A shiny app to explore clinical data
- Adverse events for a pool of trials

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Background – Wish list

- A way to investigate data **interactively**:
  - Find interesting subgroups, e.g. subjects that experience a certain AE
  - See how efficacy and safety data looks for those particular subgroups

- Single trial - after unblinding
  - Investigate data to identify things that need immediate attention

- Collection of trials - before submission
  - Investigate safety data for a pool of trials

- Exploratory work
  - Reduce number of unused outputs

- Flexibility
  - Ability to add methods for summarising data as requested by agencies

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Background – Considered solutions (I)

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	JMP	Tableau	Dash by plotly	Shiny
Getting started	Excellent	Good	Steep	Steep
Flexibility	Little	Good	Anything is possible	Anything is possible
Used by statisticians	Some	Some	Little	Much
Statistical Analyses	Little	Little	New methods implemented	New methods implemented

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Background – Decision: R with shiny

- Statistical software **R**:
  - **Documentable:** Well established method for documenting functions
  - **Testable:** Well established method for creating test suites

- R package Shiny
  - **Mature**: Tested and maintained
  - **Flexible**: Ability to add visualizations exactly as wanted

Design consideration

- Applicable for data following CDISC Analysis Data Model (ADaM) structure

- Subset data:
  - Subset data according to populations (E.g. analysis sets: FAS, SAS, and PP)
  - Subset data according to observation periods (On-treatment, in-trial, treatment-emergent, …)
  - Subset data according to any variable in the dataset

- Design different areas independently
  - Demography, efficacy, safety, … in different modules

- Ensure communication between different modules

- Ensure reproducibility by making code for producing output available for download

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Safety displays – adverse events

- Tables:
  - Total number of subjects and person years of exposure
  - Summary of adverse events
  - Adverse event listing

- Plots: adverse events with comparisons between treatment arms
  - Waterfall plots
  - Volcano plots

- Ability to analyze a pool of trials by use of the Mantel-Haenszel method

Presentation of application

- The application will be presented using a simulated pool of data

- Two trials with three treatment arms

	Comparator		Treatement 1		Treatment 2	
	N	**PYE**	**N**	**PYE**	**N**	**PYE**
NN1234-4321	384	188.13	389	191.35	370	178.76
NN1234-4322	232	109.82	219	103.15	231	109.1

- Each trial consists of a homogenous population with comparable observation time per subject

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REACTIVE
EOT

🔍 Overview

⏱ Demographics and baseline characteristics

▦ Documentation

column Panel by

studyid

Row Panel by

None

Select data   +
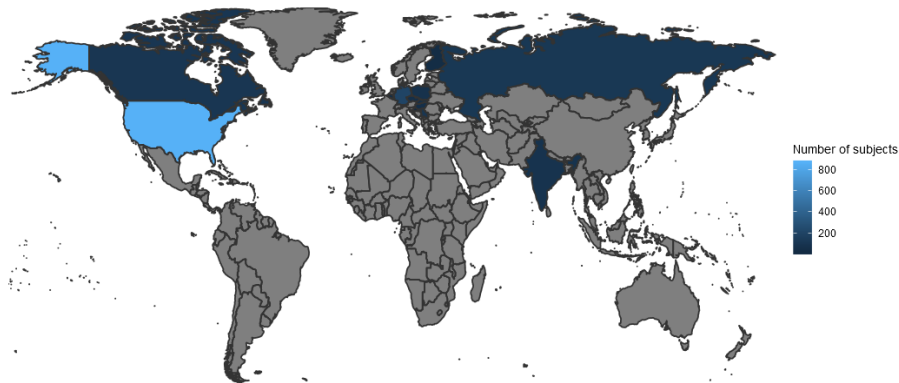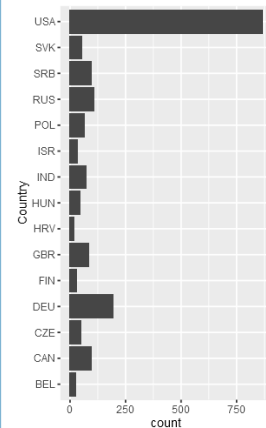
Subset data   +

Treatment   +
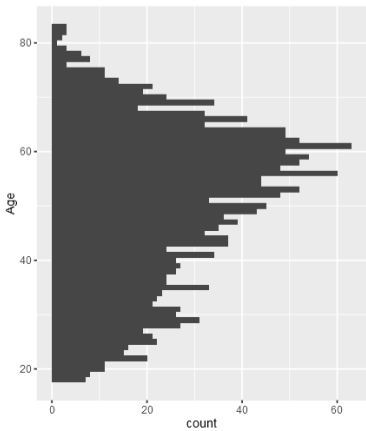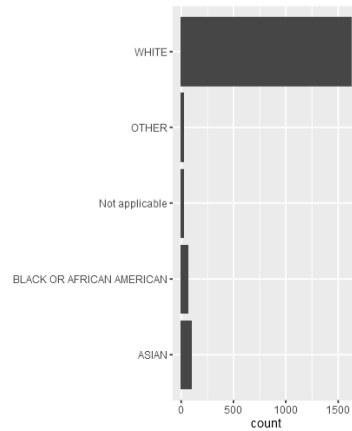
Highlight   +

World map   —

NN1234-4321   NN1234-4322

Number of subjects
100 200 300 400 500 600

Country distribution   —

NN1234-4321   NN1234-4322

USA
SVK
SRB
RUS
POL
ISR
IND
HUN
HRV
GBR
FIN
DEU
CZE
CAN
BEL

Country

0 200 400 600   0 200 400 600
count

Age distribution   —

NN1234-4321   NN1234-4322

80

60

Age

40

20

0 10 20 30 40   0 10 20 30 40
count

Race distribution   —

NN1234-4321   NN1234-4322

WHITE

OTHER

Not applicable

BLACK OR AFRICAN AMERICAN

ASIAN

0 300 600 900   0 300 600 900
count

Ethnicity distribution   —

NN1234-4321   NN1234-4322

NOT HISPANIC OR LATINO

Ethnicity

HISPANIC OR LATINO

0 300 600 900   0 300 600 900
count

REACTIVE ECT

World map

NN1234-4321 | NN1234-4322

Number of subjects
100 200 300 400 500 600

Country distribution

NN1234-4321 | NN1234-4322

USA
SVK
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DEU
CZE
CAN
BEL

Country

count
0 200 400 600 | 0 200 400 600

Overview

Demographics and baseline characteristics

Documentation

column Panel by

studyid

Row Panel by
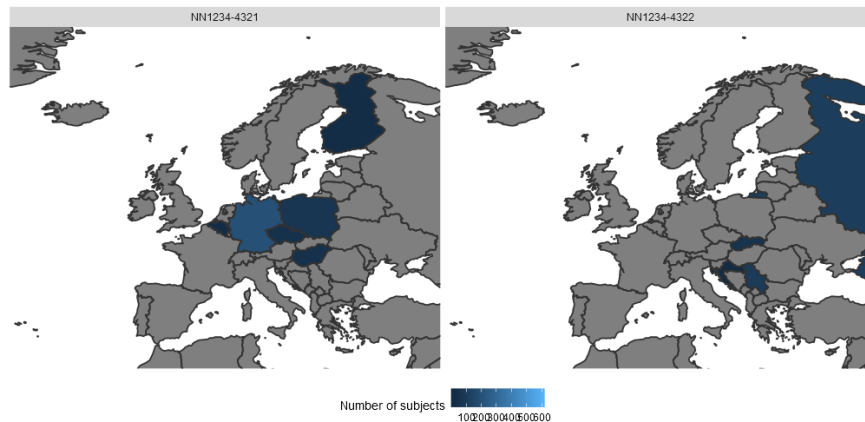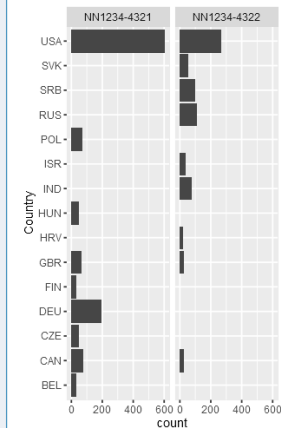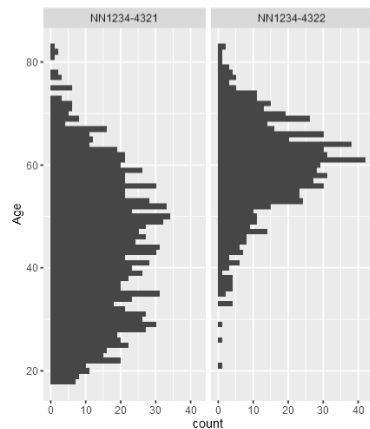
None

Select data   +

Subset data   +

Treatment   +

Highlight   −

Highlighted subjects

Europe

Name for current highlight

Save | Clear
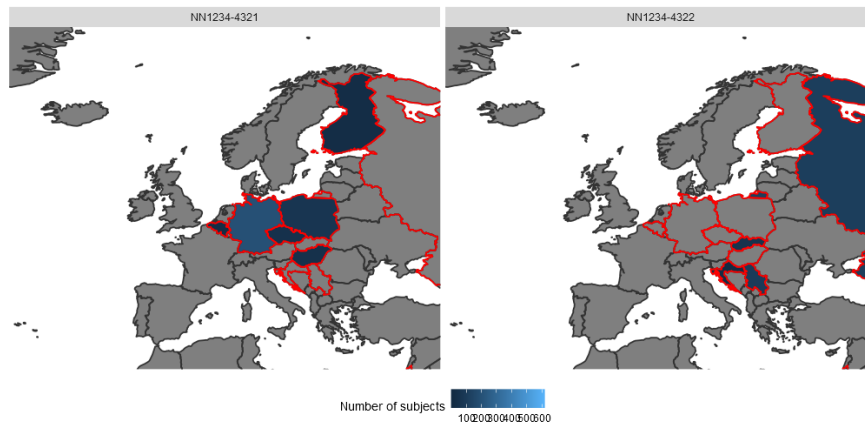
Age distribution

NN1234-4321 | NN1234-4322

Age

80

60

40

20

count
0 10 20 30 40 | 0 10 20 30 40

Race distribution

NN1234-4321 | NN1234-4322

WHITE

OTHER

Not applicable

BLACK OR AFRICAN AMERICAN

ASIAN

count
0 300 600 900 | 0 300 600 900

Ethnicity distribution

NN1234-4321 | NN1234-4322

NOT HISPANIC OR LATINO

Ethnicity

HISPANIC OR LATINO

count
0 300 600 900 | 0 300 600 900
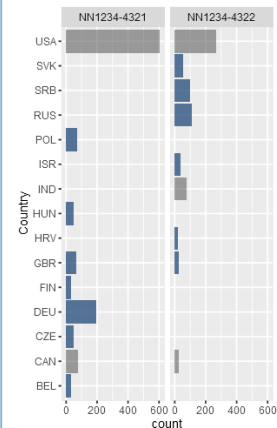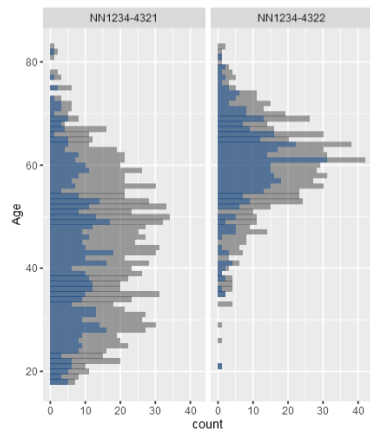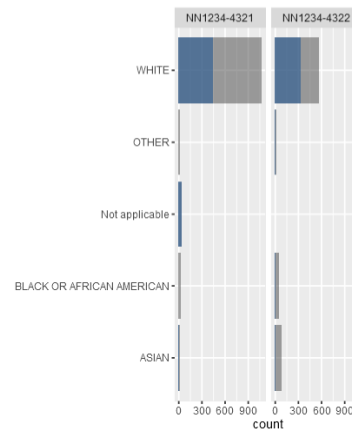
Summary of adverse events

Total number of subjects

Show 10 ▾ entries   Search: [   ]

studyid	Comparator		Treatment 1		Treatment 2	
	N	PYE	N	PYE	N	PYE
NN1234-4321	384	188.13	389	191.35	370	178.76
NN1234-4322	232	109.82	219	103.15	231	109.1

Showing 1 to 2 of 2 entries   Previous [1] Next

AE by selected term

Show 10 ▾ entries   Search: [   ]

studyid	aedecod	Comparator				Treatment 1				Treatment 2			
		N	P	E	R	N	P	E	R	N	P	E	R
NN1234-4321	Nasopharyngitis	118	30.73	181	96.21	117	30.08	156	81.53	105	28.38	154	86.15
NN1234-4321	Headache	43	11.2	67	35.61	46	11.83	91	47.56	47	12.7	85	47.55
NN1234-4321	Upper respiratory tract infection	41	10.68	52	27.64	32	8.23	42	21.95	49	13.24	59	33.01
NN1234-4322	Nasopharyngitis	21	9.05	23	20.94	22	10.05	26	25.21	18	7.79	22	20.17
NN1234-4321	Diarrhoea	29	7.55	32	17.01	17	4.37	21	10.97	21	5.68	24	13.43

Listing of adverse events

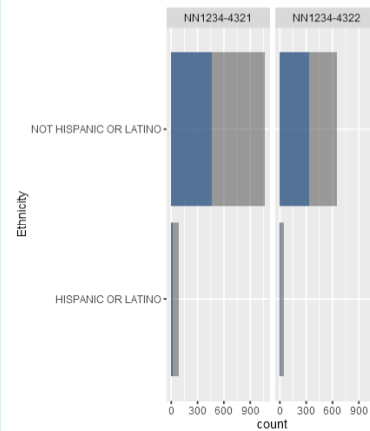## Adverse events listing   −

Show 10 ▾ entries   Search: [   ]

	subjid	country	sex	trtp	aedecod	studyid
1	101001	BEL	M	Treatment 1	Nasopharyngitis	NN1234-4321
2	101001	BEL	M	Treatment 1	Bronchitis	NN1234-4321
3	101003	BEL	F	Treatment 2	Toothache	NN1234-4321
4	101003	BEL	F	Treatment 2	Nasopharyngitis	NN1234-4321
5	101003	BEL	F	Treatment 2	Toothache	NN1234-4321
6	101003	BEL	F	Treatment 2	Cough	NN1234-4321
7	101004	BEL	F	Treatment 1	Nasopharyngitis	NN1234-4321
8	101004	BEL	F	Treatment 1	Oropharyngeal pain	NN1234-4321
9	101004	BEL	F	Treatment 1	Pyrexia	NN1234-4321
10	101004	BEL	F	Treatment 1	Infected bites	NN1234-4321

Showing 1 to 10 of 5,054 entries   Previous 1 2 3 4 5 … 506 Next
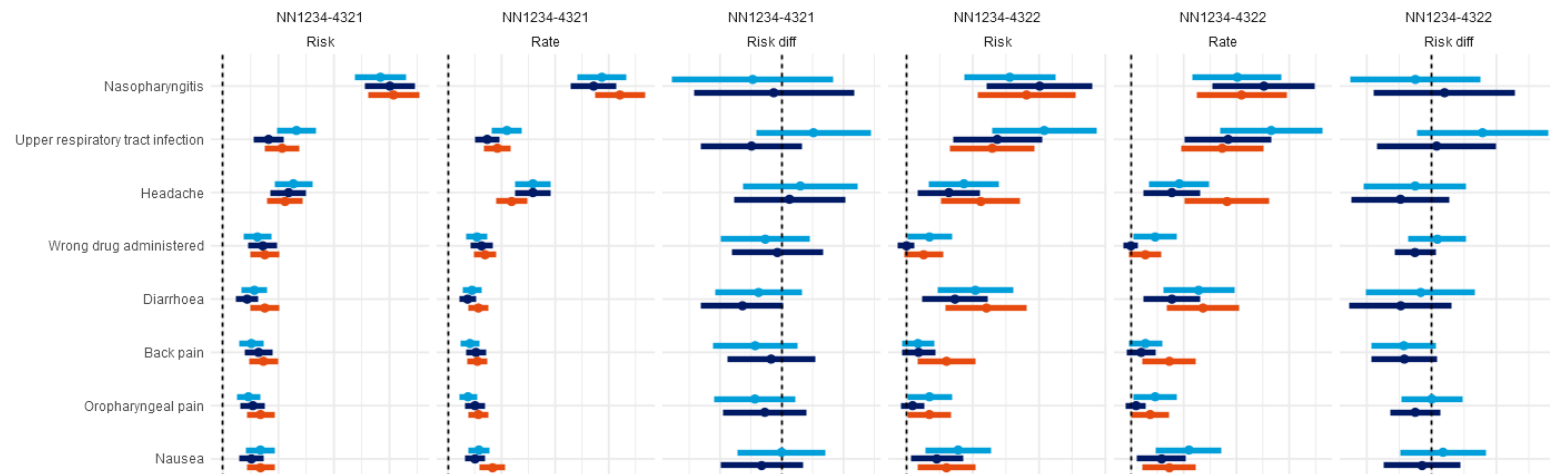
Columns to show

subjid country sex

Graphical display - I
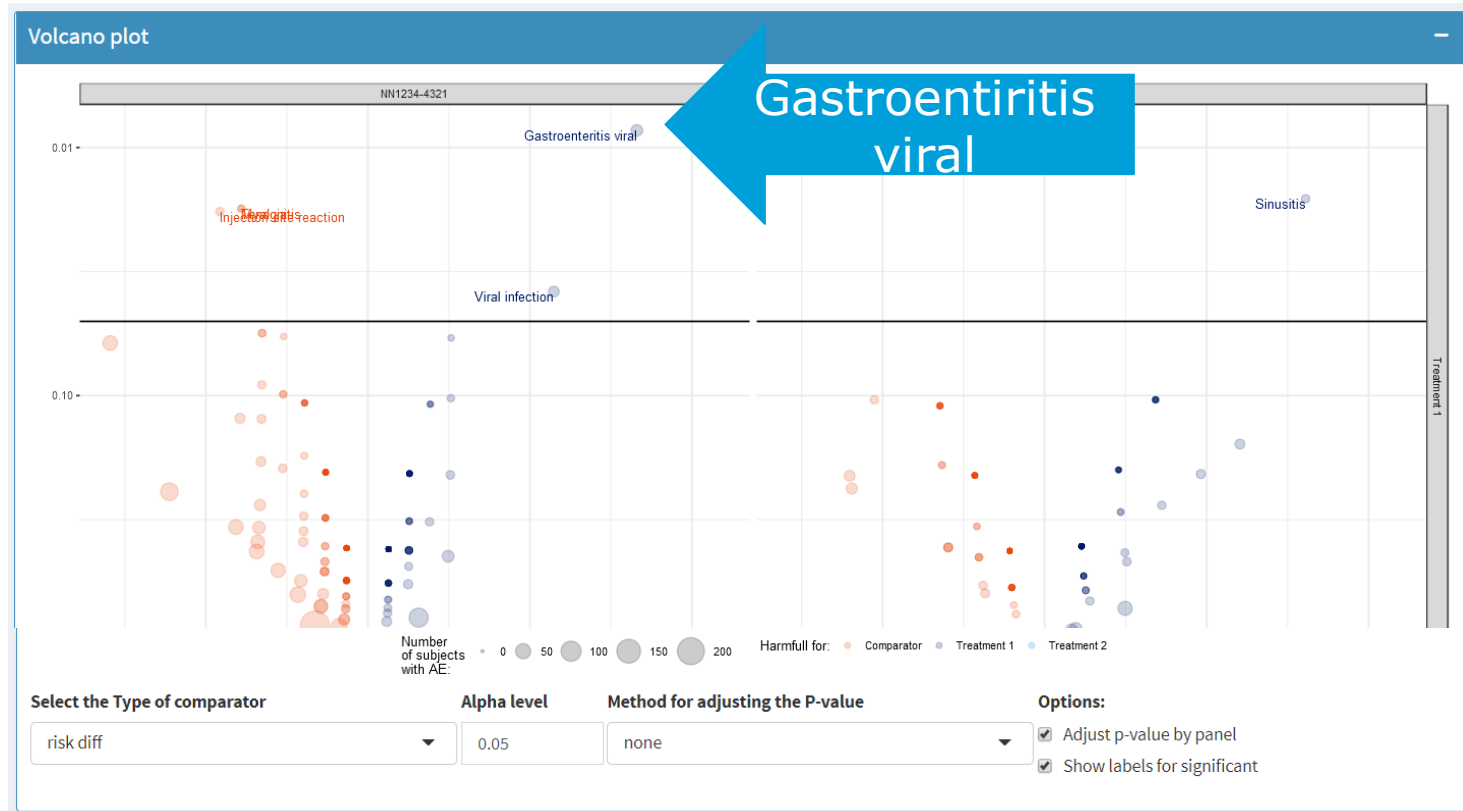
Graphical display - II

Interactivity - I

AE by selected term

Show 10 ▼ entries   Search: [   ]

studyid	aedecod	Comparator				Treatment 1				Treatment 2			
		N	P	E	R	N	P	E	R	N	P	E	R
NN1234-4321	Abdominal abscess	0	0	0	0	0	0	0	0	0	0	0	0
NN1234-4322	Abdominal abscess	0	0	0	0	1	0.46	1	0.97	0	0	0	0
NN1234-4321	Abdominal discomfort	11	2.86	13	6.91	10	2.57	12	6.27	7	1.89	7	3.92
NN1234-4322	Abdominal discomfort	3	1.29	3	2.73	0	0	0	0	2	0.87	2	1.83
NN1234-4321	Abdominal distension	1	0.26	1	0.53	0	0	0	0	2	0.54	2	1.12
NN1234-4322	Abdominal distension	1	0.43	1	0.91	1	0.46	1	0.97	1	0.43	2	1.83
NN1234-4321	Abdominal pain	4	1.04	4	2.13	5	1.29	6	3.14	6	1.62	8	4.48
NN1234-4322	Abdominal pain	1	0.43	1	0.91	0	0	0	0	4	1.73	4	3.67
NN1234-4321	Abdominal pain lower	0	0	0	0	3	0.77	3	1.57	0	0	0	0
NN1234-4322	Abdominal pain lower	0	0	0	0	0	0	0	0	0	0	0	0

Showing 1 to 10 of 1,536 entries   Previous 1 2 3 4 5 … 154 Next

Interactivity - II

Adverse events listing

Show 10 ▾ entries   Search: [   ]

	usubjid	country	sex	trtp	aedecod	studyid
1	NN1234-4321/217004	CAN	F	Treatment 1	Gastroenteritis viral	NN1234-4321
2	NN1234-4321/217004	CAN	F	Treatment 1	Inflammatory bowel disease	NN1234-4321
3	NN1234-4321/220004	CAN	F	Treatment 2	Headache	NN1234-4321
4	NN1234-4321/220004	CAN	F	Treatment 2	Abdominal discomfort	NN1234-4321
5	NN1234-4321/220004	CAN	F	Treatment 2	Skin discomfort	NN1234-4321
6	NN1234-4321/220004	CAN	F	Treatment 2	Gastroenteritis viral	NN1234-4321
7	NN1234-4321/220004	CAN	F	Treatment 2	Headache	NN1234-4321
8	NN1234-4321/220004	CAN	F	Treatment 2	Nasopharyngitis	NN1234-4321
9	NN1234-4321/220004	CAN	F	Treatment 2	Headache	NN1234-4321
10	NN1234-4321/220004	CAN	F	Treatment 2	Headache	NN1234-4321

Showing 1 to 10 of 216 entries   Previous 1 2 3 4 5 … 22 Next

Columns to show

usubjid   country   sex

Stratification by the Mantel-Haenszel method

Total number of subjects

Show [10 ▾] entries   Search: [   ]

studyid	Weight N	Weight PYE	Comparator		Treatment 1	
			N	PYE	N	PYE
NN1234-4321	193.24	94.86	384	188.13	389	191.35
NN1234-4322	112.66	53.19	232	109.82	219	103.15

Showing 1 to 2 of 2 entries   Previous [1] Next

AE by selected term

Show [10 ▾] entries   Search: [   ]

aedecod	Comparator				Treatment 1			
	N	P	E	R	N	P	E	R
Nasopharyngitis	139	22.75	204	69.17	139	22.7	182	61.29
Headache	56	9.14	87	29.36	53	8.65	99	33.26
Upper respiratory tract infection	56	9.13	71	23.93	47	7.72	61	20.68
Diarrhoea	43	6.99	47	15.81	25	4.11	29	9.82
Back pain	35	5.72	39	13.18	27	4.4	32	10.74
Nausea	33	5.39	55	18.62	25	4.09	35	11.8

Overview

AE by term

Calculate AE by term

Dictionary-Derived Term

Select the comparator

Comparator

Group calculation by

None

Stratify calculation by

None

Select data

Select data set

adae

Select analysis set

Total number of subjects

Show 10 ▼ entries

Search:

	Comparator		Treatment 1
	N ⇕	PYE ⇕	N ⇕
	616	297.94	608

Showing 1 to 1 of 1 entries

Previous

AE by selected term

Show 10 ▼ entries

Search:

aedecod ⇕	Comparator				Treatment 1			
	N ⇕	P ⇕	E ⇕	R ⇕	N ⇕	P ⇕	E ⇕	R ⇕
Abdominal abscess	0	0	0	0	1	0.16	1	0.34
Abdominal discomfort	14	2.27	16	5.37	10	1.64	12	4.07
Abdominal distension	2	0.32	2	0.67	1	0.16	1	0.34
Abdominal pain	5	0.81	5	1.68	5	0.82	6	2.04
Abdominal pain lower	0	0	0	0	3	0.49	3	1.02
Abdominal pain upper	9	1.46	13	4.36	8	1.32	11	3.74
Acanthosis nigricans	0	0	0	0	1	0.16	1	0.34

Gastroentiritis viral

Thank you for your attention