Paper PD03

Much more than TFLs – the evolving role of the Biometrician

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ABSTRACT

At Covance we recognise that planning and running clinical trials is becoming more and more complex. As a result the skills of the Biometrician are being successfully deployed to support and enhance other functional groups, in order to manage our trials more effectively.

This paper will show real life situations where Biometricians at Covance have used projected and actual data to create time saving project management tools. From modeling Data Management Resource requirements, to enabling smooth CRF retrieval from investigator sites, the role of a Biometrician at Covance has diversified. We now do much more than produce tables, figures and listings.

INTRODUCTION

Covance is a large clinical research organisation providing a variety of services to pharmaceutical organisations all around the world. Traditionally, in our industry, Biometricians have been involved in the design of the clinical trial, performed sample size calculations, analysed the data and produced tables, figures and listings (TFLs) as defined in the statistical analysis plan. However, Covance offers an opportunity for a Biometrician to combine this traditional role with that of a provider of quantitative project management tools.

This, along with an expert understanding of the impact of data decisions, allows the Biometrician at Covance to use their unique skill set to influence realistic timeline management and enhance project management decisions pre-study, at study set-up and during the study. In-tern, empowering the entire project team to increase the chances of successful delivery.

"People commonly use statistics like a drunk uses a lamppost: for support rather than for illumination"
Mark Twain

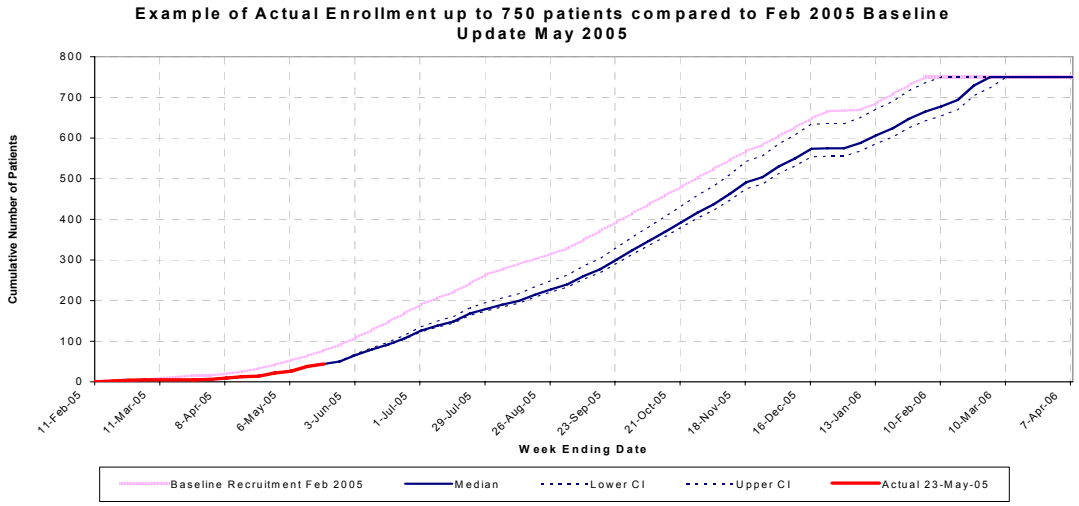
PRE-STUDY

A critical factor of any successful project is the availability and deployment of appropriate resources in accordance to workflow demands

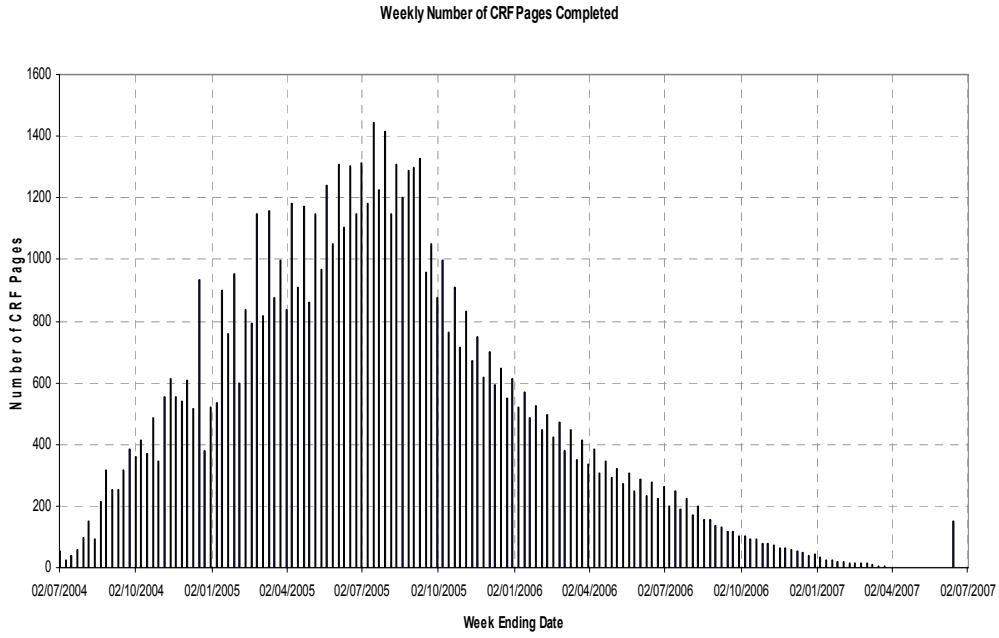
To achieve this, Project Managers require the ability to predict workflow so that they can proactively deploy resources in a timely manner. More specifically, in a Clinical trial environment, functional leads in clinical operations and data management need to know when subject data will be available to be *harvested* from site, entered onto the clinical database, reviewed and cleaned.

'MODELING'

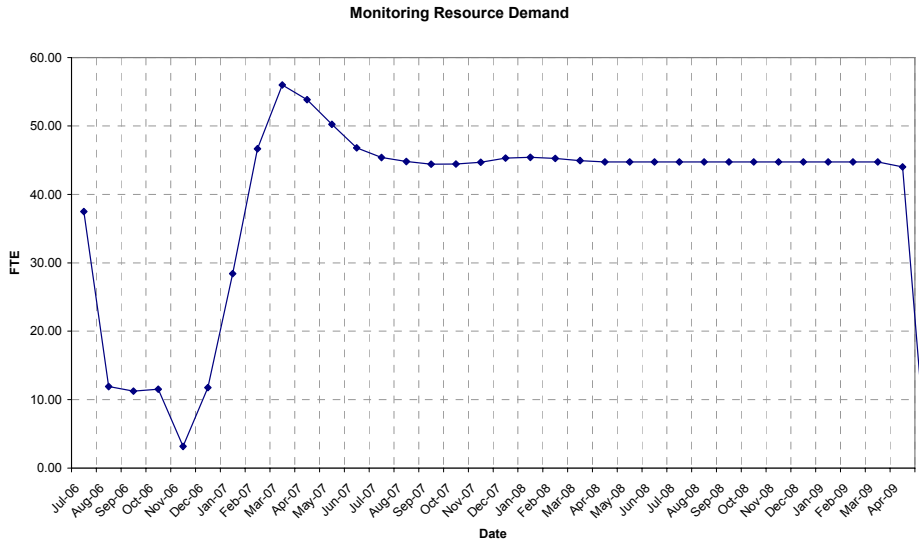
- Predicting and monitoring recruitment to achieve the correct number of patients, at the correct time. There will be no data and no analysis if we cannot recruit the required patients.



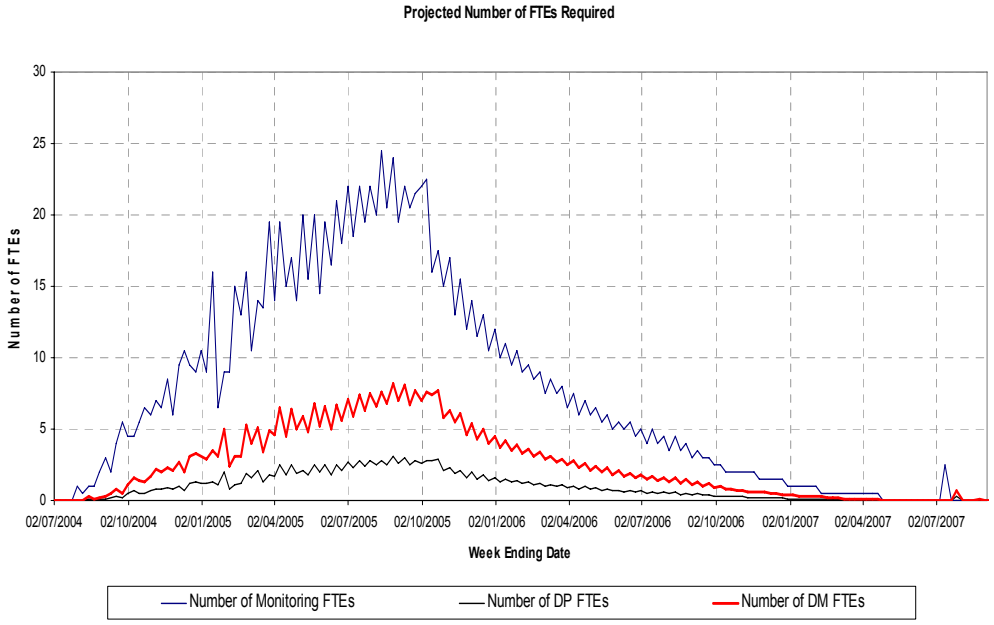
- Modeling CRF flow over time. Where and when a visit will be completed, and how many CRF pages are expected to be available over time – factoring in projected screen failure and withdrawal rates and other influences such as holidays and seasonal variations.



- Using the modeled CRF flow to predict required monitoring resources and target monitoring visits based on the data flow. Facilitating smooth and timely harvesting of CRF data from Investigator sites.



- Using the modeled CRF flow along with the predicted data harvest information to predict Data Processing and Data Management resource requirements. Allowing the adequate resources to be available as needed to process and clean the data as it becomes available.



STUDY SET-UP

Planning ahead prevents complex issues arising during the study and ensures a quality deliverable, in the minimum time.

To achieve this, the biometrician at Covance gets involved at the early stages of the study. By being involved at the planning stage, the biometrician provides valuable support to the project team during all aspects of the study set-up – through their unique understanding of clinical trial data and the implications of capturing this data in the correct way.

Good planning up-front prevents last minute remedial work which costs time and money at a point in the study when the timelines and budget do not allow that flexibility.

'CRUCIAL INPUT TO STUDY SET-UP'

- Input into timeline setting. Realistic timelines to ensure that all tasks are completed successfully whilst the overall milestones are maintained.
- Input to CRF design to prevent data issues. Good design of CRF modules to ensure that the data received better matches the requirements of the trial.
- Input to database design. Quality database set-up to prevent data capture issues and ensure the data from the CRF is accurately reflected in the database, and ultimately the end product.
- Input to the edit checks package. Using the particular skill set of a biometrician to design edit checks which give robust data. Targeted cleaning of key data points to prevent time consuming and expensive re-work at a later stage of the study.

DURING STUDY

Although all of the above goes along way to preventing a 'find and fix' approach, there is still the role for a Biometrician at Covance in enhancing the conduct of a clinical trial as it progresses.

Assessing data issues as they evolve allows the project team to identify trends and educate site staff as necessary.

By providing ongoing maintenance of trial metrics and periodically re-assessing the 'sate of play' the project manager and functional leads are given the tools to enable the continual reassessment of resource requirements.

'ONGOING TRIAL MANAGEMENT'

- Defining and identifying Protocol Violations/Deviations. Reducing the need for subjective identification by programmatically applying Protocol Violation/Deviation criteria across the whole patient population. Timely feedback of trends in Protocol Violations /Deviations to data management, monitors and sites to achieve cleaner data, first time.
- Defensive programming to capture data issues and trends. Employing a style of programming which identifies outliers and anomalies to be fed back to data management and queried.

- Identifying CRF backlog at sites using patient enrollment and withdrawal/completion data to predict CRF page availability at site. Identifying boluses of data at site by factoring in the schedule of routine monitoring visits. Enabling smoother retrieval of CRF pages, in a timely manner.

Missing Pages/CRF backlog

Country	Site No.	Subject	Visit	Total Outstanding	Expected	On Database	Status
Czech Republic	1	1	AES / CONMEDS	2	2	0	Completed
Czech Republic	1	3	Total	2	42	40	
France	2	2	VISIT 7	1	3	2	Completed
France	2	4	Total	1	42	41	
France	3	5	VISIT 8	5	5	0	Discontinued

- Query rate tracking, by CRF module in order to identify trends. Carried out regularly so that query trends can be fed back to the Investigator sites, via the monitors, to improve the ongoing data quality and reduce data management workload.

Query Matrix

country	site	N_dcfs	N_pgs_reviewed	CMED	COMP_WITHD	DEMO	DISPENSE	ECG	INCLUSION	LABTEST	PHYSEXAM	PREGTEST	RAND_SCREE	URINE_DIP	VISIT	AE	EXCLUSION	MEDHIST	VITALS	dcfs_per_page
Czech Rep	2	44	193	1	4	3	5	8	3	10	7	2	1	3	3					23%
France	11	135	592	33	3	3	3	5	8	30	20	1	2	1	8	10	2	4		23%
France	13	21	101	5	1			1		2	2				1	7	2			21%
France	14	40	136	5	3		7	1	5	4	2			1	3		1	3		29%
France	15	40	156	11	1	1	3	1		11	2		1		4			2		26%
France	19	41	160	16	4		3	1		11	3		2	2		3	2	1		26%
Hungary	22	12	63	1			1			2	3				2			3		19%
Hungary	23	108	572	11	3	3	5	4	5	30	5		4	1	13	12	2	6	1	19%
Hungary	24	15	70	5	2		1		1	2			2		1					21%
Hungary	25	25	115	3	2	2	2		3	5					6	2				22%
Netherlands	30	132	701	24	4		2	3	6	32	3		13	5		21	2	6		19%
Netherlands	31	86	893	21	5		4	2	9	17	2		4	1	5	6	1	3		10%
Netherlands	36	65	401	24	2			1	5	6	2		1	1	6	11	5			16%
Norway	40	32	177	2	1		4		1	6	2			3	5	1	1			18%
Norway	41	7	96	4									2			1				7%
Norway	43	36	223	5	5					6	2		6		8		1			16%
Poland	50	56	499	34			1	1		13				1	1	1	1			11%
Poland	58	41	184	13	6		3			5	1		1		3	8				22%
Poland	59	40	209	13	1		2	2	7	5	1		3		3	2				19%
Overall		976	5541	231	47	12	46	30	53	197	57	3	42	19	72	85	20	28	1	18%

- Ongoing timeline management by modeling CRF flow based on actual data as it becomes available. Comparing predicted data versus the real study data and adjusting subsequent work flow and resource requirements to negate the impact on timelines

THE FUTURE?

The role of the Biometrician at Covance is a constantly evolving one. New opportunities to improve the overall management of clinical trails are arising all the time and we are at the forefront of many of the current initiatives.

Examples include:

- Predicting the occurrence of endpoints.
- Producing financial metrics to create a dynamic costing model.
- Predicting safety issues and trends before they happen.
- Using CRF flow models to trigger timely investigator invoicing.
- Combining individual study resource metrics in order to model the requirements over time for entire functions.

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CONTACT INFORMATION

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