IMPERIAL

Visualisations to evaluate and communicate adverse event data in randomised controlled trials: Application of the user written Stata commands *aedot* and *aevolcano*

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Outline

- Overview of current practice for communication of adverse events in RCTs
- Demonstrate how graphics provide an improvement on current practice
- Demonstrate two user written Stata commands to produce example graphics

Background

- RCTs are typically designed around a primary efficacy outcome e.g. does drug A improve survival compared to drug B (standard care)
- Might also have known **safety** outcomes (or **harms**) as secondary outcomes
- Plus **adverse events (AEs)** that emerge during the trial
- How we analyse and report AE outcomes needs improvements
- Methods used to analyse these outcomes are less established and data is underutilised

Evaluating harm

- Prespecified events of interest + many emerging AEs
- We don’t know **what or how many AEs** will be reported
- Outcome measurement considerations:
  - **Variable type**: single occurrence and repeated AEs, time to event, continuous
  - **Duration** of each AE
  - **Severity** of each AE
  - **Timing** of each AE
- Often **low event rates**

…current practice underutilises this data

Typically we find AE data presented in tables

Table 3. Most Common Adverse Events in the Safety Population.*

Event	Daratumumab Group (N=243)		Control Group (N=237)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Common hematologic adverse event				
Thrombocytopenia	143 (58.8)	110 (45.3)	104 (43.9)	78 (32.9)
Anemia	64 (26.3)	35 (14.4)	74 (31.2)	38 (16.0)
Neutropenia	43 (17.7)	31 (12.8)	22 (9.3)	10 (4.2)
Lymphopenia	32 (13.2)	23 (9.5)	9 (3.8)	6 (2.5)
Common nonhematologic adverse events				
Peripheral sensory neuropathy	115 (47.3)	11 (4.5)	89 (37.6)	16 (6.8)
Diarrhea	77 (31.7)	9 (3.7)	53 (22.4)	3 (1.3)
Upper respiratory tract infection	60 (24.7)	4 (1.6)	43 (18.1)	2 (0.8)
Fatigue	52 (21.4)	11 (4.5)	58 (24.5)	8 (3.4)
Cough	58 (23.9)	0	30 (12.7)	0
Constipation	48 (19.8)	0	37 (15.6)	2 (0.8)
Dyspnea	45 (18.5)	9 (3.7)	21 (8.9)	2 (0.8)
Insomnia	41 (16.9)	0	35 (14.8)	3 (1.3)
Peripheral edema	40 (16.5)	1 (0.4)	19 (8.0)	0
Asthenia	21 (8.6)	2 (0.8)	37 (15.6)	5 (2.1)
Pyrexia	38 (15.6)	3 (1.2)	27 (11.4)	3 (1.3)
Pneumonia	29 (11.9)	20 (8.2)	28 (11.8)	23 (9.7)
Hypertension	21 (8.6)	16 (6.6)	8 (3.4)	2 (0.8)
Secondary primary cancer†	6 (2.5)	NA	1 (0.4)	NA

* The safety population included all patients who received at least one dose of trial treatment. Adverse events of any grade that were reported in at least 15% of patients in either treatment group and grade 3 or 4 adverse events that were reported in at least 5% of patients in either treatment group are listed. NA denotes not applicable.
† The presence of a secondary primary cancer was prespecified in the statistical analysis plan as an adverse event of clinical interest. The other adverse events of clinical interest included infusion-related reactions, infections or infestations, peripheral neuropathies, and cardiac disorders.

	Tocilizumab plus methotrexate arm (n=106)	Tocilizumab arm (n=103)	Methotrexate arm (n=108)	p value
Any AE	105 (99·1%)	99 (96·1%)	106 (98·1%)	0·32
AE rate per 100 patient-years in the study	536·7	527·0	595·1	..
Serious AEs	17 (16·0%)	19 (18·4%)	13 (12·0%)	0·44
Serious AE rate per 100 patient-years in the study	10·20	16·45	11·03	..
AEs leading to study discontinuation	9 (8·5%)	10 (9·7%)	8 (7·4%)	0·82
Serious infections	4 (3·8%)	6 (5·8%)	5 (4·6%)	0·76
Serious infection rate per 100 patient-years in the study	2·81	4·51	3·02	
Hepatic events leading to withdrawal	0	0	0	..
ALT >3 × ULN	14 (13·2%)	5 (4·9%)	12 (11·1%)	0·10
AST >3 × ULN	5 (4·7%)	1 (1·0%)	4 (3·7%)	0·37
Increase of liver enzymes leading to change in treatment	0	1 (1·0%)	2 (1·9%)	0·55
Absolute neutrophil count <1·0 × 10^9/L	7 (6·6%)	6 (5·8%)	1 (0·9%)	0·07
Platelet count <100 × 10^9/L	4 (3·8%)	3 (2·9%)	1 (0·9%)	0·37
Initiation of lipid lowering drug needed during study	16 (15·1%)	24 (23·3%)	22 (20·4%)	0·32

Data are n (%) unless otherwise specified. The strategy groups are labelled according to the randomised initial therapy. n=number of patients with at least one event. Serious adverse events were defined according to the Medical Dictionary for Regulatory Activities (MedDRA; http://www.meddra.org/). AE=adverse event. ALT=serum alanine aminotransferase. ULN=upper limit of normal. AST=serum aspartate aminotransferase. Additional safety data, including data for ALT and AST >ULN are in the appendix. Results of between three-group comparisons obtained with extended Fisher exact tests.

Table 3: Safety and laboratory data

State of play

We've got **complex**, **multifaceted** data that we **simplify** and present in contingency tables, sometimes accompanied with inappropriate hypothesis tests or alternatively undertaking no analysis at all!

We are missing a valuable opportunity for early evaluation of harm

What are we trying to do when analysing AE data?

- We're looking for **signals of adverse reactions**
- Reporting all AE data in **tables** can be **overwhelming** and **incomprehensible**
- We need summaries that are more **digestible** and allow a **clearer**, **more informative profile** to be presented

Could visualisations offer a solution?

Case study: Remdesivir in adults with severe COVID-19

Adverse events were reported in 102 (66%) of 155 patients in the remdesivir group and 50 (64%) of 78 in the control group (table 4). The most common adverse events in the remdesivir group were constipation, hypoalbuminaemia, hypokalaemia, anaemia, thrombocytopenia, and increased total bilirubin; and in the placebo group, the most common were hypoalbuminaemia, constipation, anaemia, hypokalaemia, increased aspartate aminotransferase, increased blood lipids, and increased total bilirubin. 28 (18%) seri… reported in the rem… in the resp… drome in the remdesivir group. All deaths during the observation period were judged by the site investigators to be unrelated to the intervention).

How useful is this information?

- Are they clinically important?
- Is there a numerical imbalance?
- Could they in fact relate to the underlying infection or participant comorbidity?

	Remdesivir group (n=155)		Placebo group (n=78)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Adverse events (in ≥2% of patients in any treatment group)				
Any	102 (66%)	13 (8%)	50 (64%)	11 (14%)
Hypoalbuminaemia	20 (13%)	0	12 (15%)	1 (1%)
Hypokalaemia	18 (12%)	2 (1%)	11 (14%)	1 (1%)
Increased blood glucose	11 (7%)	0	6 (8%)	0
Anaemia	18 (12%)	1 (1%)	12 (15%)	2 (3%)
Rash	11 (7%)	0	2 (3%)	0
Thrombocytopenia	16 (10%)	4 (3%)	5 (6%)	3 (4%)
Increased total bilirubin	15 (10%)	1 (1%)	7 (9%)	0
Increased blood lipids	10 (6%)	0	8 (10%)	0
Increased white blood cell count	11 (7%)	0	6 (8%)	0
Hyperlipidaemia	10 (6%)	0	8 (10%)	0
Increased blood urea nitrogen	10 (6%)	0	5 (6%)	0
Increased neutrophil	10 (6%)	0	4 (5%)	0
Aspartate aminotransferase increased	7 (5%)	0	9 (12%)	0
Constipation	21 (14%)	0	12 (15%)	0
Nausea	8 (5%)	0	2 (3%)	0
Diarrhoea	5 (3%)	0	2 (3%)	0
Vomiting	4 (3%)	0	2 (3%)	0
Reduced serum sodium	4 (3%)	0	2 (3%)	0
Increased serum potassium	4 (3%)	2 (1%)	1 (1%)	0
Serious adverse events				
Any	28 (18%)	9 (6%)	20 (26%)	10 (13%)
Respiratory failure or acute respiratory distress syndrome	16 (10%)	4 (3%)	6 (8%)	4 (5%)
Cardiopulmonary failure	8 (5%)	0	7 (9%)	1 (1%)
Pulmonary embolism	1 (1%)	1 (1%)	1 (1%)	1 (1%)
Recurrence of COVID-19	1 (1%)	0	0	0
Cardiac arrest	1 (1%)	0	0	0
Acute coronary syndrome	0	0	1 (1%)	1 (1%)
Tachycardia	0	0	1 (1%)	0
Septic shock	1 (1%)	0	1 (1%)	1 (1%)

(Table 4 continues in next column)

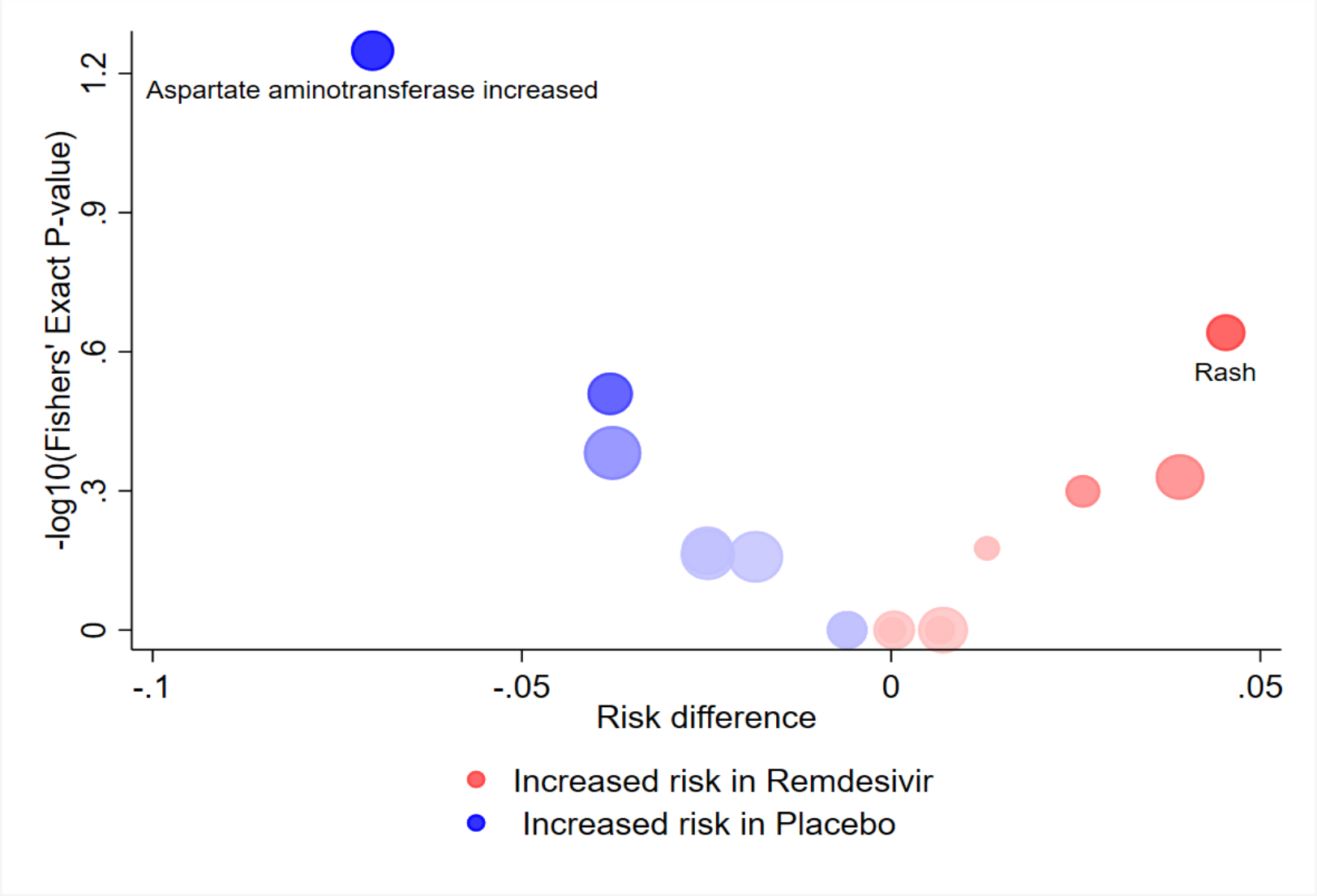
	Remdesivir group (n=155)		Placebo group (n=78)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
(Continued from previous column)				
Lung abscess	0	0	1 (1%)	1 (1%)
Sepsis	0	0	1 (1%)	1 (1%)
Bronchitis	0	0	1 (1%)	1 (1%)
Thrombocytopenia	1 (1%)	1 (1%)	0	0
Increased D-dimer	0	0	1 (1%)	1 (1%)
Haemorrhage of lower digestive tract	1 (1%)	1 (1%)	0	0
Ileus	0	0	1 (1%)	0
Deep vein thrombosis	1 (1%)	1 (1%)	1 (1%)	1 (1%)
Acute kidney injury	1 (1%)	0	0	0
Diabetic ketoacidosis	0	0	1 (1%)	1 (1%)
Multiple organ dysfunction syndrome	1 (1%)	0	2 (3%)	0
Events leading to drug discontinuation				
Any	18 (12%)	3 (2%)	4 (5%)	1 (1%)
Respiratory failure or acute respiratory distress syndrome	7 (5%)	1 (1%)	1 (1%)	0
Secondary infection	4 (3%)	0	7 (9%)	2 (3%)
Cardiopulmonary failure	3 (2%)	0	1 (1%)	0
Nausea	1 (1%)	0	0	0
Vomiting	1 (1%)	0	0	0
Ileus	0	0	1 (1%)	0
Increased alanine aminotransferase	2 (1%)	1 (1%)	0	0
Rash	2 (1%)	0	0	0
Poor appetite	1 (1%)	0	0	0
Increased total bilirubin	1 (1%)	0	0	0
Acute kidney injury	1 (1%)	1 (1%)	0	0
Seizure	0	0	1 (1%)	0
Aggravated schizophrenia	0	0	1 (1%)	1 (1%)
Aggravated depression	0	0	1 (1%)	1 (1%)

Data are n (%) and include all events reported after antiviral treatment. Some patients had more than one adverse event. 36 patients discontinued the drug, 22 because of adverse events and 14 patients for other reasons (eg, hospital discharge or early death). COVID-19=coronavirus disease 2019.

Wang, Y., et al. (2020). "Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial." The Lancet **395**(10236): 1569-1578.

Volcano plot

AEs that occurred ≥ 2% of participants



Volcano plot

Individual participant data

Install: `ssc install aevolcano` or https://ideas.repec.org/c/boc/bocode/s458736.html#download

Syntax: `aevolcano varname , treat(varname) id(varname) n1(integer) n2(integer) [options]`

`aevolcano`: requires data in long format with one row per event per participant, where `varname` indicates the variable that contains the event name/identifier. `varname` may be a numeric or a string variable.

Options

* `treat(varname)`: variable indicating treatment group assignment in the existing dataset (must be numeric)
* `id(varname)`: variable identifying unique participants in the existing dataset, multiple events (rows) per id acceptable (must be numeric)
* `n1(#)`: the total number of unique participants in the first treatment group (must be an integer value)
* `n2(#)`: the total number of unique participants in the second treatment group (must be an integer value)

Various `[options]` to edit the graph

Volcano plot

Summary level data

Install: part of the `aevolcano` package

Syntax: `aevolcs varname , n1(varname) n2(varname) tot1(varname) tot2(varname) [options]`

`aevolcs`: requires summary data in long format with one row per event, where `varname` indicates the variable that contains the event name/identifier. `varname` may be a numeric or a string variable.

Options

* `n1(varname)`: variable indicating the number of participants in the first treatment group with the event specified in `varname` (must be numeric)
* `n2(varname)`: variable indicating the number of participants in the second treatment group with the event specified in `varname` (must be numeric)
* `tot1(varname)`: variable indicating the total number of unique participants in the first treatment group (must be numeric)
* `tot2(varname)`: variable indicating the total number of unique participants in the second treatment group (must be numeric)

Various `[options]` to edit the graph

Volcano plot

Summary level data

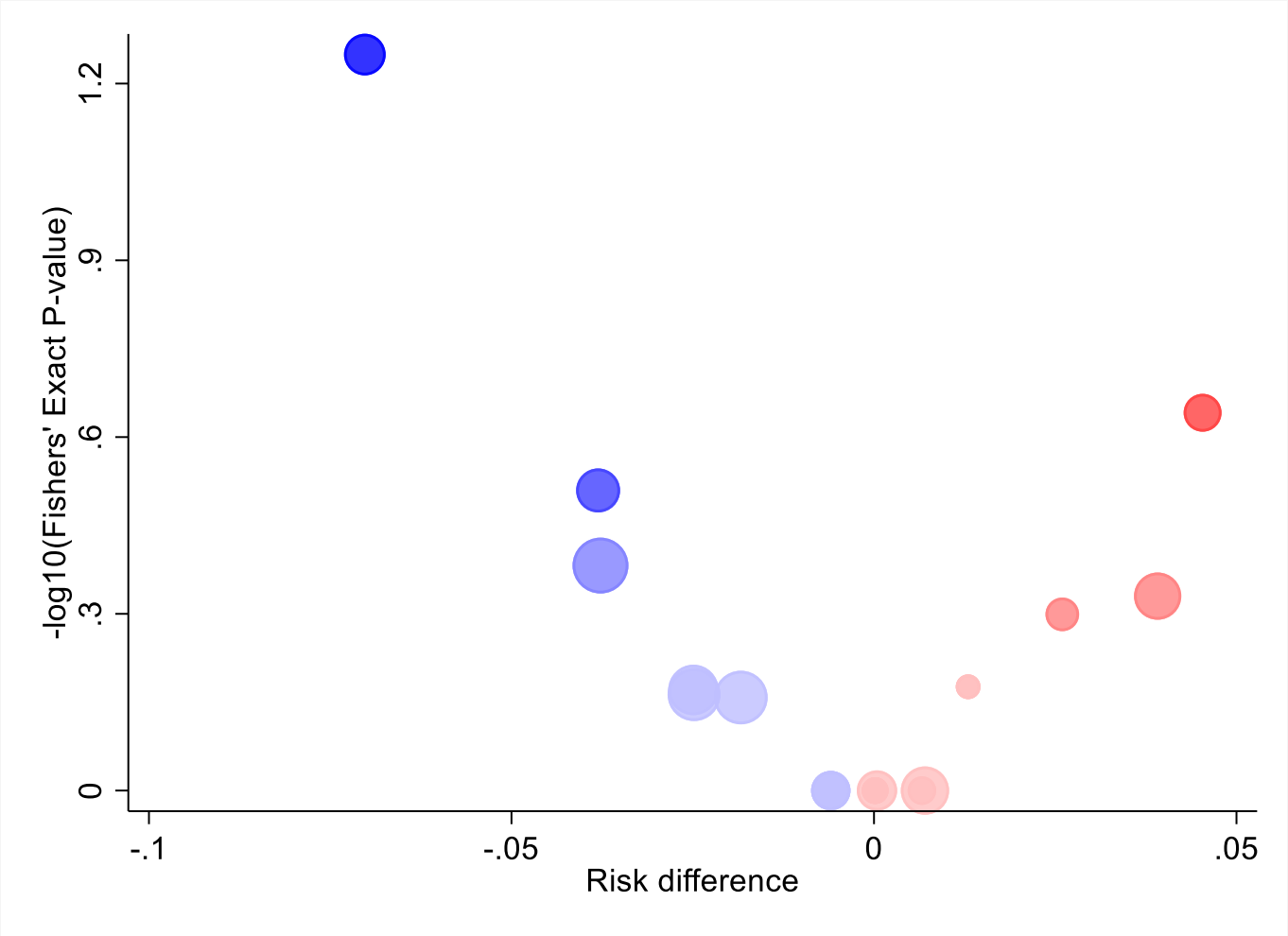
	Adverseevents	Remdesiv~G_n	Remdesivir_N	Placebo_AG_n	Placebo_N
1	Hypoalbuminaemia	20	155	12	78
2	Hypokalaemia	18	155	11	78
3	Increased blood glucose	11	155	6	78
4	Anaemia	18	155	12	78
5	Rash	11	155	2	78
6	Thrombocytopenia	16	155	5	78
7	Increased total bilirubin	15	155	7	78
8	Increased blood lipids	10	155	8	78
9	Increased white blood cell count	11	155	6	78
10	Hyperlipidaemia	10	155	8	78
11	Increased blood urea nitrogen	10	155	5	78
12	Increased neutrophil	10	155	4	78
13	Aspartate aminotransferase increased	7	155	9	78
14	Constipation	21	155	12	78
15	Nausea	8	155	2	78
16	Diarrhoea	5	155	2	78
17	Vomiting	4	155	2	78
18	Reduced serum sodium	4	155	2	78
19	Increased serum potassium	4	155	1	78

Volcano plot

Summary level data

Basic syntax:

```
aevolcs Adverseevents, n1(Remdesivir_AG_n) n2( Placebo_AG_n) tot1(Remdesivir_N)
tot2(Placebo_N)
```



Volcano plot

Summary level data

Assigns legend label for second treatment group

Specify bubble label position

Syntax with added options:

```
aevolcs Adverseevents , n1(Remdesivir_AG_n) n2(Placebo_AG_n) tot1(Remdesivir_N) tot2(Placebo_N)
legendyn(1) legend1(Remdesivir) legend2(Placebo) labelyn(1) labang(0) labpos(6) labgap(2)
```

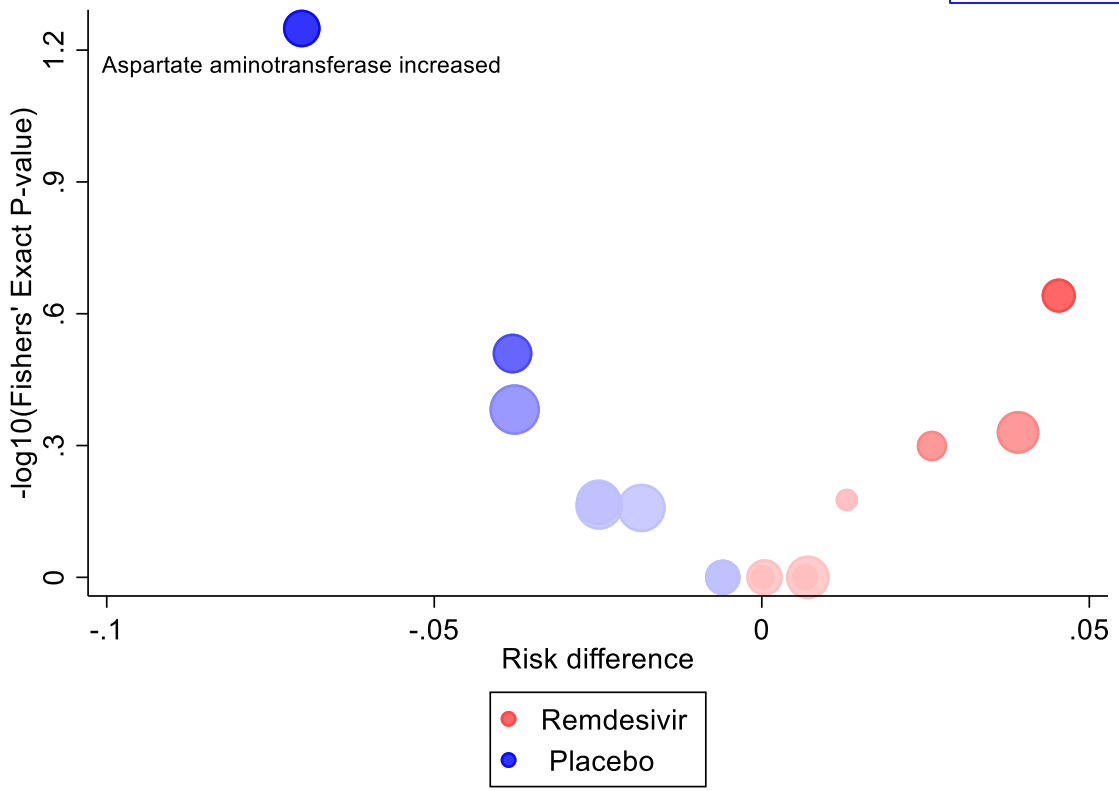
Turns legend on

Assigns legend label for first treatment group

Turns bubble labels on

Specify bubble label angle/orientation

Specify label distance from bubble



Volcano plot

Summary level data

All `[options]` detailed in the help file

Syntax

aevolcs *varname* **, n1(***varname***) n2(***varname***) tot1(***varname***) tot2(***varname***)** [*options*]

aevolcs requires summary data in long format with one row per event, where *varname* indicates the variable that contains the event name/identifier. *varname* may be a numeric or a string variable.

options	Description
* **n1(***varname***)**	variable indicating the number of participants in the first treatment group with the event specified in *varname* (must be numeric)
* **n2(***varname***)**	variable indicating the number of participants in the second treatment group with the event specified in *varname* (must be numeric)
* **tot1(***varname***)**	variable indicating the total number of unique participants in the first treatment group (must be numeric)
* **tot2(***varname***)**	variable indicating the total number of unique participants in the second treatment group (must be numeric)
saving(*filename***[, replace])**	saves the dataset with the plotted event level summary data in *filename*.dta
graphsave(*filename***[, replace])**	saves the plot in *filename*.dta
clear	if specified the newly created dataset is stored in memory. If **clear** not specified the original dataset is retained in memory.
oddsratio(#)	option to plot odds ratios; **oddsratio(1)** plots the odds ratio and **oddsratio(0)** plots the risk difference, default is **oddsratio(0)**
riskratio(#)	option to plot risk ratios; **riskratio(1)** plots the risk ratio and **riskratio(0)** plots the risk difference, default is **riskratio(0)**
pvalue(#)	option to use p-values from Pearson's chi-squared test; **pvalue(1)** uses Pearson's chi-squared p-values and **pvalue(0)** uses Fisher's exact p-values, default is **pvalue(0)**
padj(#)	option to use the false discovery rate (FDR) p-value adjustment; **padj(1)** produces FDR adjusted p-values and **padj(0)** uses no adjustment, default is **padj(0)**. See *aefdr* for full details
* **fdrhigher(***varname***)**	if **padj(1)** then **fdrhigher(varname)** required, where *varname* indicates the higher level or bodysystem event variable
* **fdrlower(***varname***)**	if **padj(1)** then **fdrlower(varname)** required, where *varname* indicates the lower level or preferred term event variable
fdrval(#)	indicates the alpha value the FDR adjustment is carried out on. The FDR procedure flags events with adjusted event and bodysystem p-values below this specified value (must be numeric), default is **fdrval(0.1)**
labelyn(#)	used to turn bubble labels on by specifying **labelyn(1)**; default is bubble label off **labelyn(0)**
label(#)	if **labelyn(1)** then **label** used to indicate p-value threshold below which bubbles will be labelled; default is **label(1)** so variables with log10(p-value)>1 will be labelled, this equates to a p-value<0.1
labelnum(#)	used to specify if bubble labels required when *varname* numeric; default is **labelnum(0)** which indicates number labels not required, **labelnum(1)** labels assigned numeric values, **labelnum(2)** labels assigned label values
labcol(*colorstyle***)**	label text colour; default is **labcol(black)**
labcol1(*colorstyle***)**	label text colour for events where the risk is largest in the first treatment group; default **labcol1(black)**
labcol2(*colorstyle***)**	label text colour for events where the risk is largest in the second treatment group; default **labcol2(black)**
labang(#)	label angle; default **labang(90)** to give vertical labels
labang1(#)	label angle for events where the risk is largest in the first treatment group; default **labang1(90)** to give vertical labels
labang2(#)	label angle for events where the risk is largest in the second treatment group; default **labang2(90)** to give vertical labels
labpos(#)	label position; default **labpos(12)** to give labels above the bubble
labpos1(#)	label position for events where the risk is largest in the first treatment group; default **labpos1(12)** to give labels above the bubble
labpos2(#)	label position for events where the risk is largest in the second treatment group; default **labpos2(12)** to give labels above the bubble
labgap(#)	gap between label and bubble; default **labgap(5)**
labgap1(#)	gap between label and bubble for events where the risk is largest in the first treatment group; default **labgap1(5)**
labgap2(#)	gap between label and bubble for events where the risk is largest in the second treatment group; default **labgap2(5)**
xaxismin(#)	allows user to extend the x-axis beyond the minimum plotted value; default is 0 so minimum value used
xaxismax(#)	allows user to extend the x-axis beyond the maximum plotted value; default is 0 so maximum value used
yaxismin(#)	allows user to extend the y-axis beyond the minimum value; default is 0 so minimum value used
yaxismax(#)	allows user to extend the y-axis beyond the maximum value; default is 0 so maximum value used
xaxisticks(#)	allows user to specify how the x-axis ticks are spaced; default is 4
yaxisticks(#)	allows user to specify how the y-axis ticks are spaced; default is 4
xaxisdp(#)	allows the user to specify the unit x-axis values are rounded to; default is 0.1
yaxisdp(#)	allows the user to specify the unit y-axis values are rounded to; default is 0.1
ylineyn(#)	allows the user to specify if a horizontal line is plotted by specifying **ylineyn(1)**; default is **ylineyn(0)** which does not plot a line
yline(*numlist***)**	allows the user to specify the y-axis value where the horizontal line is plotted if **ylineyn(1)**; default is **yline(1)** which equates to a p-value of 0.1, unless **padj(1)**
ylinepat(*linepattern***)**	style of **yline()**; default is **ylinepat(dash)**
ylinecol(*colorstyle***)**	colour of **yline()**; default is **ylinecol(bluishgrey)**

Volcano plot

Pros

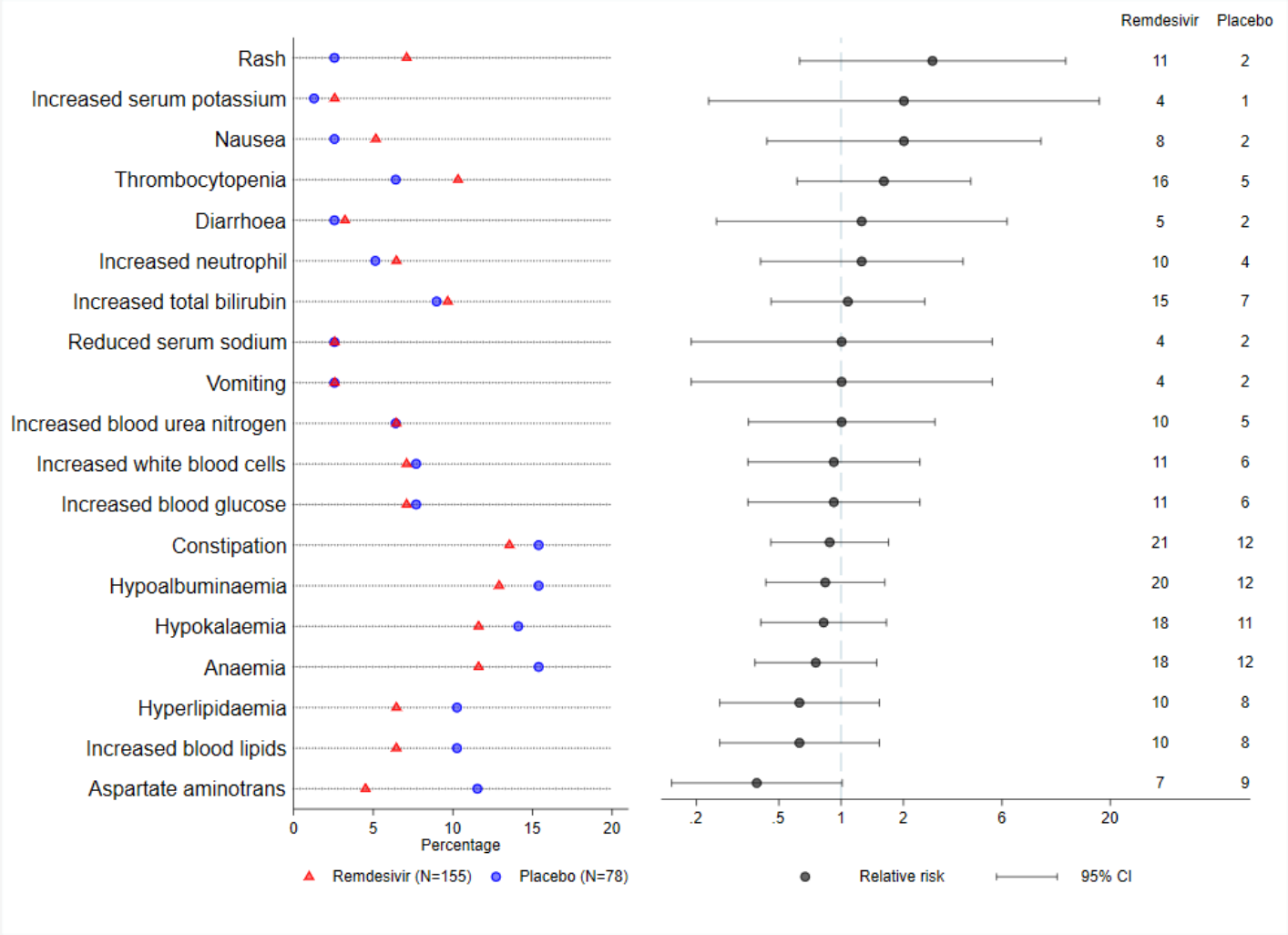
- Immediate communication of extreme differences in AE - any asymmetry in the plot
- Effective way to communicate signals for adverse reactions

Cons/cautions

- Less effective when there are few AEs in total, or where several AEs share the same frequency
  - ➢ Useful when ≈ 10 events or more and not dominated by low frequency counts, e.g. 0 and 1
- Precision of the estimate not transparent
  - ➢ Possible to give a misleading impression when the event numbers are small
- Still need to check if it communicates a fair representation of the raw data
- Presentation of more detailed information in a table is still needed

Dot plot

AEs that occurred ≥ 2% of participants



Dot plot

Individual participant data

Install: `ssc install aedot` or https://ideas.repec.org/c/boc/bocode/s458735.html

Syntax: `aedot varname , treat(varname) id(varname) n1(integer) n2(integer) [options]`

`aedot`: requires data in long format with one row per event per participant, where `varname` indicates the variable that contains the event name/identifier. `varname` may be a numeric or a string variable.

Options

* `treat(varname)`: variable indicating treatment group assignment in the existing dataset (must be numeric)
* `id(varname)`: variable identifying unique participants in the existing dataset, multiple events (rows) per id acceptable (must be numeric)
* `n1(#)`: the total number of unique participants in the first treatment group (must be an integer value)
* `n2(#)`: the total number of unique participants in the second treatment group (must be an integer value)

Various `[options]` to edit the graph

Dot plot

Summary level data

Install: part of the `aedot` package

Syntax: `aedots varname , n1(varname) n2(varname) tot1(varname) tot2(varname) [options]`

`aedots`: requires summary data in long format with one row per event, where `varname` indicates the variable that contains the event name/identifier. `varname` may be a numeric or a string variable.

Options

* `n1(varname)`: variable indicating the number of participants in the first treatment group with the event specified in `varname` (must be numeric)
* `n2(varname)`: variable indicating the number of participants in the second treatment group with the event specified in `varname` (must be numeric)
* `tot1(varname)`: variable indicating the total number of unique participants in the first treatment group (must be numeric)
* `tot2(varname)`: variable indicating the total number of unique participants in the second treatment group (must be numeric)

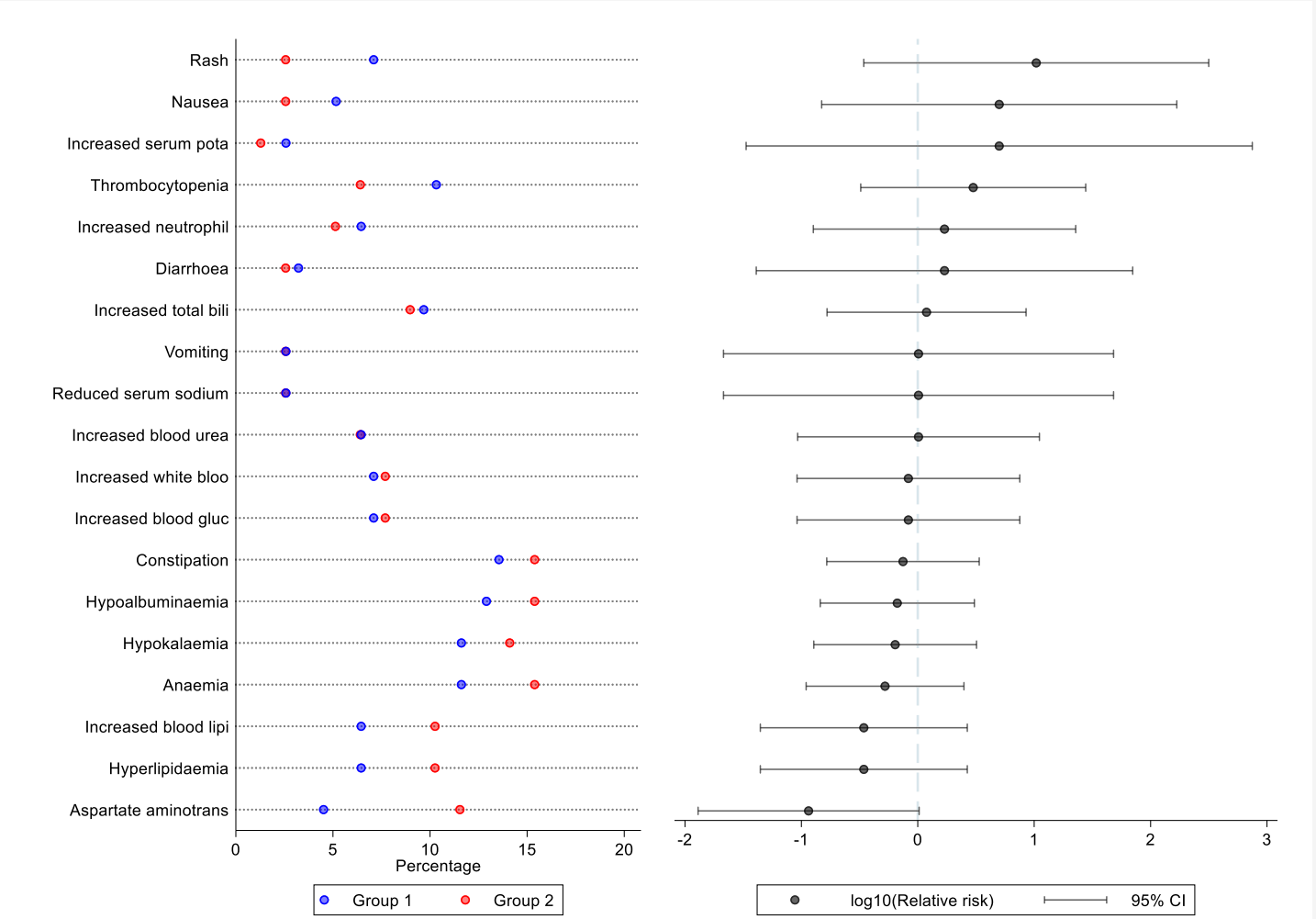
Various `[options]` to edit the graph

Dot plot

Summary level data

Basic syntax:

```
aedots Adverseevents, n1(Remdesivir_AG_n) n2(Placebo_AG_n) tot1(Remdesivir_N)
tot2(Placebo_N)
```



Dot plot

Summary level data

Syntax with added options:

```
aedots Adverseevents , n1(Remdesivir_AG_n) n2(Placebo_AG_n) tot1(Remdesivir_N) tot2(Placebo_N)
logoff(1) leftcolor1(red) leftcolor2(green) leftsymb1(triangle) legendleft1(Remdesivir (N=155))
legendleft2(Placebo (N=78)) brightmargin(3.5) leftlabsize(1.3) rightxline(1) rightxlabel(0.2 0.5 1 2 6 20)
nummargin(1) margin(30) event1pos(35) event2pos(90)  event1name(Remdesivir)  event2name(Placebo)
marginpos(r)
```

Changes marker colour

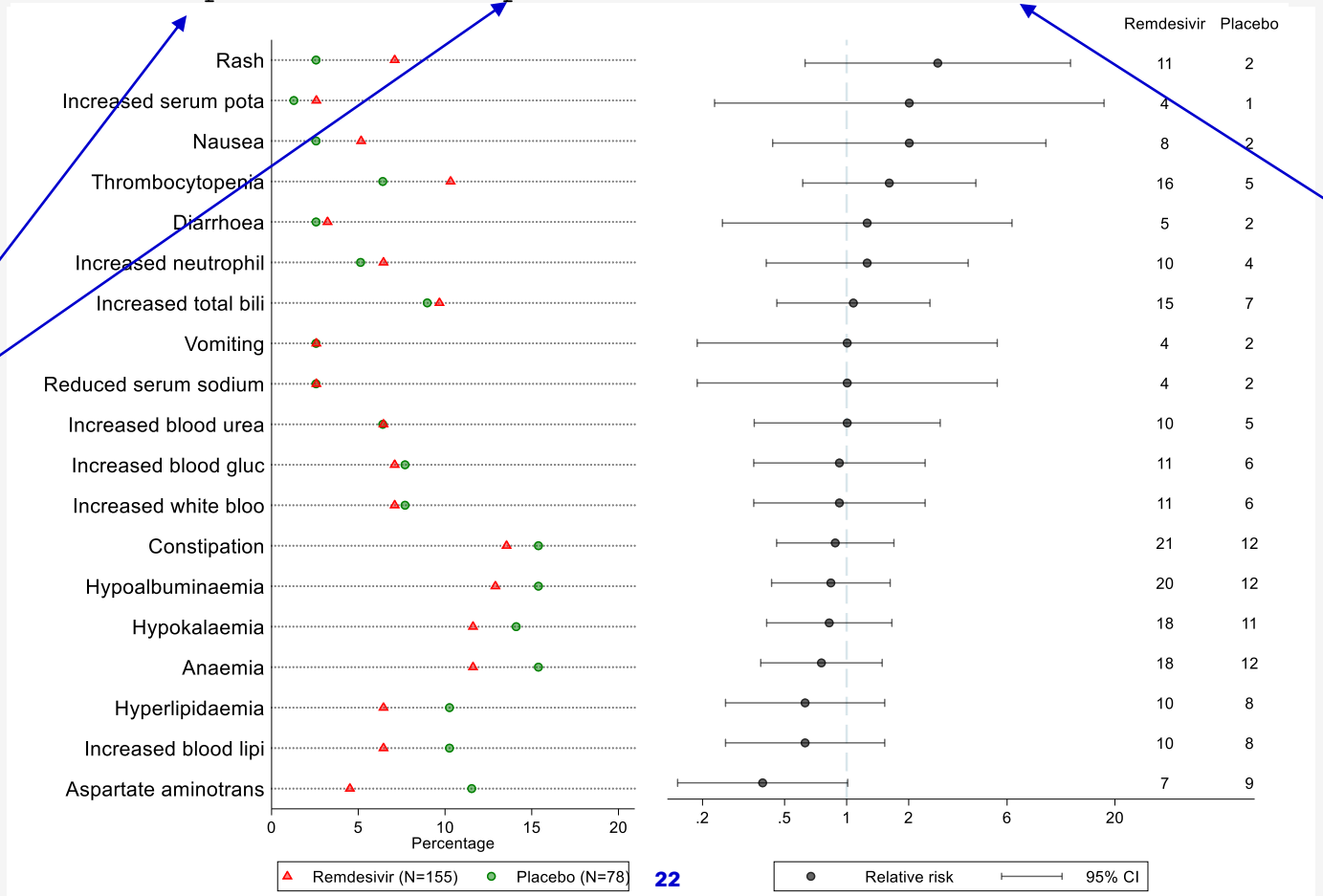
Changes marker symbol

Includes the data table

Specify the position of the data table

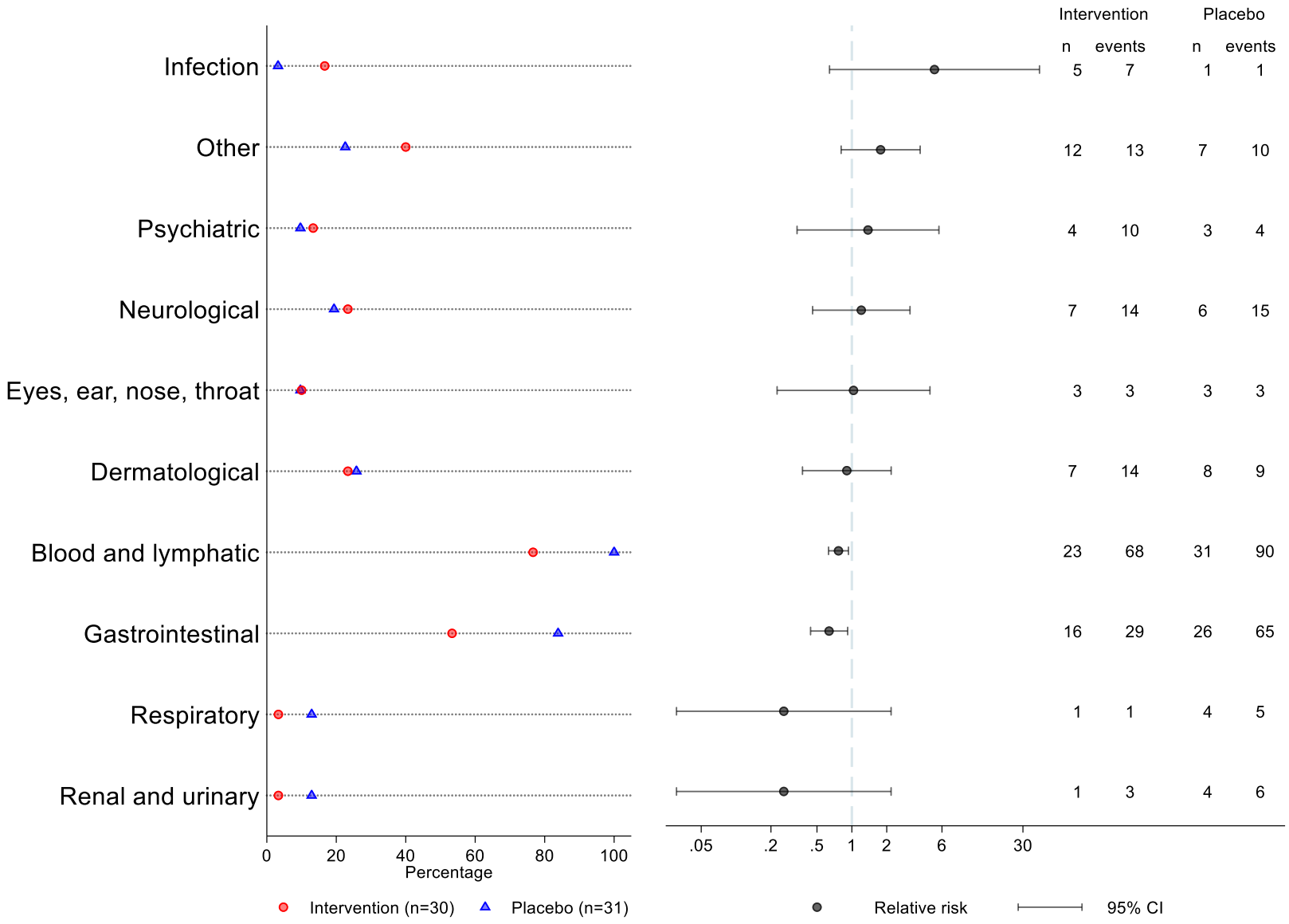
Specify position of data table columns relative to x-axis

Specify the labels for the columns of the data table



Dot plot

Individual participant data



Dot plot

Individual participant data

All `[options]` detailed in the help file

Syntax

aedot *varname* **, treat(***varname***) id(***varname***) n1(***integer***) n2(***integer***)** [*options*]

aedot requires data in long format with one row per event per participant, where *varname* indicates the variable that contains the event name/identifier. *varname* may be a numeric or a string variable.

options	Description
* **treat(***varname***)**	variable indicating treatment group assignment in the existing dataset (must be numeric)
* **id(***varname***)**	variable identifying unique participants in the existing dataset, multiple events (rows) per **id** acceptable (must be numeric)
* **n1(#)**	the total number of unique participants in the first treatment group (must be an integer value)
* **n2(#)**	the total number of unique participants in the second treatment group (must be an integer value)
saving(*filename***[, replace])**	saves the dataset with event level summary data used for the plot in *filename*.dta
graphsave(*filename***[, replace])**	saves the plot in *filename*.gph
clear	if specified the newly created dataset is stored in memory. Without **clear** the original dataset is retained in memory
riskdiff(#)	specify whether relative risk or risk difference plotted; **riskdiff(0)** plots the relative risk and **riskdiff(1)** plots the risk difference, default is **riskdiff(0)**
logoff(#)	specify whether log relative risk or relative risk plotted; **logoff(0)** plots the log relative risk and **logoff(1)** plots the relative risk, default is **logoff(0)**
leftxtitle(*string***)**	title for the x-axis on the plot on the left; the default label is *"Percentage"*
leftcolor1(*colorstyle***)**	marker colour for the first treatment group values on the plot on the left; default is **leftcolor1(blue)**
leftcolsat1(#)	marker colour saturation for the first treatment group values on the plot on the left; default is **leftcolsat1(50)**
leftcolor2(*colorstyle***)**	marker colour for the second treatment group values on the plot on the left; default is **leftcolor2(red)**
leftcolsat2(#)	marker colour saturation for the second treatment group values on the plot on the left; default is **leftcolsat2(50)**
leftsymb1(*symbolstyle***)**	marker symbol for the first treatment group values on the plot on the left; default symbol is **leftsymb1(circle)**
leftsymb2(*symbolstyle***)**	marker symbol for the second treatment group values on the plot on the left; default symbol is **leftsymb2(circle)**
leftlabsize(#)	size of labels on the y-axis for the plot on the left; default is **leftlabsize(1)**
leftlabang(#)	label angle on the y-axis for the plot on the left; default is **leftlabang(0)** to give horizontal labels
leftlabel(*string***)**	used to override y-axis labels on the plot on the left. See *graph dot* **relabel** for further details
rightxline(#)	vertical line position on the plot on the right; default is **rightxline(0)**
rightxlinepat(*linepattern***)**	vertical line style on the plot on the right; default is **rightxlinepat(dash)**
rightxlinecol(*colorstyle***)**	vertical line colour on the plot on the right; default is **rightxlinecol(bluishgray)**
rightdcolor(*colorstyle***)**	horizontal grid line colour on the plot on the right; default is **rightdcolor(white)**
rightdotcol(*colorstyle***)**	marker colour on the plot on the right; default is **rightdotcol(black)**
rightdotsat(#)	marker colour saturation on the plot on the right; default is **rightdotsat(60)**
rightlincol(*colorstyle***)**	line colour of the confidence interval on the plot on the right; default is **rightlincol(black)**
rightlinsat(#)	colour saturation of the confidence interval on the plot on the right; default is **rightlinsat(60)**
rightxlabel(*numlist***)**	allows the user to specify the x-axis value labels on the plot on the right
legendleftyn(#)	specify whether legend appears on the plot on the left; **legendleftyn(#)** takes values 0 to indicate legend off or 1 to indicate legend on, default is **legendleftyn(1)**
legendleft1(*string***)**	specify text for the legend to describe the first treatment group for the plot on the left; default text is *"Group 1"*
legendleft2(*string***)**	specify text for the legend to describe the second treatment group for the plot on the left; default text is *"Group 2"*
legendleftpos(#)	specify position of the legend on the plot on the left; default is **legendleftpos(6)**
legendleftcol(#)	number of columns in the legend on the plot on the left; default is **legendleftcol(2)**
legendleftrow(#)	number of rows in the legend on the plot on the left; default is **legendleftrow(1)**
legendrightyn(#)	specify whether legend appears on the plot on the right; **legendrightyn(#)** takes values 0 to indicate legend off or 1 to indicate legend on, default is **legendrightyn(1)**
legendright1(*string***)**	specify text to describe the point estimate in the legend on the plot on the right; default text is *"log10(Relative risk)"* if **riskdiff(0)** and *"Risk difference"* if **riskdiff(1)**
legendright2(*string***)**	specify text to describe the 95% confidence interval in the legend on the plot on the right; default text is *"95% CI"*
legendrightpos(#)	specify position of the legend on the plot on the right; default is **legendrightpos(6)**
legendrightcol(#)	number of columns in the legend on the plot on the right; default is **legendrightcol(2)**
legendrightrow(#)	number of rows in the legend on the plot on the right; default is **legendrightrow(1)**
bleftmargin(#)	adds a margin of empty space to the bottom of the plot on the left; default is **bleftmargin(0)**. This can be used to help align the plots.

Dot plot

Pros

- Includes more detailed information - absolute risk by arm and relative between-arm comparison
- Could replace the typical AE frequency table presented
- Allows for more scrutiny

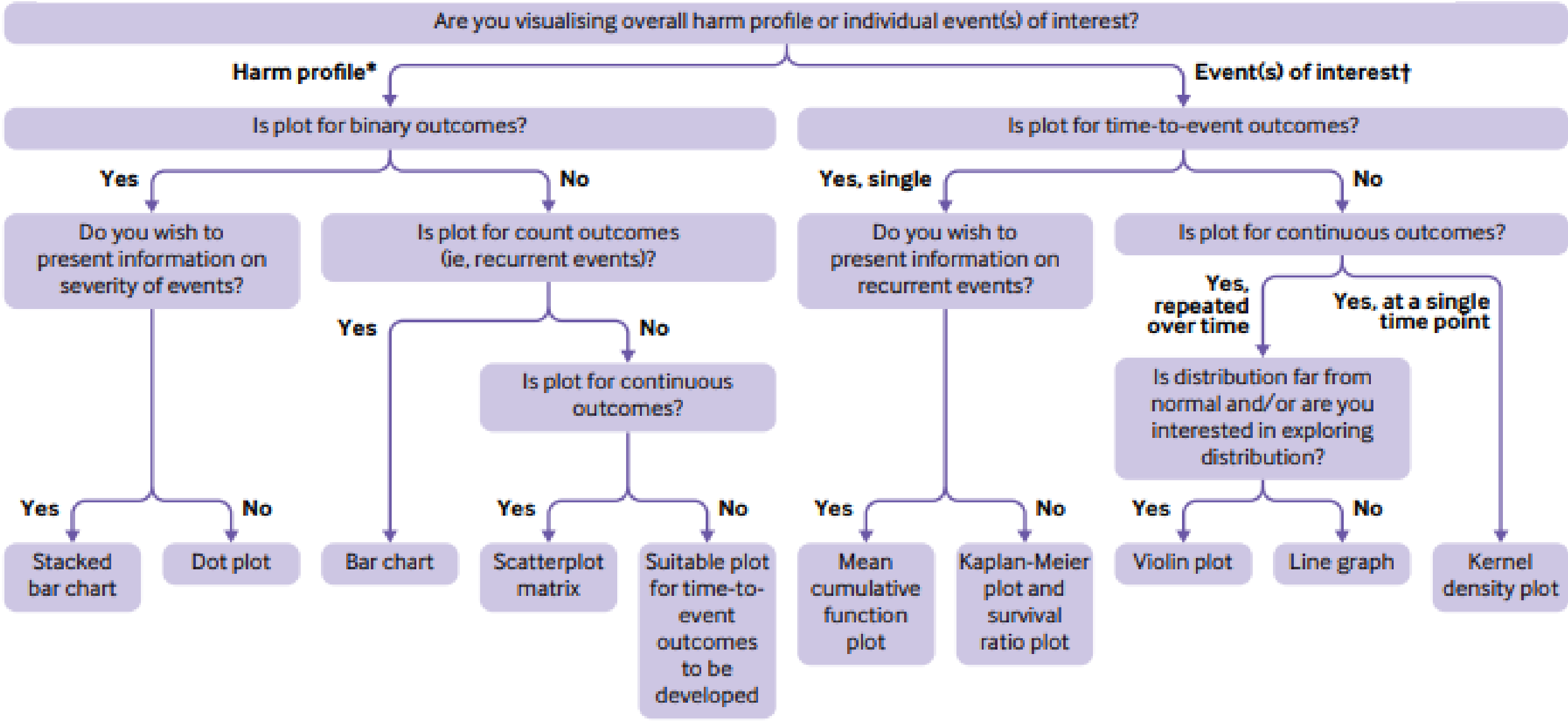
Cons/cautions

- Inclusion of 95% CIs for the relative statistic strongly encourages the temptation to interpret as a test of no statistical difference

Summary

- Visualisations provide an alternative way to communicate risk of harms
- Allows assimilation of large volumes of data
- Encourages informal between-arm comparisons
- Provide different emphasis on inferences
- Recommend trialists examine both crude numbers along with graphical displays

Decision tree to help researchers decide which plot(s) to use to visualise data on harm outcomes



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Thank you

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