

Lumping and Splitting Approach to Analyzing High Dimensional Sparse Counts Data

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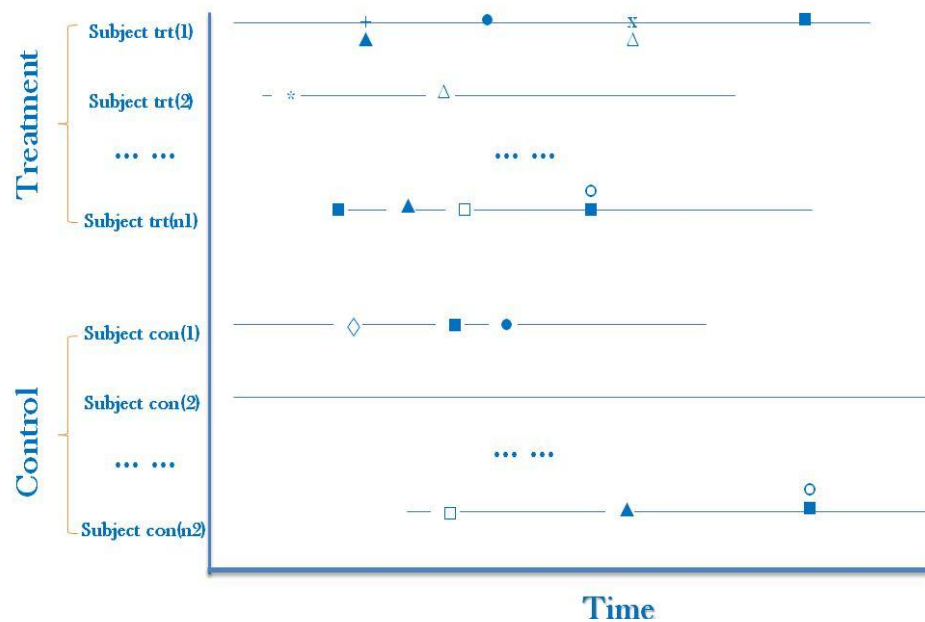
SCT 2013 - BOSTON

Multiple Counts Data

- Non-negative integers
- Represent the number of occurrences within a fixed time
- Both events and duration can be parameterized
- Variance increases with the expected number of events

- Quite common in clinical studies

- multiple efficacy endpoints
- multiple safety endpoints
- imaging count data
- genomic count data
- cognitive function data
- etc



Multiple Endpoints: ■ □ △ ▲ × ◇ ○ ● + *

Data Capture

ID	Onset Time	End Time	Event	Other Variables
S_1	mmddyyyy	mmddyyyy	E_7
S_2	mmddyyyy	mmddyyyy	E_5
...
S_{n-1}	mmddyyyy	mmddyyyy	E_8
S_n	mmddyyyy	mmddyyyy	E_1

Data Formation

- Multiple Counts Data
- Longitudinal Data
- Time-to-Events Data

High Dimensional Sparse Counts Data

m Events

n Subjects	ID	E ₁	E ₂	E ₃	E ₄	E ₅	E ₆	E ₇	E ₈	...	E _{m-1}	E _m
	S ₁	0	0	0	0	0	0	1	0	...	0	0
	S ₂	0	1	0	0	0	0	0	0	...	0	0
	S ₃	0	0	0	0	0	0	0	0	...	0	0
	S ₄	0	0	0	0	0	0	0	0	...	0	0
	S ₅	0	0	0	0	0	0	0	0	...	0	0
	S ₆	0	0	0	0	0	0	0	0	...	0	0
	S ₇	0	0	0	0	0	0	0	0	...	0	0
	S ₈	0	0	0	0	0	0	0	0	...	2	0

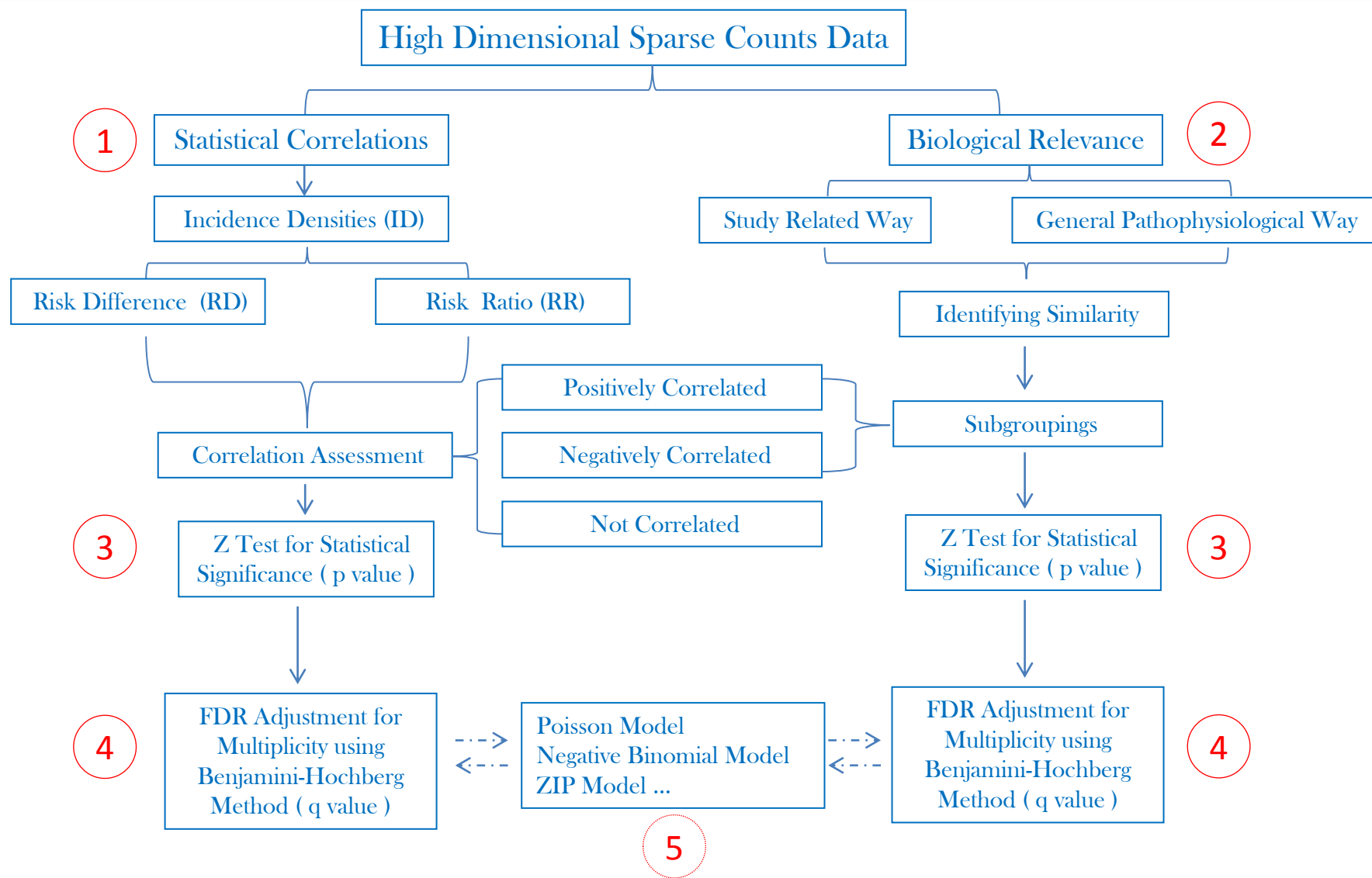
	S _{n-1}	0	0	0	0	0	0	0	1	...	0	0
	S _n	1	0	0	0	0	0	0	0	...	0	0

- n subjects, m endpoints, $m \gg n$
- too many zeros

Issues for Such Data Analysis

- Power Issue (Rare Incidence)
- Multiplicity Issue (Many Features)
- Competing Risk Issue (Multiple Events)

Analysis Approach



Data Analysis: An Example

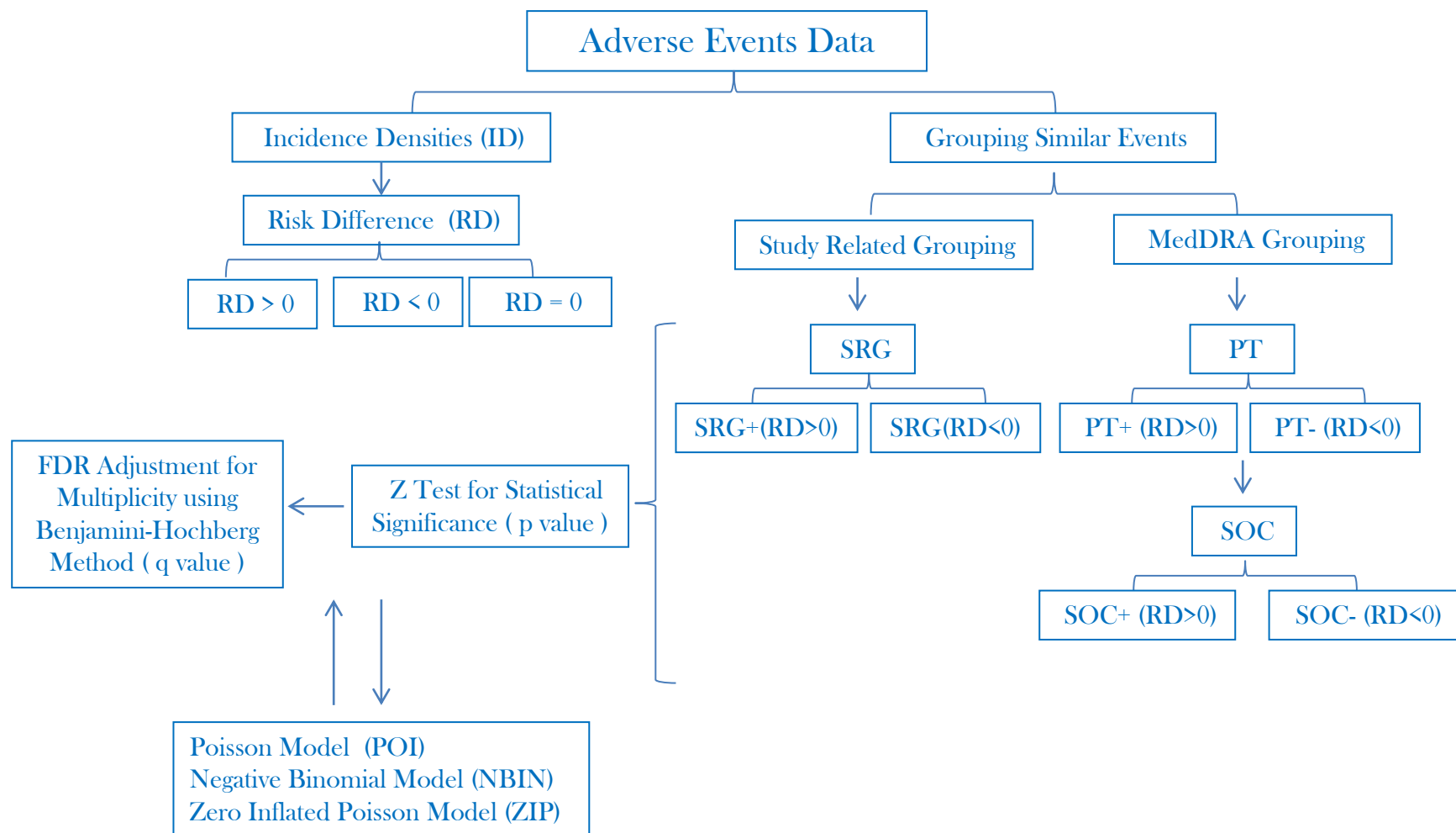
Clinical Trial

- A placebo-controlled, double-blind, randomized multi-center trial
- 212 subjects enrolled at 16 centers during 4.5 years
- 108 randomized to treatment group (trt) and 104 to placebo group (plb)

Data

- Adverse events (AE) data used as multiple endpoints
- 1348 AE observed during the study
- 864 distinct AE symptoms

Data Analysis Pipeline



Summary of AE Analysis Results

Grouping Method	Analysis Category	m	# p < 0.05 (%)	# q<0.05 (%)
No Grouping	Individual Events (IE)	864	11 (1.27)	1 (0.12)
PT Level Grouping	PT	372	17 (4.57)	5 (1.34)
	PT(Correlation)	462	48 (10.39)	7 (1.52)
SOC Level Grouping	SOC	23	5 (21.74)	4 (17.39)
	SOC (Correlation)	43	25 (58.14)	22 (51.16)
Study Related Grouping	SRG	113	11 (9.73)	4 (3.54)
	SRG(Correlation)	158	32 (20.25)	6 (3.80)

Analysis based on Individual Events

#	Individual Events (IE)	ID (trt)	ID (plb)	RD	Z	p	q
1	AUTONOMIC DYSREFLEXIA	0.1167	0.0042	0.1124	7.7076	0.0000	0.0000
2	ELEVATED TEMPATURE	0.0316	0.0021	0.0295	3.6588	0.0003	NS
3	ELEVATED ALT	0.0257	0.0000	0.0257	3.6528	0.0003	NS
4	ANAEMIA	0.0178	0.0000	0.0178	3.0271	0.0025	NS
5	HYPERGLYCEMIA	0.0099	0.0000	0.0099	2.2472	0.0246	NS
6	HYPONATREMIA	0.0099	0.0000	0.0099	2.2472	0.0246	NS
7	HYPERKALAEMIA	0.0138	0.0021	0.0117	2.0885	0.0368	NS
8	FEVER	0.0178	0.0042	0.0136	2.0539	0.0400	NS
9	NAUSEA AND VOMITING	0.0000	0.0085	-0.0085	2.0086	0.0446	NS
10	ELEVATED AST	0.0079	0.0000	0.0079	2.0080	0.0447	NS
11	ELEVATED PLATELETS	0.0079	0.0000	0.0079	2.0080	0.0447	NS

Lumping AE into Preferred Terms

#	Preferred Terms (PT)	ID (trt)	ID (plb)	RD	Z	p	q
1	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1167	0.0043	0.1124	7.7076	0.0000	0.0000
2	ALANINE AMINOTRANSFERASE INCREASED	0.0455	0.0000	0.0455	4.9088	0.0000	0.0002
3	PYREXIA	0.0989	0.0297	0.0692	4.4888	0.0000	0.0009
4	HEPATIC ENZYME INCREASED	0.0435	0.0021	0.0414	4.4422	0.0000	0.0009
5	BODY TEMPERATURE INCREASED	0.0613	0.0170	0.0443	3.6283	0.0003	0.0216
6	ASPARTATE AMINOTRANSFERASE INCREASED	0.0198	0.0000	0.0198	3.1940	0.0014	NS
7	BLOOD POTASSIUM INCREASED	0.0138	0.0000	0.0138	2.6643	0.0077	NS
8	BLOOD PRESSURE INCREASED	0.0138	0.0000	0.0138	2.6643	0.0077	NS
9	HYPOTENSION	0.0237	0.0043	0.0195	2.6325	0.0085	NS
10	PLATELET COUNT INCREASED	0.0119	0.0000	0.0119	2.4642	0.0137	NS
11	DEBRIDEMENT	0.0158	0.0021	0.0137	2.3059	0.0211	NS
12	HYPERKALAEMIA	0.0158	0.0021	0.0137	2.3059	0.0211	NS
13	VOMITING	0.0119	0.0340	-0.0221	2.2934	0.0218	NS
14	ANAEMIA	0.0237	0.0064	0.0174	2.2558	0.0241	NS
15	HAEMOGLOBIN DECREASED	0.0178	0.0043	0.0136	2.0539	0.0400	NS
16	BLOOD ALKALINE PHOSPHATASE INCREASED	0.0000	0.0085	-0.0085	2.0086	0.0446	NS
17	OPEN WOUND	0.0040	0.0170	-0.0130	1.9813	0.0476	NS

Lumping AE into Preferred Terms

Positive Correlation

#	Preferred Terms (PT)	ID (trt)	ID (plb)	RD	Z	p	q
1	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1167	0.0042	0.1124	7.7076	0.0000	0.0000
2	PYREXIA	0.1009	0.0064	0.0945	6.8057	0.0000	0.0000
3	ALANINE AMINOTRANSFERASE INCREASED	0.0455	0.0000	0.0455	4.9088	0.0000	0.0001
4	BODY TEMPERATURE INCREASED	0.0514	0.0021	0.0493	4.9063	0.0000	0.0001
5	HEPATIC ENZYME INCREASED	0.0435	0.0021	0.0414	4.4422	0.0000	0.0008
6	DECUBITUS ULCER	0.0336	0.0000	0.0336	4.1942	0.0000	0.0021
7	ANAEMIA	0.0218	0.0000	0.0218	3.3533	0.0008	0.0461
8	ASPARTATE AMINOTRANSFERASE INCREASED	0.0198	0.0000	0.0198	3.1940	0.0014	NS
9	RASH	0.0198	0.0000	0.0198	3.1940	0.0014	NS
10	HYPOTENSION	0.0237	0.0021	0.0216	3.0464	0.0023	NS
11	CELLULITIS	0.0178	0.0000	0.0178	3.0271	0.0025	NS
12	WOUND COMPLICATION	0.0178	0.0000	0.0178	3.0271	0.0025	NS
13	HAEMOGLOBIN DECREASED	0.0178	0.0000	0.0178	3.0271	0.0025	NS
14	DEBRIDEMENT	0.0158	0.0000	0.0158	2.8511	0.0044	NS
15	BLOOD POTASSIUM INCREASED	0.0138	0.0000	0.0138	2.6643	0.0077	NS
16	BLOOD PRESSURE INCREASED	0.0138	0.0000	0.0138	2.6643	0.0077	NS
17	PLATELET COUNT INCREASED	0.0119	0.0000	0.0119	2.4642	0.0137	NS
18	HYPERGLYCAEMIA	0.0119	0.0000	0.0119	2.4642	0.0137	NS
19	PLEURAL EFFUSION	0.0119	0.0000	0.0119	2.4642	0.0137	NS
20	HYPERKALAEMIA	0.0158	0.0021	0.0137	2.3059	0.0211	NS
21	OSTEOMYELITIS	0.0099	0.0000	0.0099	2.2472	0.0246	NS
22	RBC SEDIMENTATION RATE INCREASED	0.0099	0.0000	0.0099	2.2472	0.0246	NS
23	WBC COUNT INCREASED	0.0099	0.0000	0.0099	2.2472	0.0246	NS
24	HYPONATRAEMIA	0.0099	0.0000	0.0099	2.2472	0.0246	NS
25	MUSCULOSKELETAL PAIN	0.0099	0.0000	0.0099	2.2472	0.0246	NS
26	HYPERTENSION	0.0099	0.0000	0.0099	2.2472	0.0246	NS
27	GGTINCREASED	0.0178	0.0042	0.0136	2.0539	0.0400	NS
28	STAPHYLOCOCCAL INFECTION	0.0079	0.0000	0.0079	2.0080	0.0447	NS
29	WOUND	0.0079	0.0000	0.0079	2.0080	0.0447	NS
30	BLOOD UREA INCREASED	0.0079	0.0000	0.0079	2.0080	0.0447	NS
31	ANXIETY	0.0079	0.0000	0.0079	2.0080	0.0447	NS
32	DYSPNOEA	0.0079	0.0000	0.0079	2.0080	0.0447	NS

Lumping AE into Preferred Terms

Negative Correlation

#	Preferred Terms (PT)	ID (trt)	ID (plb)	RD	Z	p	q
1	PYREXIA	0.0000	0.0234	-0.0234	3.3560	0.0008	NS
2	OSTEOMYELITIS	0.0020	0.0234	-0.0214	2.9549	0.0031	NS
3	DECUBITUS ULCER	0.0020	0.0234	-0.0214	2.9549	0.0031	NS
4	OPEN WOUND	0.0000	0.0170	-0.0170	2.8528	0.0043	NS
5	VOMITING	0.0099	0.0340	-0.0241	2.5518	0.0107	NS
6	FALL	0.0000	0.0127	-0.0127	2.4652	0.0137	NS
7	CELLULITIS	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
8	FUNGAL SKIN INFECTION	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
9	CONTUSION	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
10	WOUND	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
11	PREALBUMIN DECREASED	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
12	RBC SEDIMENTATION RATE INCREASED	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
13	RASH	0.0000	0.0106	-0.0106	2.2480	0.0246	NS
14	CLOSTRIDIAL INFECTION	0.0000	0.0085	-0.0085	2.0086	0.0446	NS
15	BLOOD ALKALINE PHOSPHATASE INCREASED	0.0000	0.0085	-0.0085	2.0086	0.0446	NS
16	MUSCULOSKELETAL PAIN	0.0000	0.0085	-0.0085	2.0086	0.0446	NS

Lumping AE into Body Systems

#	System Organ Classes (SOC)	ID (trt)	ID (plb)	RD	Z	p	q
1	INVESTIGATIONS	0.3817	0.1613	0.2204	8.0257	0.0000	0.0000
2	NERVOUS SYSTEM DISORDERS	0.1543	0.0276	0.1267	7.1370	0.0000	0.0000
3	VASCULAR DISORDERS	0.0613	0.0127	0.0486	4.0977	0.0000	0.0003
4	GENERAL DISORDERS & ADMINISTRATION SITE CONDITION	0.1424	0.0807	0.0617	3.0907	0.0020	0.0115
5	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0.1127	0.0722	0.0406	2.1996	0.0278	NS

Lumping AE into Body Systems

Negative Correlation

#	System Organ Classes (SOC)	ID (trt)	ID (plb)	RD	Z	p	q
1	INVESTIGATIONS	0.0237	0.0934	-0.0697	4.6387	0.0000	0.0000
2	GASTROINTESTINAL DISORDERS	0.0218	0.0828	-0.0610	4.2807	0.0000	0.0001
3	INFECTIONS AND INFESTATIONS	0.0396	0.1083	-0.0687	4.1055	0.0000	0.0002
4	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0.0218	0.0658	-0.0441	3.3531	0.0008	0.0031
5	GENERAL DISORDERS & ADMINISTRATION SITE CONDITION	0.0178	0.0488	-0.0310	2.6885	0.0072	0.0124
6	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0.0020	0.0170	-0.0150	2.3922	0.0168	0.0360
7	SURGICAL AND MEDICAL PROCEDURES	0.0079	0.0276	-0.0197	2.3121	0.0208	0.0425
8	NERVOUS SYSTEM DISORDERS	0.0020	0.0149	-0.0129	2.1781	0.0294	NS
9	REPRODUCTIVE SYSTEM AND BREAST DISORDERS	0.0000	0.0085	-0.0085	2.0086	0.0446	NS

Lumping AE into Body System

Positive Correlation

#	System Organ Classes (SOC)	ID (trt)	ID (plb)	RD	Z	p	q
1	INVESTIGATIONS	0.3580	0.0679	0.2901	11.9516	0.0000	0.0000
2	NERVOUS SYSTEM DISORDERS	0.1523	0.0127	0.1396	8.3099	0.0000	0.0000
3	GENERAL DISORDERS & ADMINISTRATION SITE CONDITION	0.1246	0.0318	0.0928	5.5318	0.0000	0.0000
4	VASCULAR DISORDERS	0.0613	0.0085	0.0528	4.6027	0.0000	0.0000
5	INFECTIONS AND INFESTATIONS	0.2650	0.1571	0.1079	4.1813	0.0000	0.0002
6	METABOLISM AND NUTRITION DISORDERS	0.0494	0.0064	0.0431	4.1763	0.0000	0.0002
7	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0.0989	0.0425	0.0564	3.4828	0.0005	0.0021
8	SURGICAL AND MEDICAL PROCEDURES	0.0316	0.0043	0.0274	3.2847	0.0010	0.0037
9	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0.0475	0.0127	0.0347	3.2230	0.0013	0.0042
10	PSYCHIATRIC DISORDERS	0.0218	0.0021	0.0196	2.8764	0.0040	0.0124
11	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	0.0494	0.0170	0.0325	2.8649	0.0042	0.0124
12	RENAL AND URINARY DISORDERS	0.0237	0.0043	0.0195	2.6325	0.0085	0.0214
13	GASTROINTESTINAL DISORDERS	0.0969	0.0552	0.0417	2.4764	0.0133	0.0317
14	BLOOD AND LYMPHATIC SYSTEM DISORDERS	0.0257	0.0064	0.0193	2.4374	0.0148	0.0335
15	EAR AND LABYRINTH DISORDERS	0.0099	0.0000	0.0099	2.2472	0.0246	0.0481
16	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0.0257	0.0085	0.0172	2.0972	0.0360	NS

Lumping AE into Study Related Groups

#	Study Related Grouping (SRG)	ID (trt)	ID (plb)	RD	Z	p	q
1	LIVER FUNCTION TEST ABNORMAL	0.1305	0.0085	0.1220	7.8397	0.0000	0.0000
2	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1167	0.0043	0.1124	7.7076	0.0000	0.0000
3	FEVER	0.1642	0.0510	0.1132	5.8538	0.0000	0.0000
4	HIGH POTASSIUM	0.0297	0.0021	0.0275	3.5143	0.0004	0.0124
5	HIGH BLOOD PRESSURE	0.0237	0.0043	0.0195	2.6325	0.0085	NS
6	TREATMENT PROBLEM	0.0237	0.0043	0.0195	2.6325	0.0085	NS
7	PLATELET COUNT INCREASED	0.0119	0.0000	0.0119	2.4642	0.0137	NS
8	LOW BLOOD PRESSURE	0.0257	0.0064	0.0193	2.4374	0.0148	NS
9	HIGH BLOOD GLUCOSE	0.0455	0.0212	0.0243	2.1280	0.0333	NS
10	HEARING IMPAIRED	0.0079	0.0000	0.0079	2.0080	0.0447	NS
11	DISORIENTATION	0.0040	0.0170	-0.0130	1.9813	0.0476	NS

Lumping AE into Study Related Groups

Positive Correlation

#	Study Related Grouping (SRG)	ID (trt)	ID (plb)	RD	Z	p	q
1	LIVER FUNCTION TEST ABNORMAL	0.1305	0.0085	0.1220	7.8397	0.0000	0.0000
2	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1167	0.0043	0.1124	7.7076	0.0000	0.0000
3	FEVER	0.1602	0.0467	0.1135	5.9770	0.0000	0.0000
4	HIGH POTASSIUM	0.0297	0.0021	0.0275	3.5143	0.0004	0.0174
5	SKIN COMPLICATIONS	0.0831	0.0318	0.0512	3.4847	0.0005	0.0174
6	ANAEMIA	0.0435	0.0106	0.0329	3.2165	0.0013	0.0342
7	TREATMENT PROBLEM	0.0237	0.0021	0.0216	3.0464	0.0023	NS
8	HAEMORRHAGE	0.0158	0.0000	0.0158	2.8511	0.0044	NS
9	LOW BLOOD PRESSURE	0.0257	0.0043	0.0215	2.8061	0.0050	NS
10	WOUND COMPLICATION	0.0336	0.0085	0.0251	2.7730	0.0056	NS
11	VASCULAR DISORDERS	0.0138	0.0000	0.0138	2.6643	0.0077	NS
12	HIGH BLOOD PRESSURE	0.0237	0.0043	0.0195	2.6325	0.0085	NS
13	INFECTION	0.0316	0.0085	0.0232	2.6136	0.0090	NS
14	PAIN	0.0415	0.0149	0.0267	2.5455	0.0109	NS
15	MENTAL DISORDER	0.0178	0.0021	0.0157	2.5080	0.0121	NS
16	INFLAMMATIONS	0.0119	0.0000	0.0119	2.4642	0.0137	NS
17	NEUROLOGIC DISFUNCTION	0.0119	0.0000	0.0119	2.4642	0.0137	NS
18	PLATELET COUNT INCREASED	0.0119	0.0000	0.0119	2.4642	0.0137	NS
19	RESPIRATORY COMPLICATIONS	0.0158	0.0021	0.0137	2.3059	0.0211	NS
20	SEPSIS	0.0237	0.0064	0.0174	2.2558	0.0241	NS
21	HIGH BLOOD GLUCOSE	0.0455	0.0212	0.0243	2.1280	0.0333	NS
22	URINARY DISORDERS	0.1562	0.1125	0.0437	2.0116	0.0443	NS
23	GASTROINTESTINAL OBSTRUCTION	0.0079	0.0000	0.0079	2.0080	0.0447	NS
24	HEARING IMPAIRED	0.0079	0.0000	0.0079	2.0080	0.0447	NS

Lumping AE into Study Related Groups

Negative Correlation

#	Study Related Grouping (SRG)	ID (trt)	ID (plb)	RD	Z	p	q
1	INFLAMMATIONS	0.0059	0.0318	-0.0259	2.9505	0.0032	NS
2	GASTROOESOPHAGEAL DISORDER	0.0000	0.0127	-0.0127	2.4652	0.0137	NS
3	SKIN COMPLICATIONS	0.0158	0.0403	-0.0245	2.3062	0.0211	NS
4	VOMITING/NAUSEA	0.0119	0.0340	-0.0221	2.2934	0.0218	NS
5	INFECTION	0.0237	0.0509	-0.0272	2.2335	0.0255	NS
6	BLOOD ENZYME INCREASED	0.0000	0.0085	-0.0085	2.0086	0.0446	NS
7	DISORIENTATION	0.0040	0.0170	-0.0130	1.9813	0.0476	NS
8	WOUND COMPLICATION	0.0158	0.0361	-0.0203	1.9811	0.0476	NS

Summary of the AE Analysis

■ No Grouping

#	Individual Events (IE)	RD	RR	q
1	AUTONOMIC DYSREFLEXIA	0.1124	27.48	0.0000

■ Grouping based on Biological Information

#	Preferred Terms (PT)	RD	RR	q
1	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1124	27.46	0.0000
2	ALANINE AMINOTRANSFERASE INCREASED	0.0454	>999.00	0.0002
3	PYREXIA	0.0691	3.33	0.0012
4	HEPATIC ENZYME INCREASED	0.0413	20.52	0.0012
5	BODY TEMPERATURE INCREASED	0.0443	3.61	0.0216



#	Study Related Grouping (SRG)	RD	RR	q
1	LIVER FUNCTION TEST ABNORMAL	0.1220	15.37	0.0000
2	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1124	27.46	0.0000
3	FEVER	0.1132	3.22	0.0000
4	HIGH POTASSIUM	0.0275	14.00	0.0124

Summary of the AE Analysis

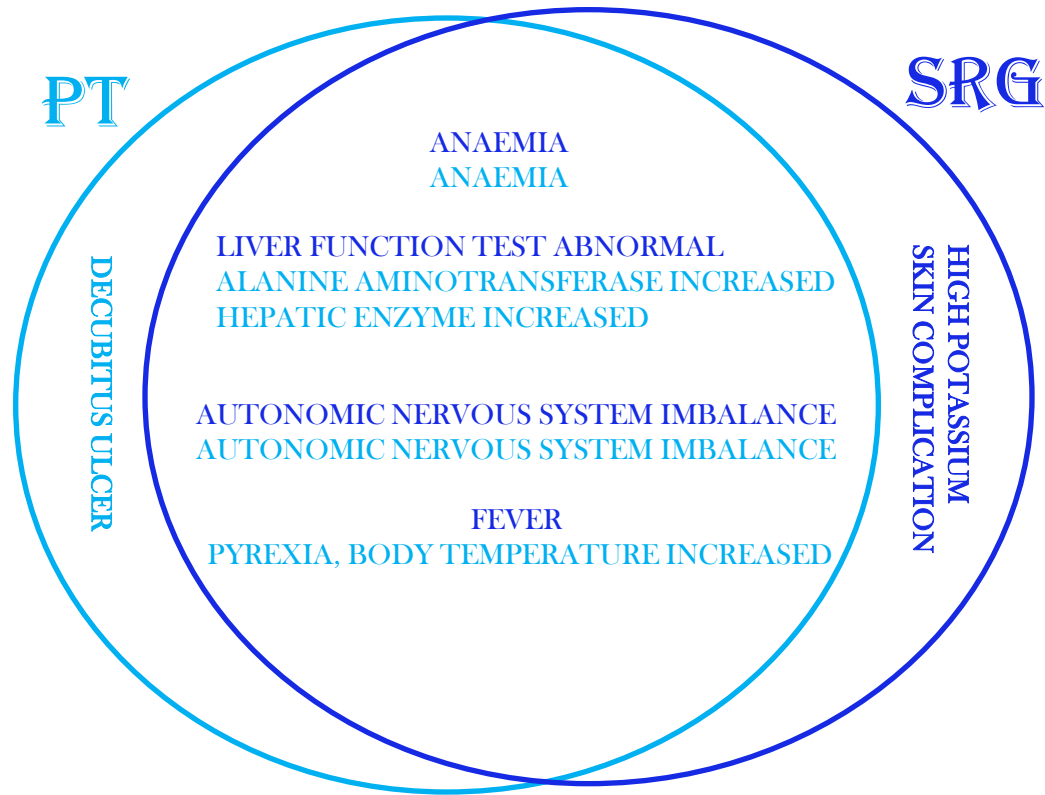
- Grouping based on Biological Information and Statistical Correlation

#	Preferred Terms (PT)	RD	RR	q
1	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1124	27.48	0.0000
2	PYREXIA	0.0945	15.84	0.0000
3	ALANINE AMINOTRANSFERASE INCREASED	0.0455	>999.00	0.0001
4	BODY TEMPERATURE INCREASED	0.0493	24.22	0.0001
5	HEPATIC ENZYME INCREASED	0.0414	20.49	0.0008
6	DECUBITUS ULCER	0.0336	>999.00	0.0021
7	ANAEMIA	0.0218	>999.00	0.0461



#	Study Related Grouping (SRG)	RD	RR	q
1	LIVER FUNCTION TEST ABNORMAL	0.1220	15.37	0.0000
2	AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.1124	27.46	0.0000
3	FEVER	0.1135	3.43	0.0000
4	HIGH POTASSIUM	0.0275	14.00	0.0174
5	SKIN COMPLICATIONS	0.0512	2.61	0.0174
6	ANAEMIA	0.0329	4.10	0.0342

Summary of the AE Analysis



Model Analysis

Preferred Terms (PT)	POI		ZIP		NBIN	
	p	q	p	q	p	q
AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.0000	0.0001	0.0000	0.0000	NS	NS
PYREXIA	0.0002	0.0156	0.0002	0.0153	0.0136	NS
ALANINE AMINOTRANSFERASE INCREASED	0.0000	0.0000	0.0000	0.0004	0.0000	0.0009
BODY TEMPERATURE INCREASED	0.0002	0.0156	0.0310	NS	NS	NS
HEPATIC ENZYME INCREASED	0.0000	0.0000	0.0000	0.0014	0.0000	0.0020
DECUBITUS ULCER	NS	NS	NS	NS	NS	NS
ANAEMIA	0.0002	0.0156	0.0332	NS	NS	NS



Study Related Grouping (SRG)	POI		ZIP		NBIN	
	p	q	p	q	p	q
LIVER FUNCTION TEST ABNORMAL	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
AUTONOMIC NERVOUS SYSTEM IMBALANCE	0.0000	0.0000	0.0000	0.0000	NS	NS
FEVER	0.0000	0.0018	0.0000	0.0007	0.0098	NS
HIGH POTASSIUM	0.0000	0.0000	0.0024	NS	0.0035	NS
SKIN COMPLICATIONS	NS	NS	NS	NS	NS	NS
ANAEMIA	0.0224	NS	NS	NS	NS	NS

Conclusions

- A grouping method is proposed to analyze high dimensional sparse counts data by incorporating data correlation information into biological pathway to reduce data dimension
- Statistical inference is adjusted for multiplicity by controlling FDR
- Regression models with count data (POI, NBIN, ZIP ...) are used to cross checking the inference results based on RD/RR
- The proposed analytical pipeline is illustrated and validated using a clinical trial data with 864 safety binary endpoints
- The proposed method increases the inferential power

THANK YOU