EMEA Performance Indicators Pre-Authorisation

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EMEA

EMEA-EFPIA Info Day 2009

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Analysis Period

- EMEA Data Set: All applications with outcome between 1 January 2003 and 31 December 2008
  - Period of questionnaires follows annual reporting to Management Board
  - Source:
    - Questionnaires to (co-)rapporteurs
    - Scientific Memory Database
- EFPIA Data Set: October 06-October 08

EMEA Questionnaires

- Two versions have been used in 2003-2008
- “Old” version, implemented in 2000
  - 10-point Scale (0 dissatisfied to 10 satisfied)
- “New” version implemented in 2007
  - Keep some of the same domains from “old” questionnaire
  - Includes new domains (e.g., Scientific Advice)
  - 5-point Likert Scale (1 agree to 5 disagree)
  - Note: validation ongoing
- Questionnaires administered after day 80
- Average scores between Rapporteur/Co-rapporteur, per product
- Exclusion of duplicates

EMEA Questionnaires Compared

Item	V2000	No.	V2007	No.
Dossier Presentation	Q NC C	3	Q NC C	3
Evidence-Data/Design	Q NC C	3	Q NC C	11
Overview	NC C	2	-	
Summary	Q NC C	3	-	
Study Reports	Q NC C	3	-	
SPC, PL, Labelling	Yes	3	-	
Scientific Advice	-		Yes	4
Communication	-		Yes	1
RMP/PVP	-		Yes	5

Q= quality, NC=non-clinical, C=clinical, CPh=clinical pharmacology; CE=clinical efficacy, CS=clinical safety, PVP=pharmacovigilance plan.

Data Set 2003-2008 (N=209)

- Allows to explore 2 domains and Parts of Dossier
  - **Presentation** of the Dossier for Q, NC and C
  - **Evidence** (Data/Studies) included in the dossier for Q, NC and C

Year	2003	2004	2005	2006	2007	2008	Total
No. Questionnaires ("new" + "old")	21	32	33	43	36	44	209
No. "old" quest.	21	32	33	43	35	14	178
No. "new" quest.					1	30	31
No. Outcomes	30	36	36	50	59	70	281
Compliance (%)	70	89	92	86	61	63	74

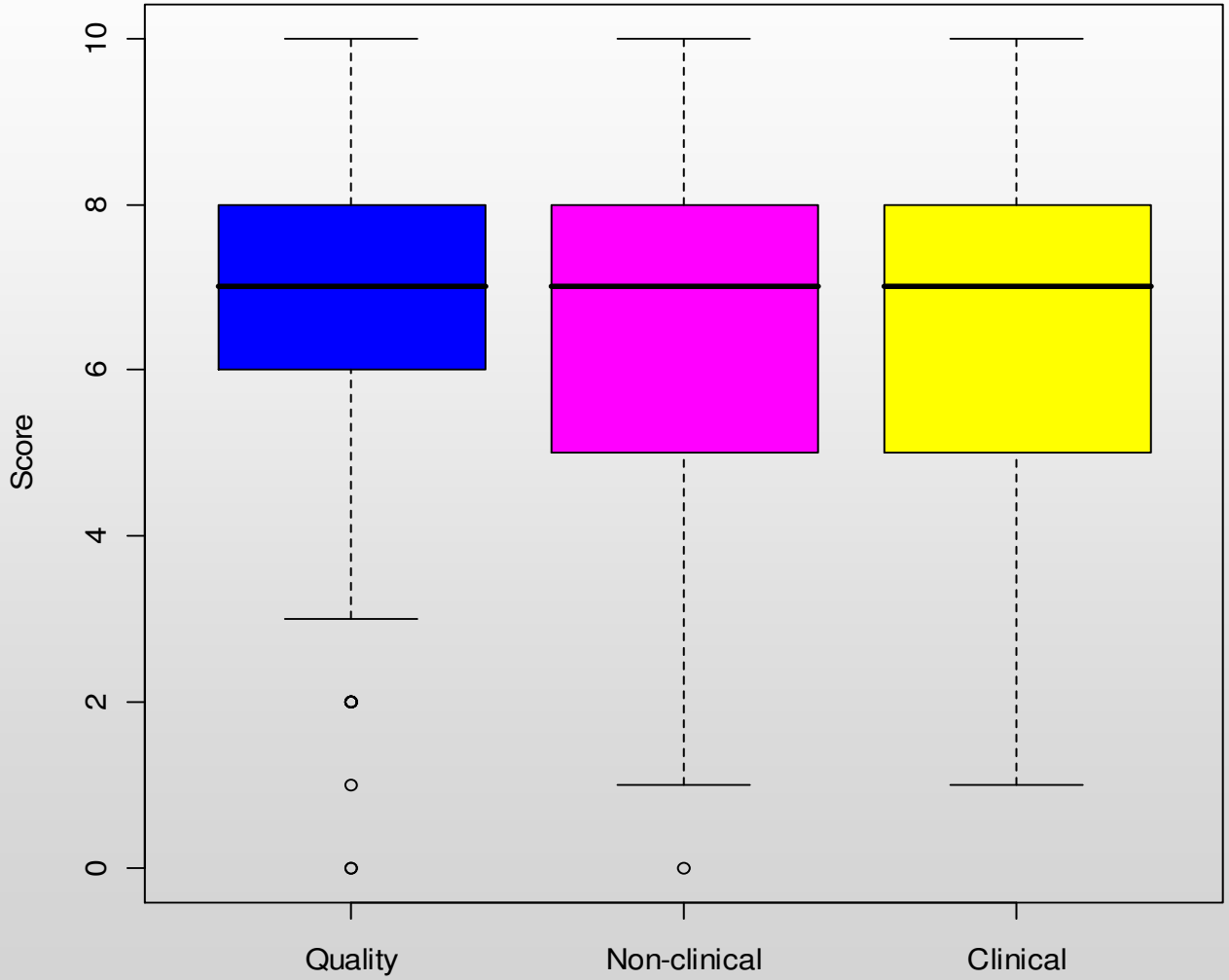
Product Characteristics (N=209)

		Frequency	Percent
Orphan Status		56	26.79
ATC	A	29	13.88
	B	11	5.26
	C	15	7.18
	J	37	17.70
	L	50	23.92
	N	23	11.00
	V	15	7.18
	Other	29	13.87
Outcome	Positive	157	75.12
Scientific Advice		85	40.67

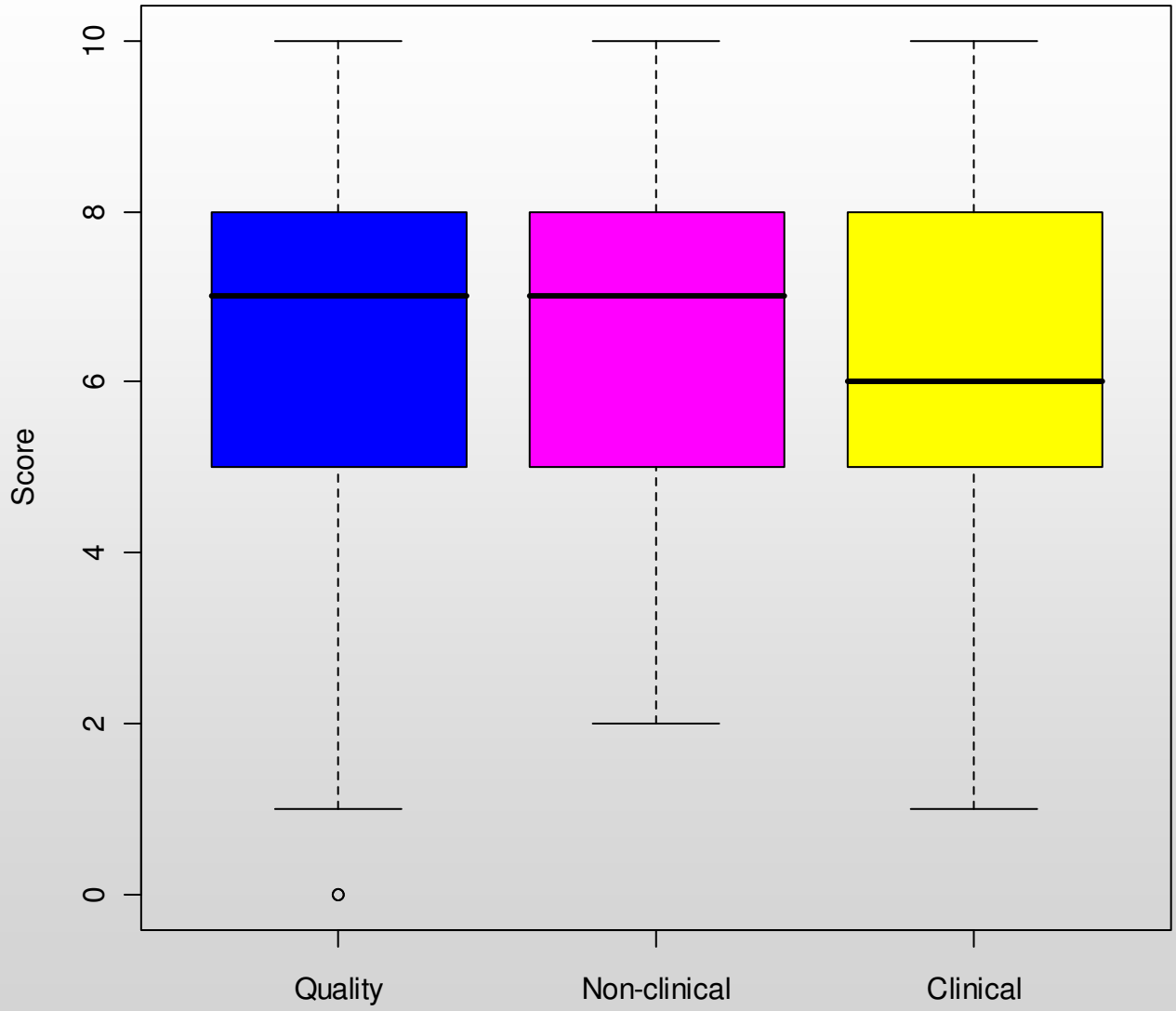
Questionnaire Results

- All scores converted to 10-point Scale (0 dissatisfied to 10 satisfied)

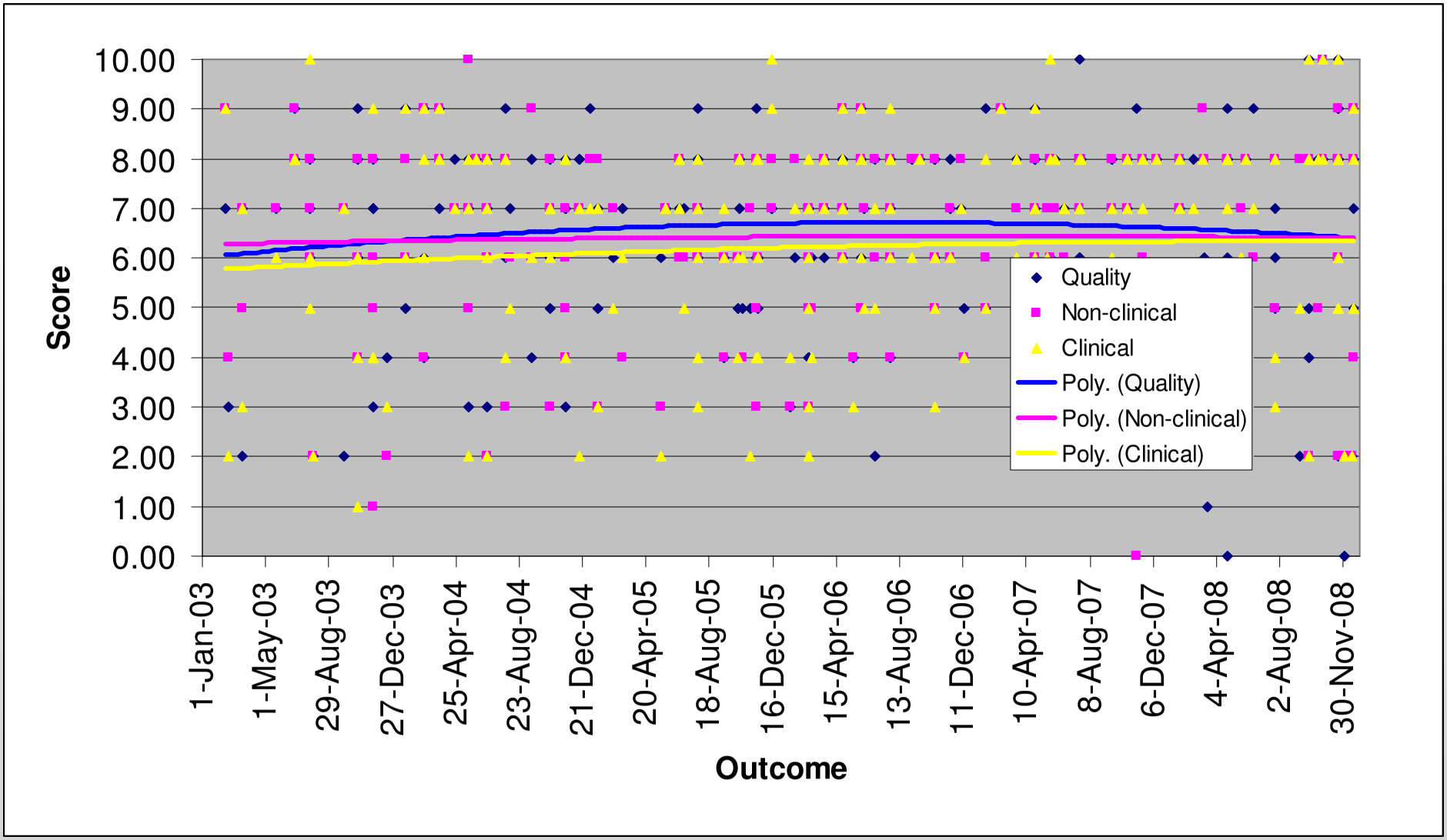
Presentation of Dossier (N=209)



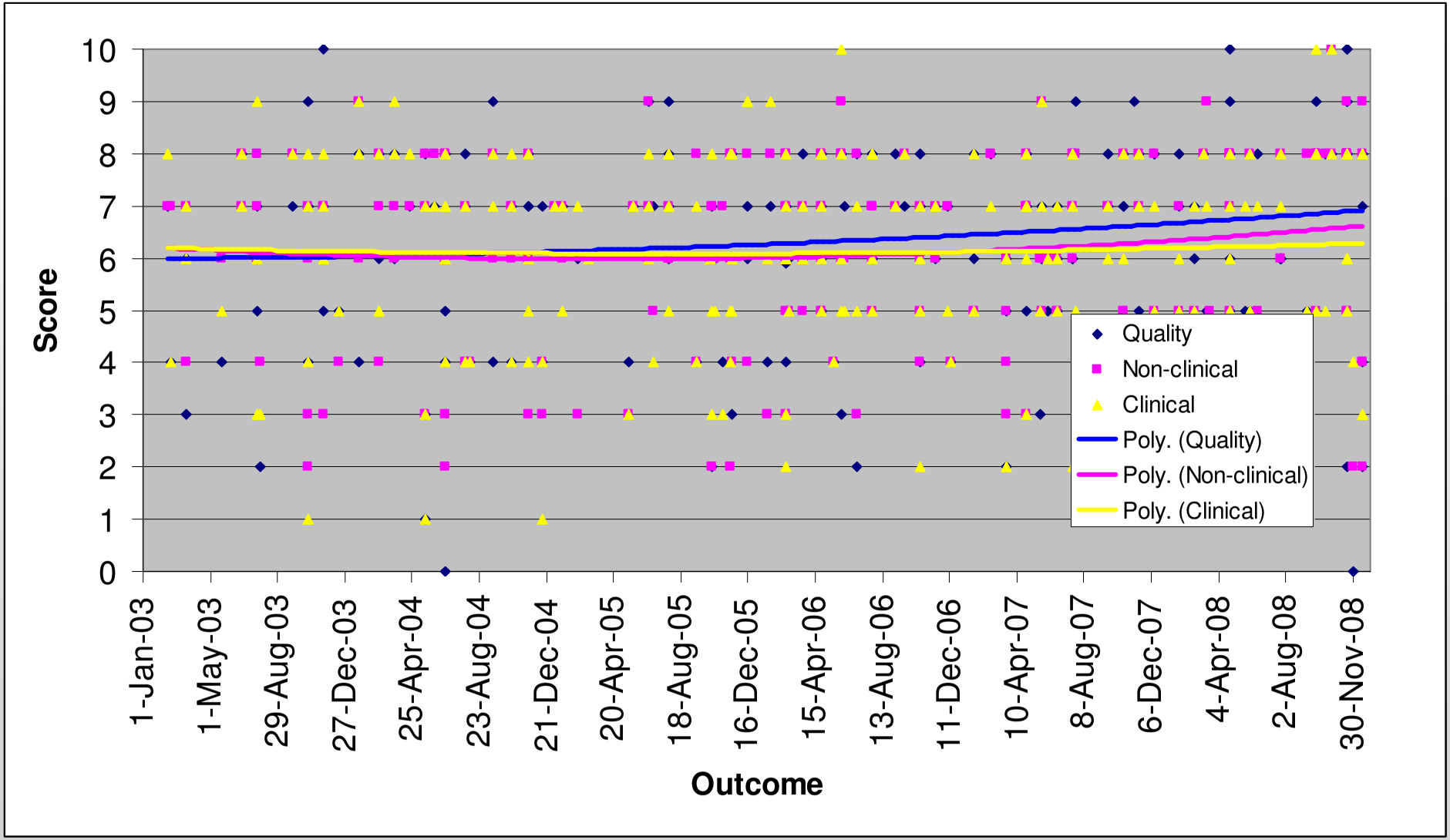
Evidence by Module (N=209)



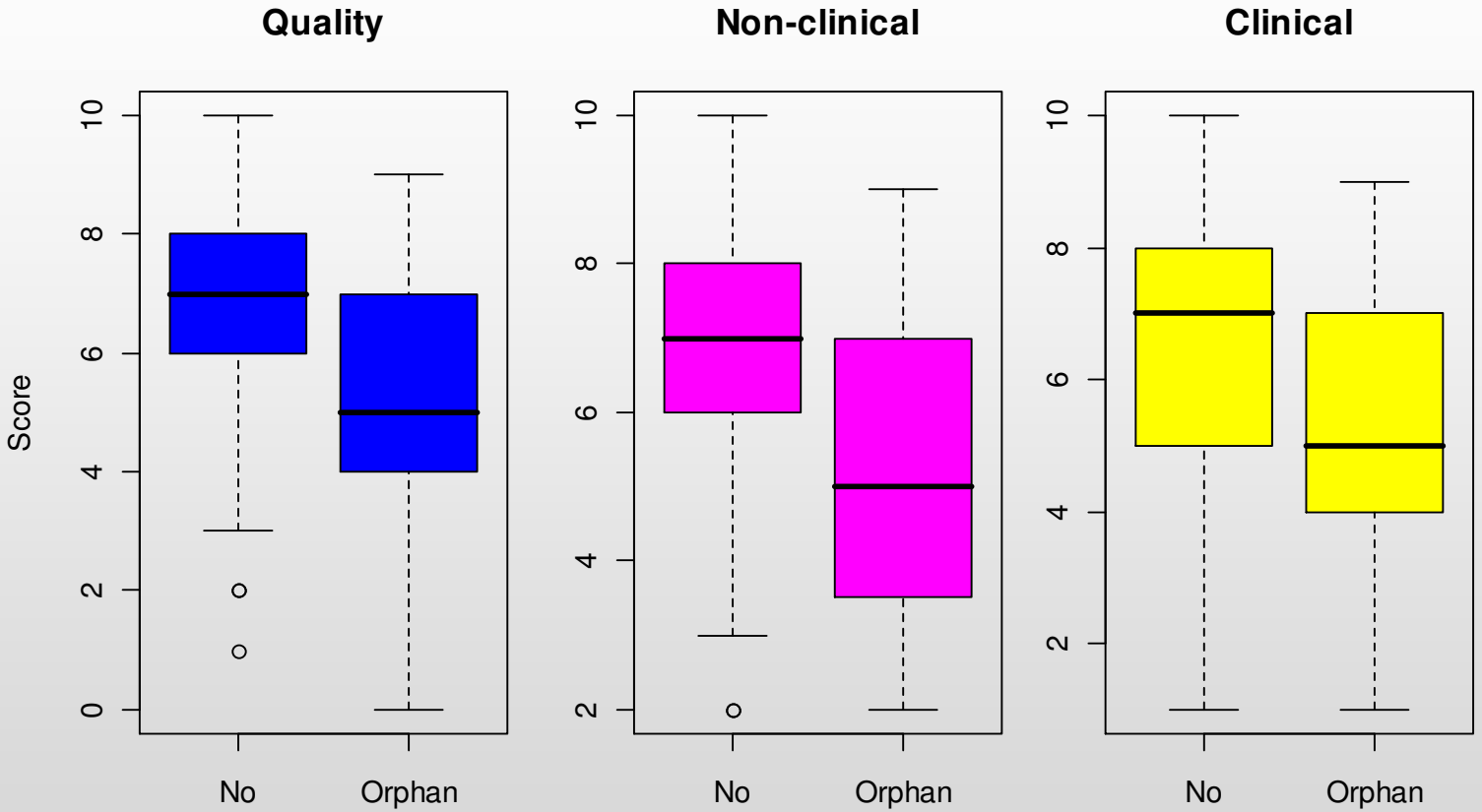
Presentation By Time (N=209)



Evidence by Module by Time (N=209)



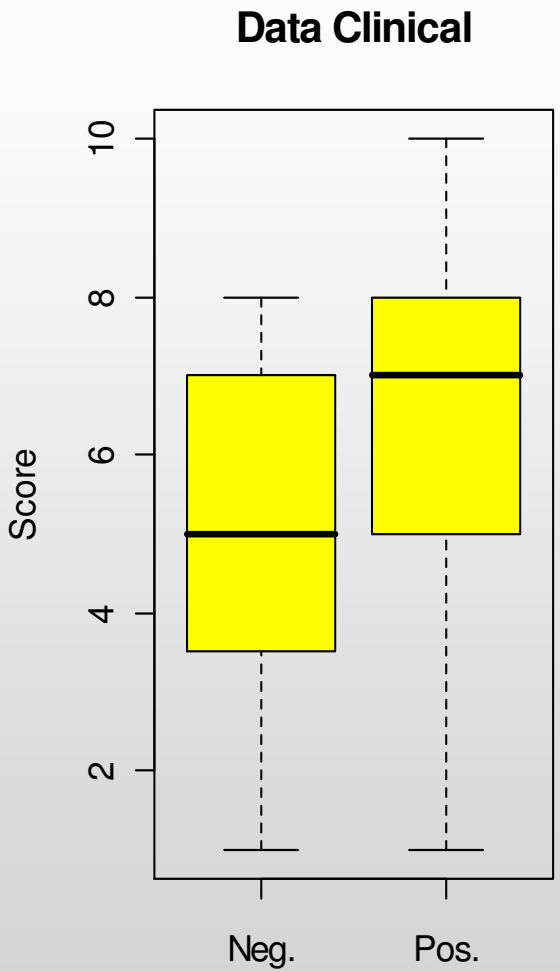
Evidence by Orphan (N=209)



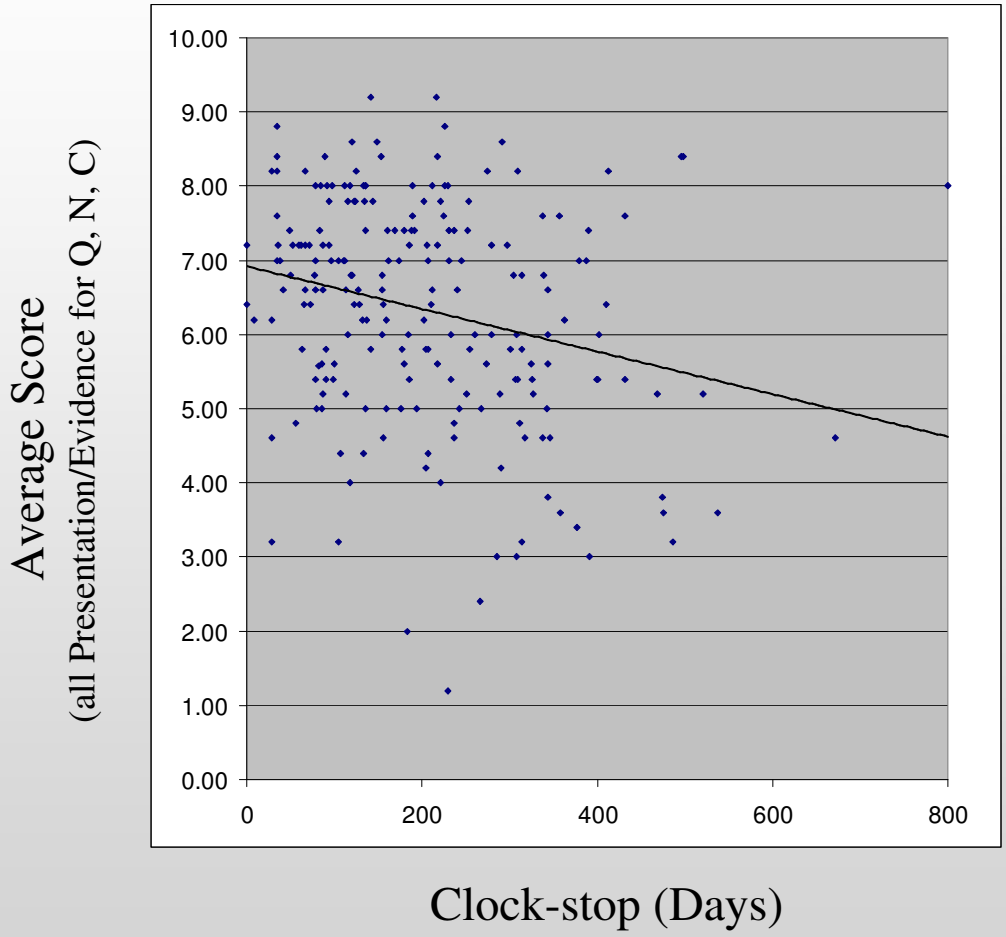
Is the Score Associated with Outcome and Clock-stop?

Success by Outcome Year (N=209)

Clinical Evidence versus Outcome (N=209)



Average Score and Clock-stop (N=209)



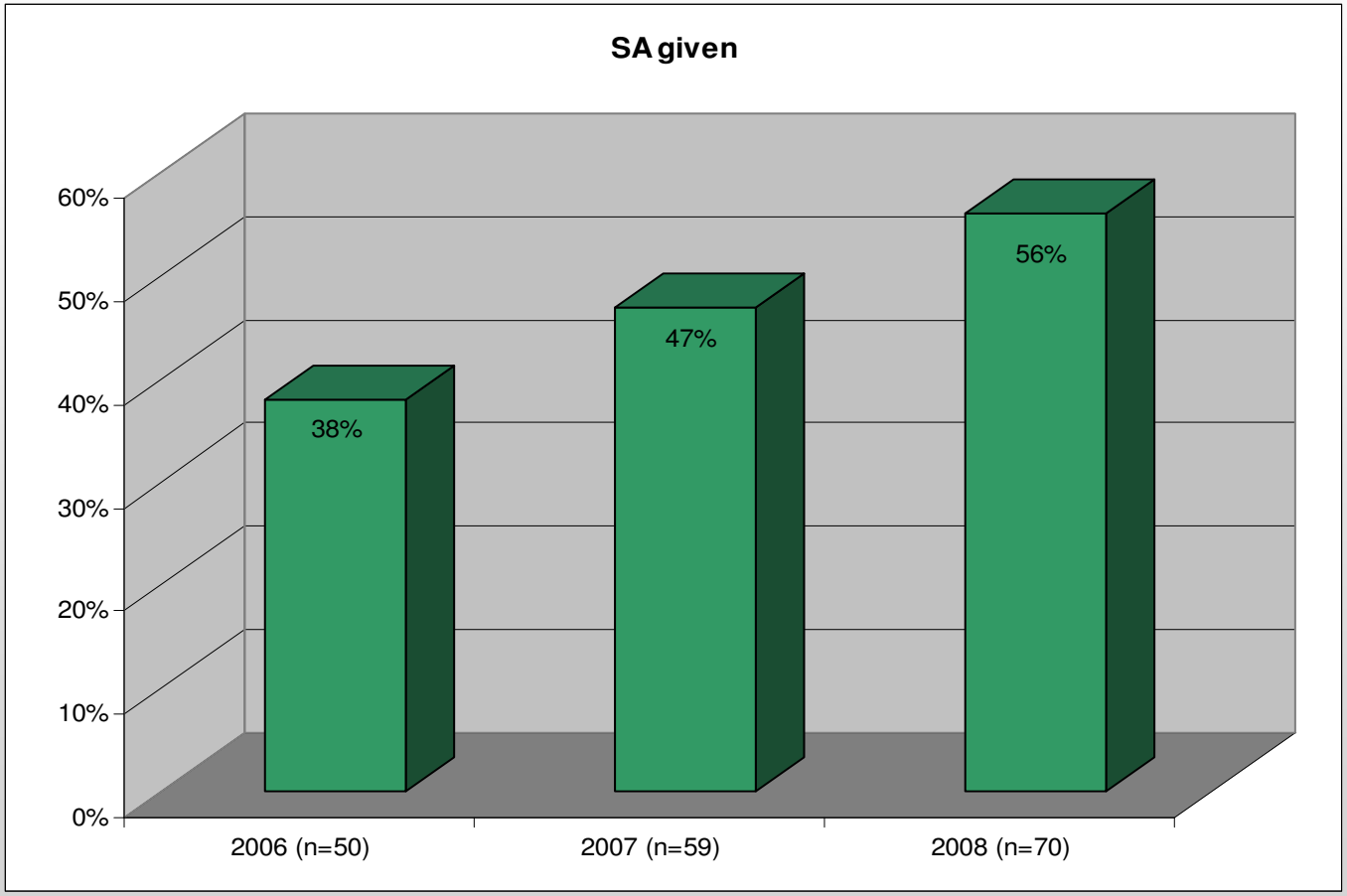
Summary

- Majority satisfaction
  - No new time trends
  - Orphan status associated with lower satisfaction with Evidence for all modules (and Presentation, data not shown)
- Satisfaction with Clinical Evidence associated with outcome and clock-stop
- Need to improve compliance with questionnaire
- Future
  - Further validate new questionnaire and explore new domains (work in progress)
  - Predictors of Outcome (work in progress)

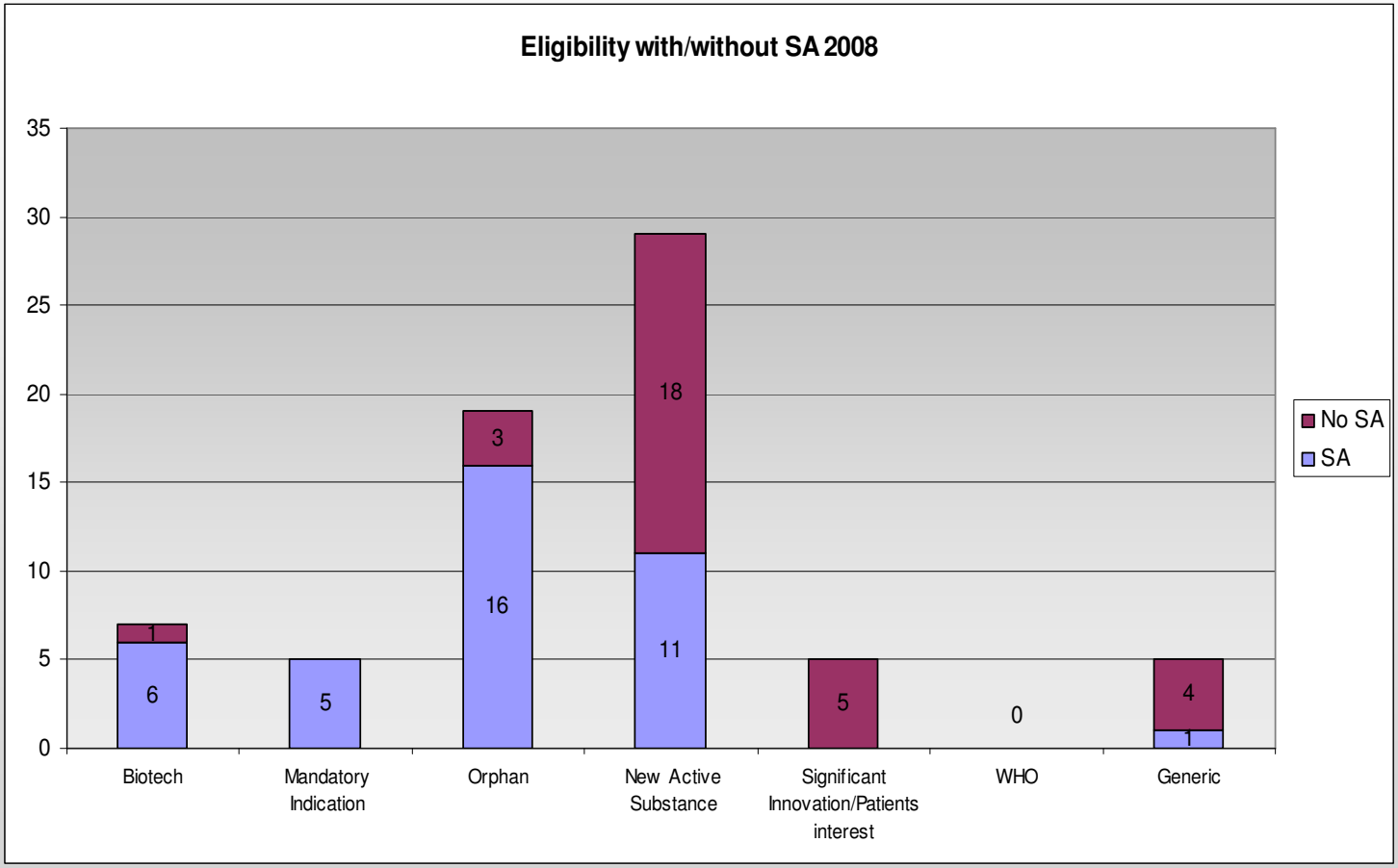
Predictors for Outcome - SA

Work in progress

Proportion of MAAs that received SA (by outcome year)

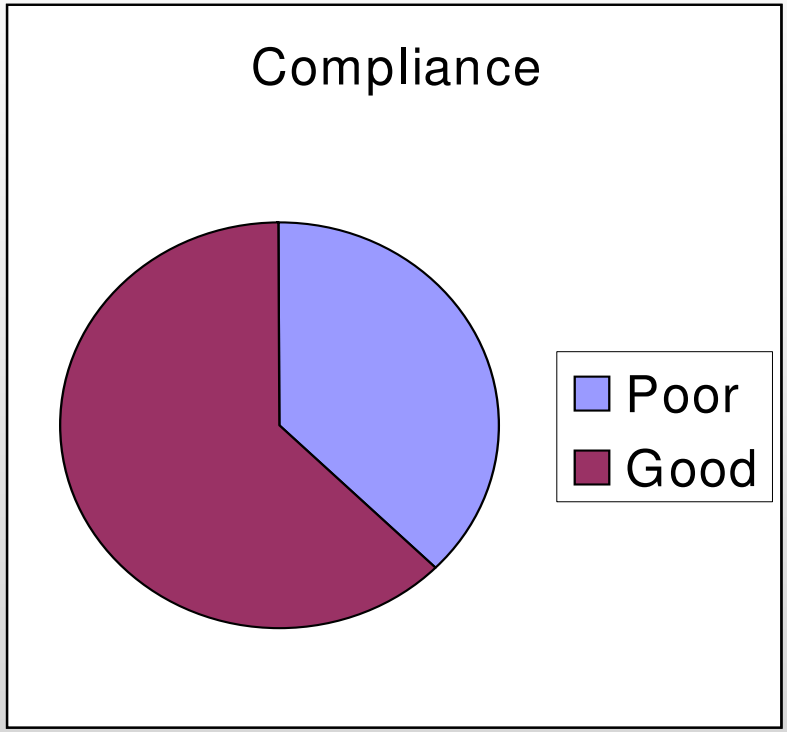


Distribution of Scientific Advice over eligibility -2008



Did the Company follow SA?

- 31 “new” questionnaires in study period
  - 16 with SA given
  - **6/16 (35%) show poor compliance according to Rapporteurs (score <5)**
- Is SA or compliance to SA related to outcome?



Size of company, success rate and Compliance with SA

Pharma size	Number applications	Success rate	Proportion with SA	Compliance with SA
Top 20 largest*	83	**89%**	46%	**84%**
21-150**	53	**72%**	34%	**63%**
151+***	56	**50%**	29%	**36%**

Regnstroem et al., (in manuscript)

*Top 20 largest (n=83) defined as being among the 20 largest companies
**21-150 (n=53) defined as being among the 21 – 150 largest companies
***151+ (n=56) defined as not being among the 150 largest companies
based on Total revenues 2005 according to Scrips Pharmaceutical League Tables 2006.

Predictors of Outcome

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Company Size (1: 151+; 2: 21-150; 3: Top 20 largest)	1.904	1.079	3.36
Clinical Evidence (0-10)	1.485	1.16	1.901
Major Objection on RCT (No vs Yes)	0.301	0.122	0.744
SA & Compliant *vs*. (No SA or Not Compliant)	9.593	1.175	78.311

Data on ranking was only available for 148 applications (work in progress)
Stepwise logistic regression. Compliance, retrospectively assigned in Regnstroem et al. (in manuscript)

Conclusions

- Most important factors associated with outcome
  - Compliance with Scientific Advice
  - Company Size
  - Rapporteurs' satisfaction with Clinical Evidence submitted
  - Major Objections on the Lack or Randomised Controlled Trials

Acknowledgments

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