

Consolidating Study Outcomes in a Standardised, SEND-Compatible Structure

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Retrieval of critical toxicological findings and differentiating these from incidental ones is a key requirement for the analysis of large pre-clinical data sets.

The eTRANSafe project has identified the need to consolidate pre-clinical study outcomes, as expressed in study reports, with the corresponding study measurement data it holds in its SEND-based pre-clinical data warehouse.

It has created a Study Report (SR) 'Domain' which allows sponsors to assemble the important findings from a study report in a structured, SEND-compatible format.

The SR Domain has been populated manually by eTRANSAFE consortium members (EFPIA) and found to be fit for purpose.

Methods for automatically populating the SR Domain using text mining and data analytics are currently under investigation.

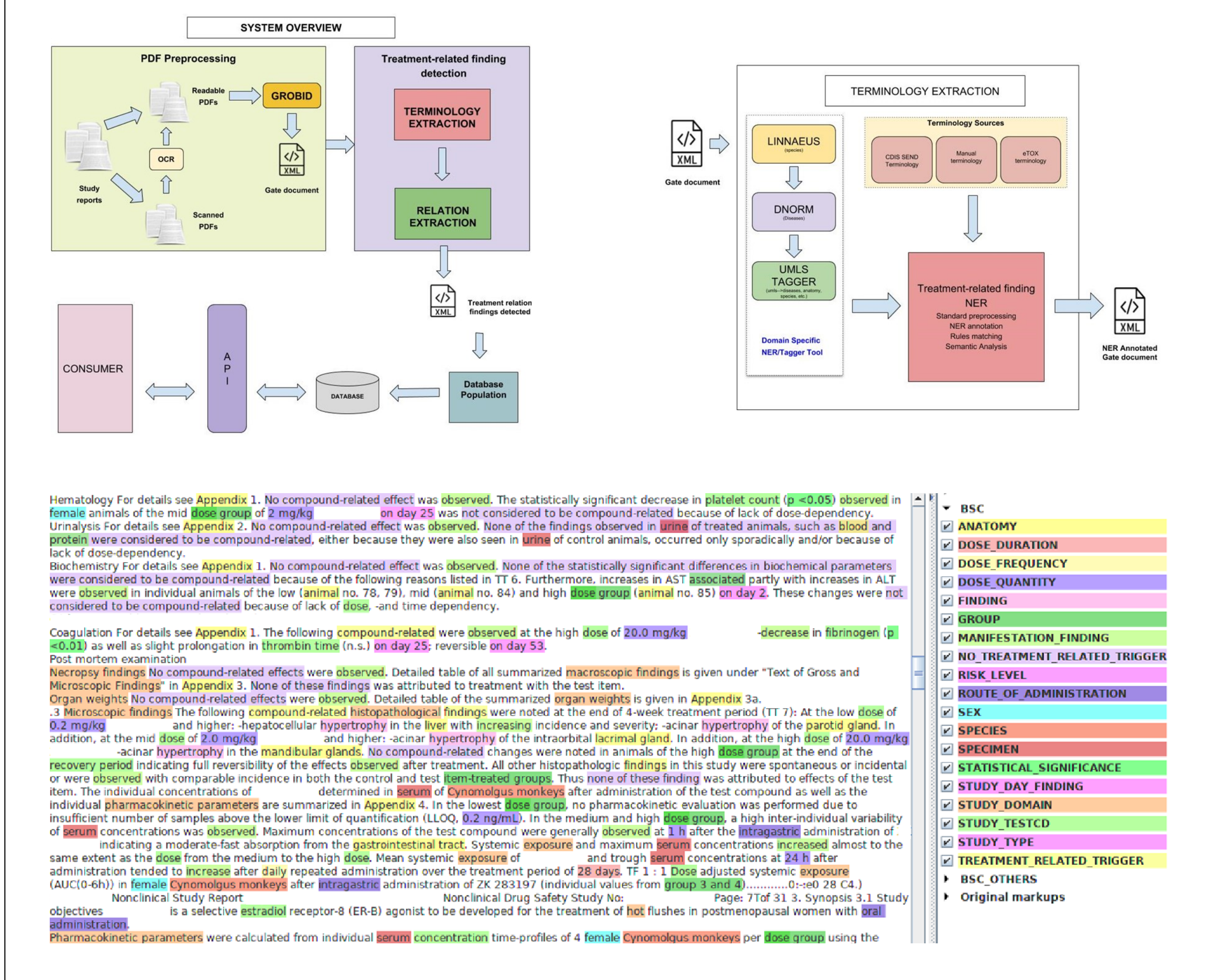
Since the linking of treatment effects to measurement data is critically important, the SR Domain could form the basis of a standard that is adopted and maintained by CDISC, as an extension to the SEND standard.

Text Mining Method

Purpose: Automatically populate SR-Domains from Study Reports (PDF)

Usage: Individual/bulk processing of legacy Study Reports

Dependencies: Resulting SR-Domains require 100% QA



Study Report (SR) Domain



Variable Name	Variable Label	Type	Controlled Terms, CodeList or Format	Role	Notes	Core
STUDID	Study Identifier	Char		Identifier	Unique identifier for a study within a SEND submission.	Req
DOMAIN	Domain Abbreviation	Char	SR	Identifier	Two character abbreviation for the domain.	Req
SRIRK	Risk Level Associated with this Finding	Char		Record Qualifier	A toxicity risk indicator. Can be one of: NOEL, LOEL, NOAEL or LOAEL.	Perm
SRGRP	Group Identifier	Num		Record Qualifier	Number of the treatment group in which the finding was observed.	Req
SRNGE	Scale of this Finding	Num		Record Qualifier	An estimate (range) of the number of subjects in the treatment group that were affected this severity (SSV) of the finding.	Perm
SRSEX	Sex	Char	(SEX)	Record Qualifier	Sex of the animal in which the finding was observed.	Req
SRDY	Day of Finding	Num		Timing	Day on which the finding was observed. Can be blank for time course observations (e.g. severity, bodyweight, bodyweight gain, etc.).	Perm
RODMAN	Domain of Finding	Char	(SDOMAN)	Topic	Domain in which the finding was observed. Supported domains are: BW, BG, CL, DD, FW, LA, MA, MI, OMP, PD, TF, VS, CV, CY and RE. Out of scope domains are: PM, PC and all Trial Design domains.	Req
SRSPC	Specimen of Finding	Char	(SPEC), (BODYVS)	Record Qualifier	Specimen in which the finding was observed. This is not required for all domains. For CL (Clinical Signs) domain, (BODYVS) is used instead of (SPEC).	Perm
SRTESTCD	Test Short Name	Char	(BGETESTCD), (BWTESTCD), (DGETESTCD), (EGETESTCD), (LEFTESTCD), (OMGETESTCD), (PEPARAMCD), (SCVTESTCD), (SPRTESTCD), (TFTESTCD), (VSTESTCD)	Record Qualifier	Short name of the measurement, test, or examination relating to the finding. The controlled term list is determined by the Domain in which the finding was observed. For some domains (e.g. CL, MA, MI, etc.) there is no associated test so this field can remain blank.	Perm
SRINDG	Finding	Char	(FINDINDG), (NOCLAPMA), (NONNOE)	Record Qualifier	Finding in those cases where there is no associated test (such as for domains CL, MA, MI, etc.) which may be controlled terms (depending on the domain). If not, the finding can be obtained from a local list (created and maintained) via the Ontobrowser.	Perm
SRDESV	Manifestation of Finding	Char		Result Qualifier	"I" = Increase, "D" = Decrease, "P" = Present.	Req
SRQESQ	Observation Qualifier	Char		Result Qualifier	"R" = Reversible, "T" = Transitory. This is an extensible list – to be agreed.	Perm
SRSSV	Severity of finding	Char	(SEV)	Variable Qualifier	Severity of the observation – can be blank.	Perm
SRSIGF	Statistical Significance	Char		Variable Qualifier	Statistical significance of the observation: + p < 0.01, ++ p < 0.001, +++ p < 0.001. Can be blank.	Perm
SRTRTEF	Treatment-Related?	Char	(NY)	Variable Qualifier	"Y" = finding is treatment-related; "N" = finding is not treatment-related; "U" = uncertain; "NA" = not applicable.	Req

Clinical Observations

Pale faeces were noted under the cages of males and females receiving 2500 or 5000 mg/kg/day (Groups 4 and 5) from Week 6. There were no other clinical findings attributable to treatment with the test article.

Bodyweight

Females receiving 2500 or 5000 mg/kg/day gained slightly less body weight than the control group ($p<0.05$ and $p<0.01$ respectively for Week 0 to 13 gain) during the course of the study. Other groups of females had similar body weight curves to that of the control. There was no consistent pattern of variation in the male body weights to indicate an effect of treatment.

Clinical Chemistry

Alkaline phosphatase activities for high dose females tended to be higher than those of the controls. The difference is of small magnitude and as there was no similar finding for males its relationship to treatment was regarded as uncertain. Alkaline phosphatase activities for the other female groups and all groups of treated males were comparable with those of the controls. There was no consistent pattern of variation in the other parameters to indicate an effect of treatment.

Relative Organ Weights

Kidney weights for treated males were higher ($p < 0.05$ or $p < 0.01$) than those of the control. There was no relationship to dose and, in the absence of any similar finding in the females, this finding was considered of doubtful toxicological significance. Kidney weights for treated females showed no pattern of variation to indicate an effect of treatment. Although in some instances variations from control attained levels of statistical significance, they were either of insufficient magnitude or showed no pattern to indicate an effect of treatment.

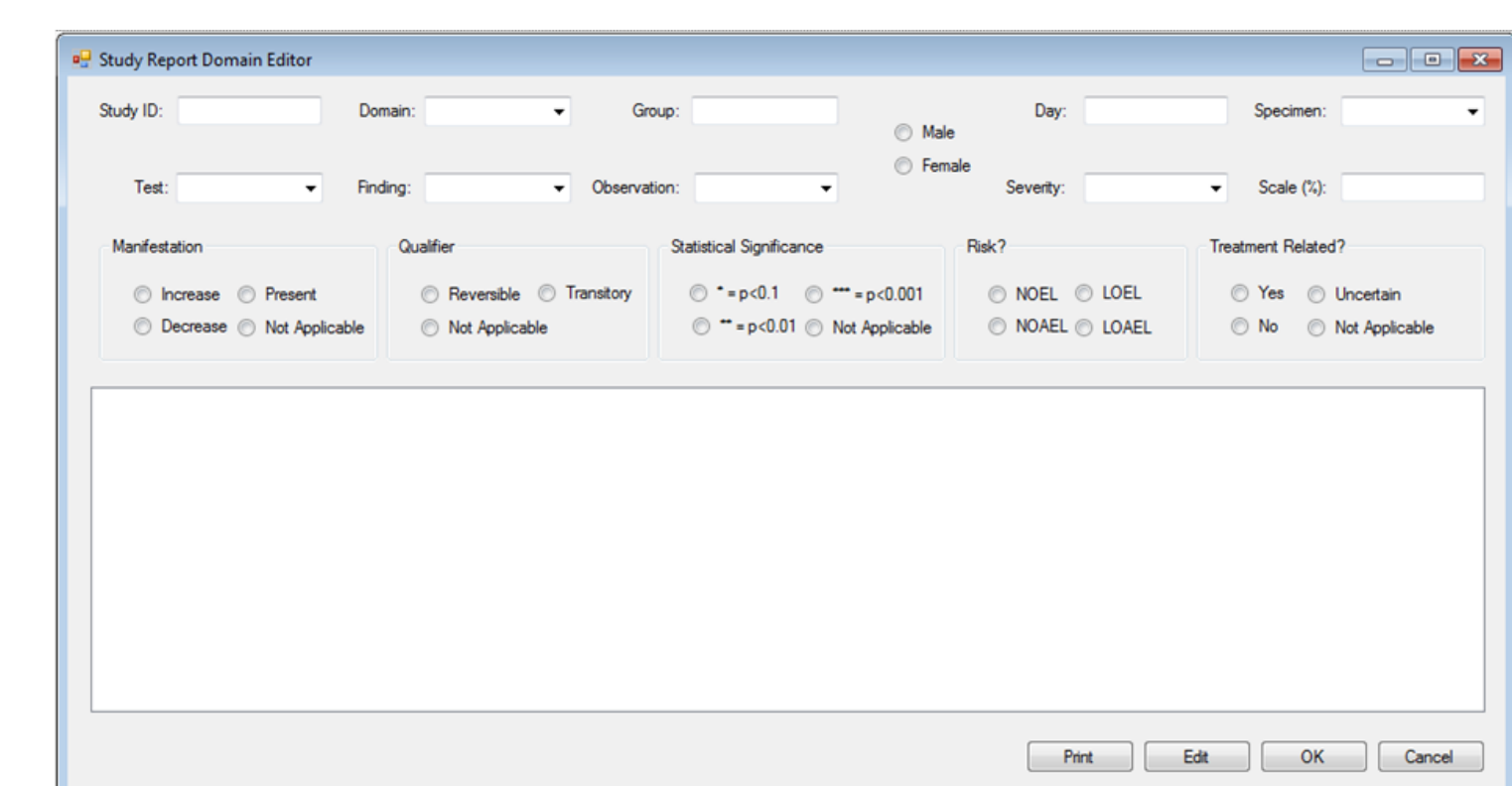
STUDY ID	DOMAIN	SRSSEQ	SRSRSC	SRSRSP	SRSRSG	SRSRSE	SRSRDY	RDOMAIN	SRSPEC	SRTSTDCT	SRSFNGDG	SRSROBSV	SRSRBSQ	SRSRSEV	SRSRSGV	SRTTREF
<Study ID>	SR	1	LOEL	4	100	M		CL	FECES		PALE	Increase				Y
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<Study ID>	SR	1	LOEL	5	100	F	91	LB	WHOLE BLOOD	ALP		Increase		MILD	*	U
<Study ID>	SR	1	LOEL	2	100	M	93	OM	KIDNEY	OWBWI		Increase		MILD	*	N

Manual Method

Purpose:	Manually populate SR-Domains from Study Reports; edit SR-Domains created by Text Mining and Computational Methods
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Usage: Transcription from Study Reports or as a companion to Report writing

Dependencies: SR-Domain creation/editing requires specialist staff (e.g. Study Director)

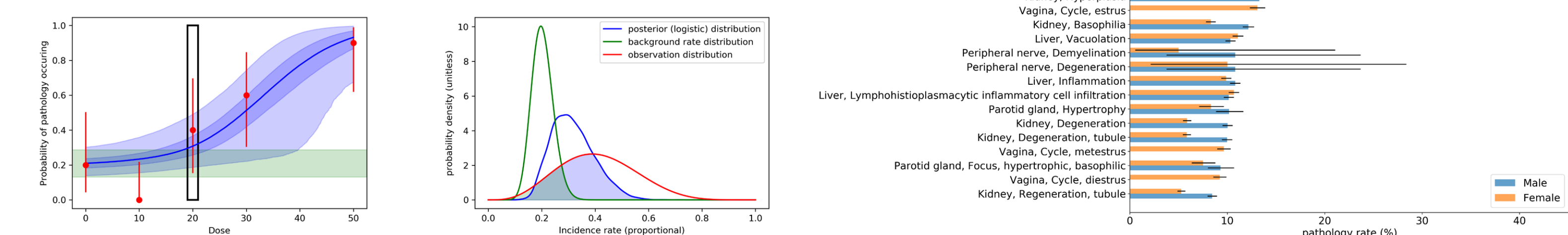


Computational Method

Purpose: Automatically populate SR-Domains directly from SEND datasets

Usage: Individual/bulk processing of study datasets

Dependencies: Resulting SR-Domains require 100% QA



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