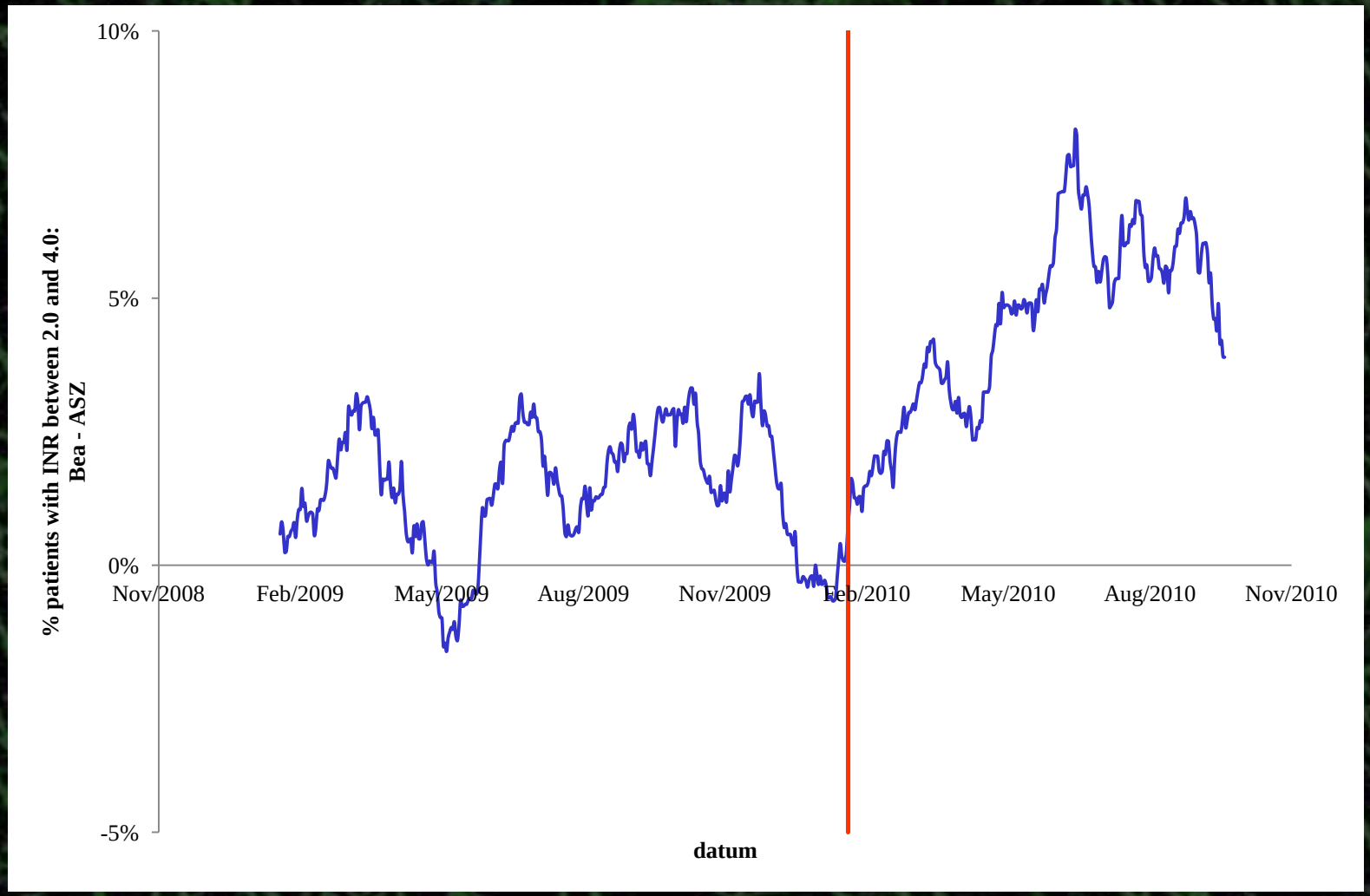
Innovin versus Hepatoquick:

- "Quality-difference" seen nationally between clinics is partially explained by the type of thromboplastin used (2006 to 2009).
- "Proof of the pudding":
  - Does quality improve *locally* if a different thromboplastin is used?
- Our situation:
  - INR's are measured in two separate hospitals. (Dordrecht and Gorinchem)
  - Innovin is used in both.
- Study design:
  - Switch from Innovin to Hepatoquick for INR-measurement in one hospital (Gorinchem), while keeping all other parameters the same.

Innovin vs Hepatoquick in Gorinchem



Gorinchem vs Dordrecht



Cross-section of the files:

1st target range	n	< 2 months	2 – 6 months	> 6 months
2009	431	64%	77%	70%
2010	415	66%	79%	72%
2nd target range	**n**	**< 2 months**	**2 – 6 months**	**> 6 months**
2009	99	58%	67%	63%
2010	110	61%	75%	75%

Time within range:

1st target range	n	< 2 months	2 – 6 months	> 6 months
2009	311	53%	69%	72%
2010	346	53%	70%	76%
2nd target range	**n**	**< 2 months**	**2 – 6 months**	**> 6 months**
2009	84	49%	54%	51%
2010	93	55%	62%	70%

Conclusions:

- Quality depends on the choice of thromboplastin, as :
  - A *difference* in quality is seen nationally (2006 – 2009) with different thromboplastins
  - A *change* in quality is seen locally with a change in thromboplastin
- Possible explanations:
  - Hepatoquick is a *tissue* thromboplastin (rabbit brain)
  - Innovin is a *recombinant* thromboplastin
- Remijn *et al*.: recombinant thromboplastins are more sensitive to small changes in factor VII than tissue thromboplastins
- Besselaar *et al*.: Recombinant thromboplastin is more sensitive to minor contamination than tissue thromboplastin (Becton Dickenson).