

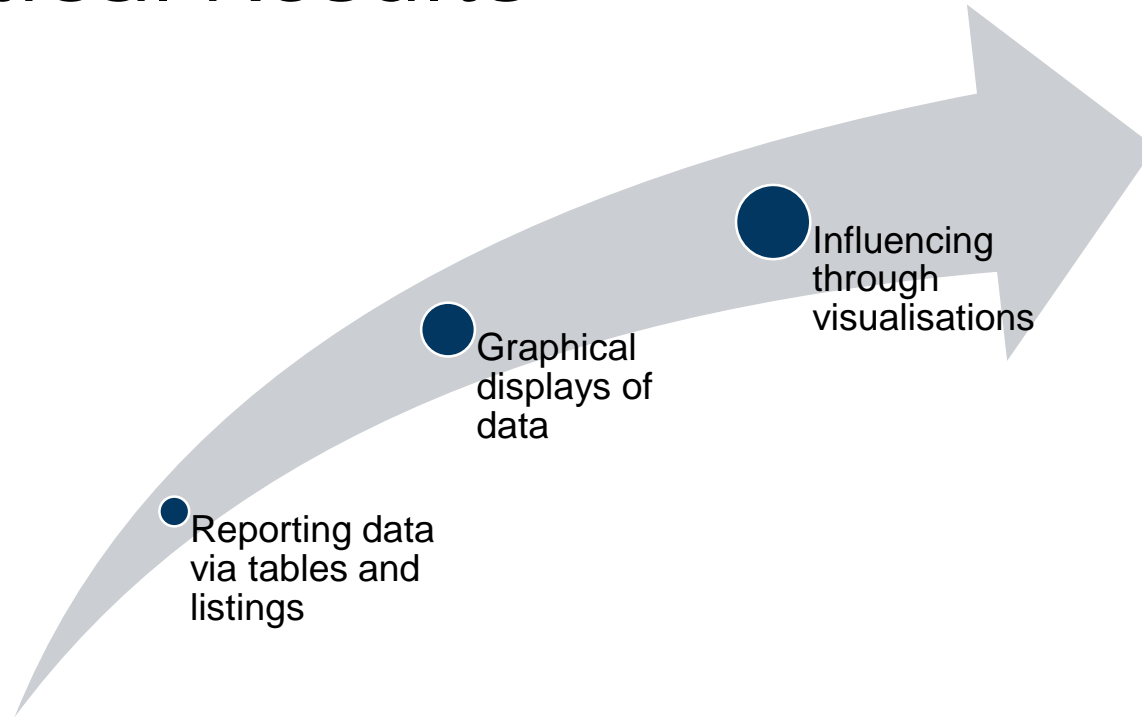
Global Drug Development



Show me the question: Putting the questions front and centre

Andrew Wright
RSS Conference, September 2019

Evolution in the Communication of Statistical Results



Current Flow from Questions to Results in Clinical Trial Setting

Question:
What are the questions of interest?

Objectives:
How do these questions translate into trial objectives?

Design:
What is the best design to address the objectives?

Measurements:
What should we measure in the trial?

Case Report Forms:
How do we collect the data from the measurements?

Database:
How do we database these data?

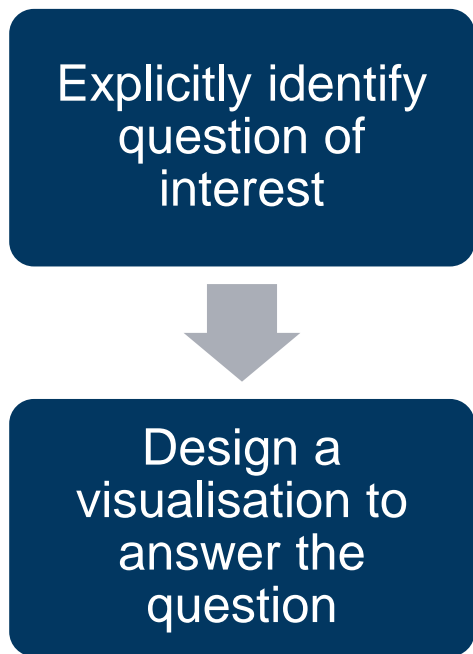
Datasets:
How do we convert the database into usable datasets?

Results:
How do we display the data in the datasets?

At the end of this chain, do we still remember the question we started from?

Question-Based Visualisations (QBV)

A Top-Down Approach



This approach encourages:

- Clear **alignment** on the purpose of each visualisation **before** it is produced
- Clear **understanding** of the purpose of each visualisation **after** it is produced

Three Applications of QBVs

Replacement for tables, listings and figures in static reports

Structure for interactive Shiny apps

Framework for exploratory data analyses

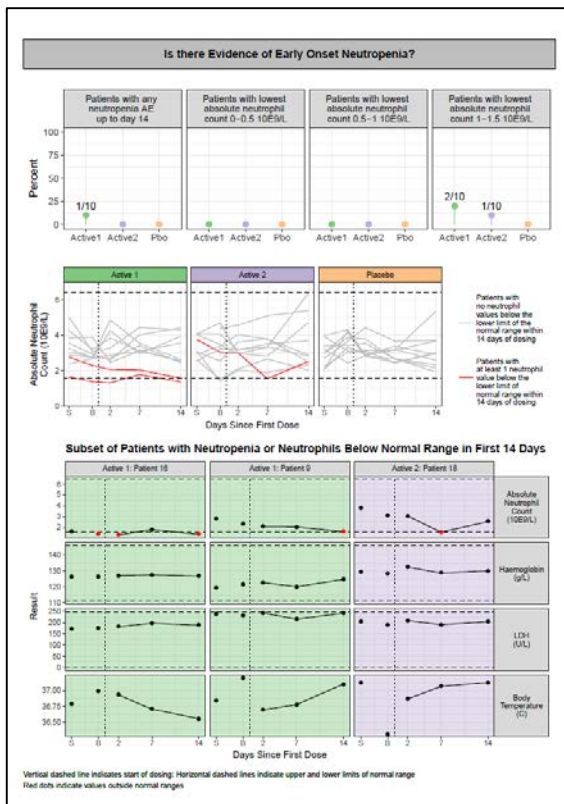
Three Applications of QBVs

Replacement for tables, listings and figures in static reports

Structure for interactive Shiny apps

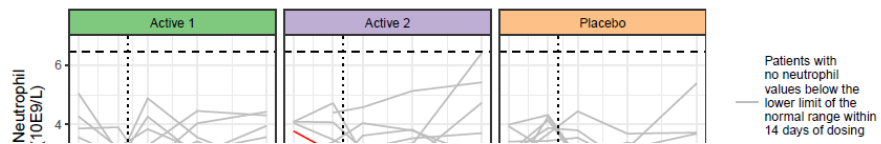
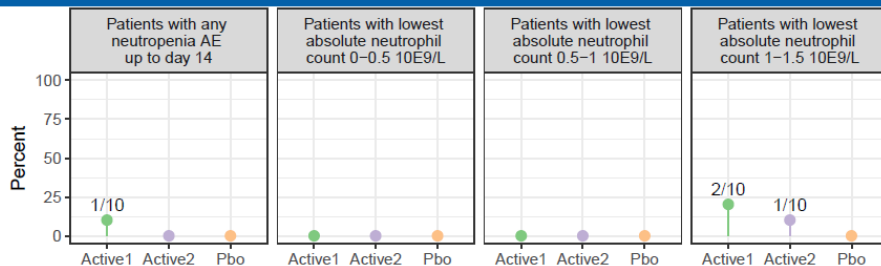
Framework for exploratory data analyses

QBVVs in Static Reports



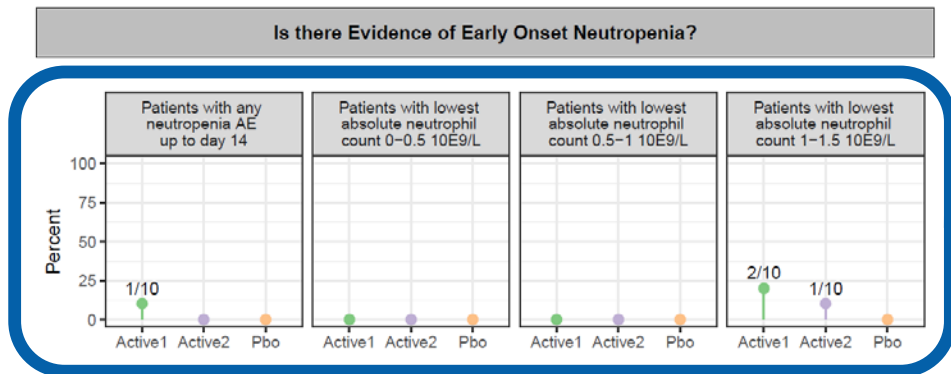
QBVVs in Static Reports

Is there Evidence of Early Onset Neutropenia?

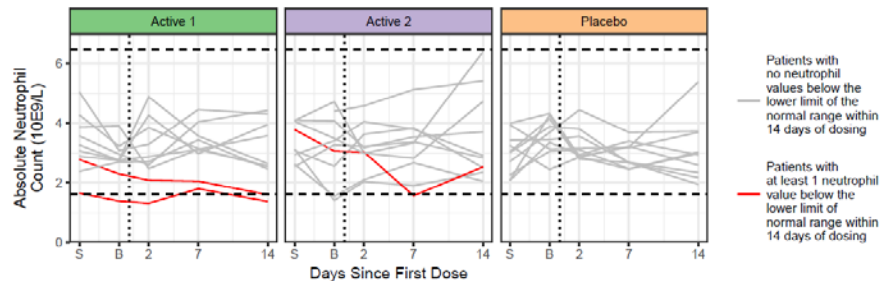


This visualisation is designed to address the question of whether there is evidence of a known potential safety concern: early onset neutropenia

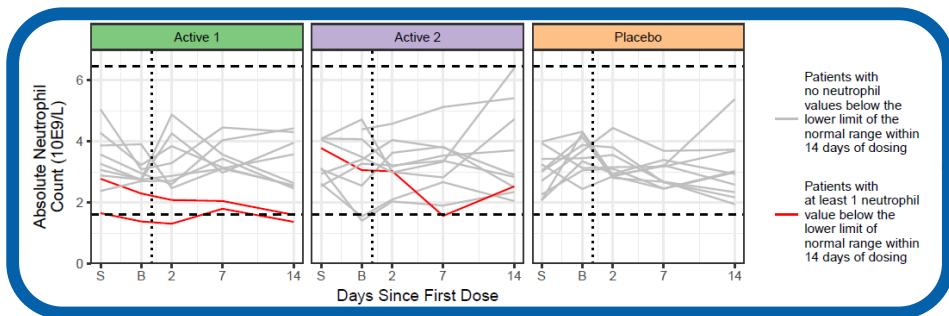
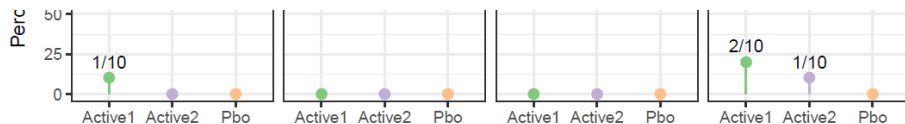
QBV's in Static Reports



The first part of the visualisation provides a high level summary of whether there are any clear signals in the data

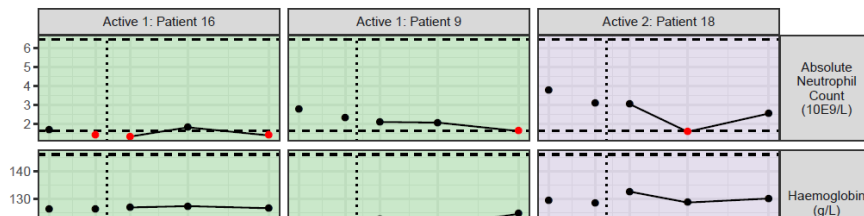


QBVVs in Static Reports

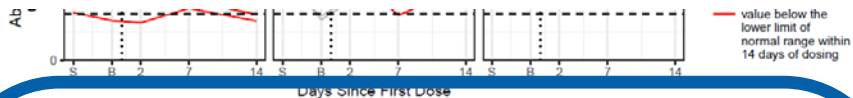


The second plot highlights potential patients of concern and contrasts them with other patients in the study

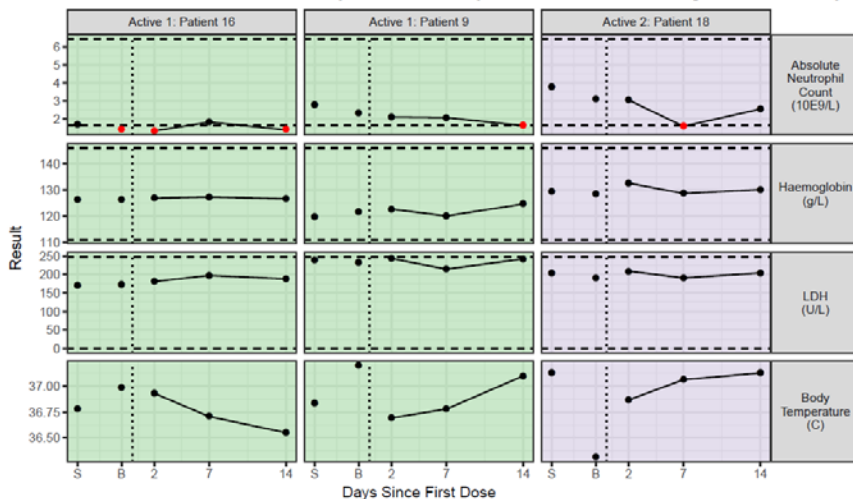
Subset of Patients with Neutropenia or Neutrophils Below Normal Range in First 14 Days



QBVVs in Static Reports



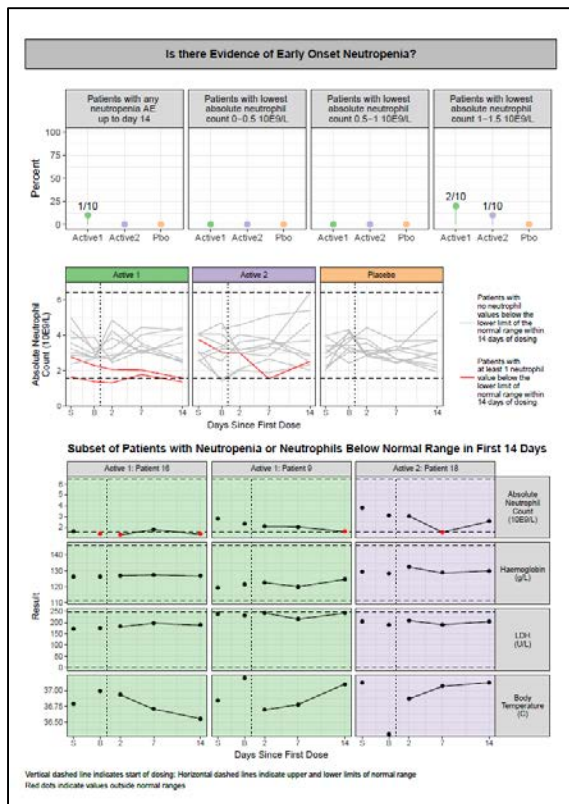
Subset of Patients with Neutropenia or Neutrophils Below Normal Range in First 14 Days



Vertical dashed line indicates start of dosing; Horizontal dashed lines indicate upper and lower limits of normal range
Red dots indicate values outside normal ranges

The last plot focuses on the patients of concern to address whether neutrophil changes are consistent with other markers of a compromised immune system

Key Attributes of QBVs



- Title **explicitly** states the question of interest
- All information required to answer question are presented on **one page**
- Combination of summary statistics and individual data, descriptive and inferential statistics
- Data from many data domains displayed together

Three Applications of QBVs

Replacement for tables, listings and figures in static reports (e.g. CSRs)

Structure for interactive Shiny apps

Framework for exploratory data analyses

Interactive Shiny App Structured around Questions

The screenshot displays a Shiny application interface with a dark blue header and a light blue sidebar. The main content area is white with blue accents. The sidebar on the left contains a 'Data Dashboard' title, a 'Home' button, and a 'Choose studies' section with three checkboxes for 'Study 001' (purple), 'Study 002' (orange), and 'Study 003' (green). Below this are navigation links for 'Home', 'Overview', 'Population', 'Signs & Symptoms', 'Biomarkers', and 'Patient Profiles', each with a corresponding icon and a right-pointing arrow. The main content area features a top navigation bar with a hamburger menu icon and the text 'Home'. Below this is a large blue header for the 'Overview' section, titled 'Overview' and subtitled 'Key efficacy & safety results'. The main content is organized into three columns. The left column is titled 'Population' with the question 'What type of patients were recruited?' and contains two blue buttons: 'Demographics' and 'Disease Characteristics'. The middle column is titled 'Signs & Symptoms' with the question 'What is the effect on...?' and contains three blue buttons: 'Overall Disease Activity', 'Symptom 1', and 'Symptom 2'. The right column is titled 'Biomarkers' with the question 'What is the effect on...?' and contains two blue buttons: 'Proximal Markers' and 'Distal Markers'. At the bottom of the main content area is a blue header for the 'Patient Profiles' section, which contains three blue buttons: 'Efficacy', 'PK/PD', and 'Safety'.

Interactive Shiny App Structured around Questions

The screenshot displays a Shiny application interface for a clinical trial data dashboard. The interface is organized into several key sections:

- Header:** A blue bar at the top contains the text "Data Dashboard" on the left and a hamburger menu icon followed by "Home" on the right.
- Left Sidebar:** A dark grey sidebar contains the following elements:
 - Choose studies:** Three checkboxes are shown, each with a colored square: "Study 001" (purple), "Study 002" (orange), and "Study 003" (green). All three are checked.
 - Navigation:** A list of menu items with icons and arrows:
 - Home (house icon)
 - Overview (document icon)
 - Population (person icon)
 - Signs & Symptoms (pill icon)
 - Biomarkers (microscope icon)
 - Patient Profiles (document icon)
- Main Content Area:** A large blue area with a white background containing several panels:
 - Overview:** A top panel with the title "Overview" and subtitle "Key efficacy & safety results".
 - Population:** A panel titled "Population" with the question "What type of patients were recruited?". It contains two buttons: "Demographics" and "Disease Characteristics".
 - Signs & Symptoms:** A panel titled "Signs & Symptoms" with the question "What is the effect on...?". It contains three buttons: "Overall Disease Activity", "Symptom 1", "Symptom 2", and "Symptom 3".
 - Biomarkers:** A panel titled "Biomarkers" with the question "What is the effect on...?". It contains two buttons: "Proximal Markers" and "Distal Markers".
 - Patient Profiles:** A bottom panel titled "Patient Profiles" containing three buttons: "Efficacy", "PK/PD", and "Safety".

Question-Based Visualisations Are the Backbone of the App

The screenshot displays a web application interface for a 'Data Dashboard'. The main header is 'Population: Disease Characteristics'. On the left, a dark sidebar contains navigation options: 'Home', 'Overview', 'Population', 'Demographics', 'Disease Characteristics', 'Signs & Symptoms', 'Biomarkers', and 'Patient Profiles'. Under 'Choose studies', three studies are listed: 'Study 001', 'Study 002', and 'Study 003'. The main content area features a toggle switch for 'Display answers for all questions at once?' set to 'OFF'. Below this is a search bar with the placeholder text 'Click to select questions or type keyword to search'. The content is organized into three columns: 'Physician Assessments', 'Patient Assessments', and 'Others'. Each column contains several questions related to disease activity endpoints and patient characteristics at baseline.

Data Dashboard | Population: Disease Characteristics

Choose studies:
Study 001
Study 002
Study 003

Home
Overview
Population
Demographics
Disease Characteristics
Signs & Symptoms
Biomarkers
Patient Profiles

Display answers for all questions at once? OFF

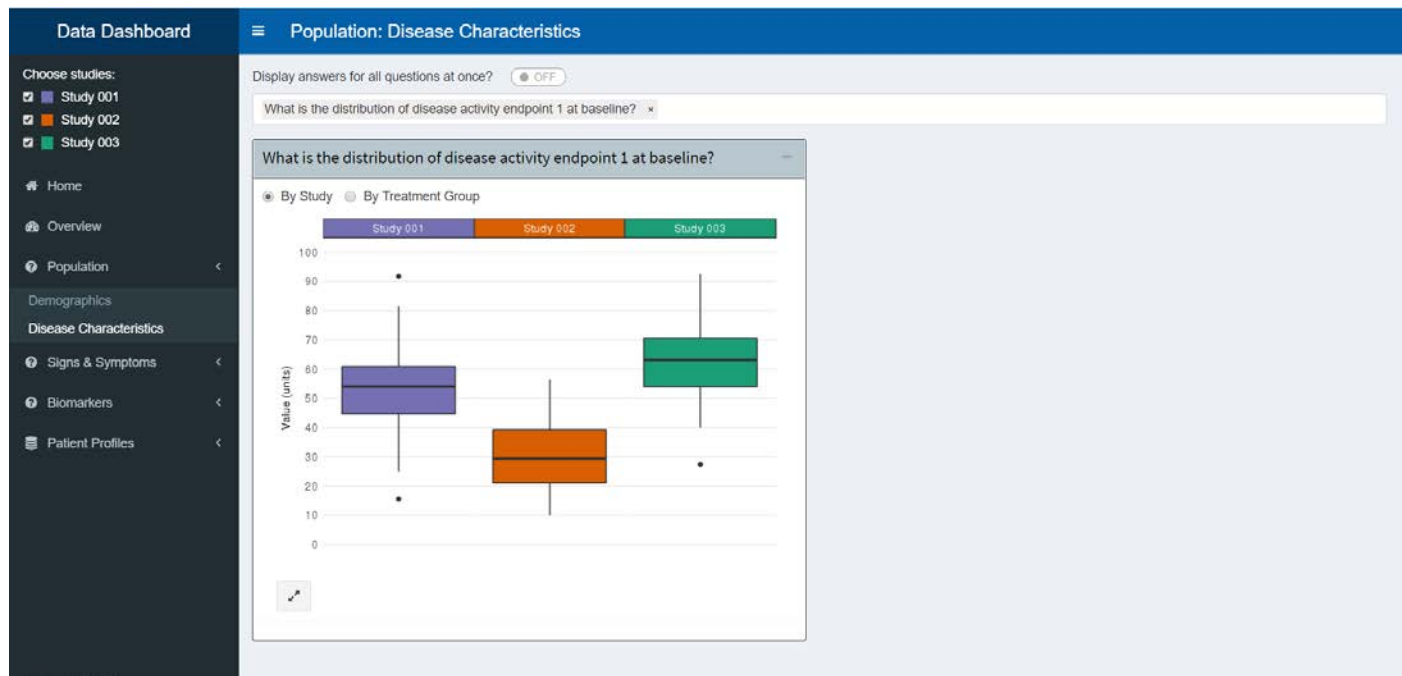
Click to select questions or type keyword to search

Physician Assessments
What is the distribution of disease activity endpoint 1 at baseline?
What is the distribution of disease activity endpoint 2 at baseline?
Is there a correlation between baseline disease activity endpoint 1 and 2?

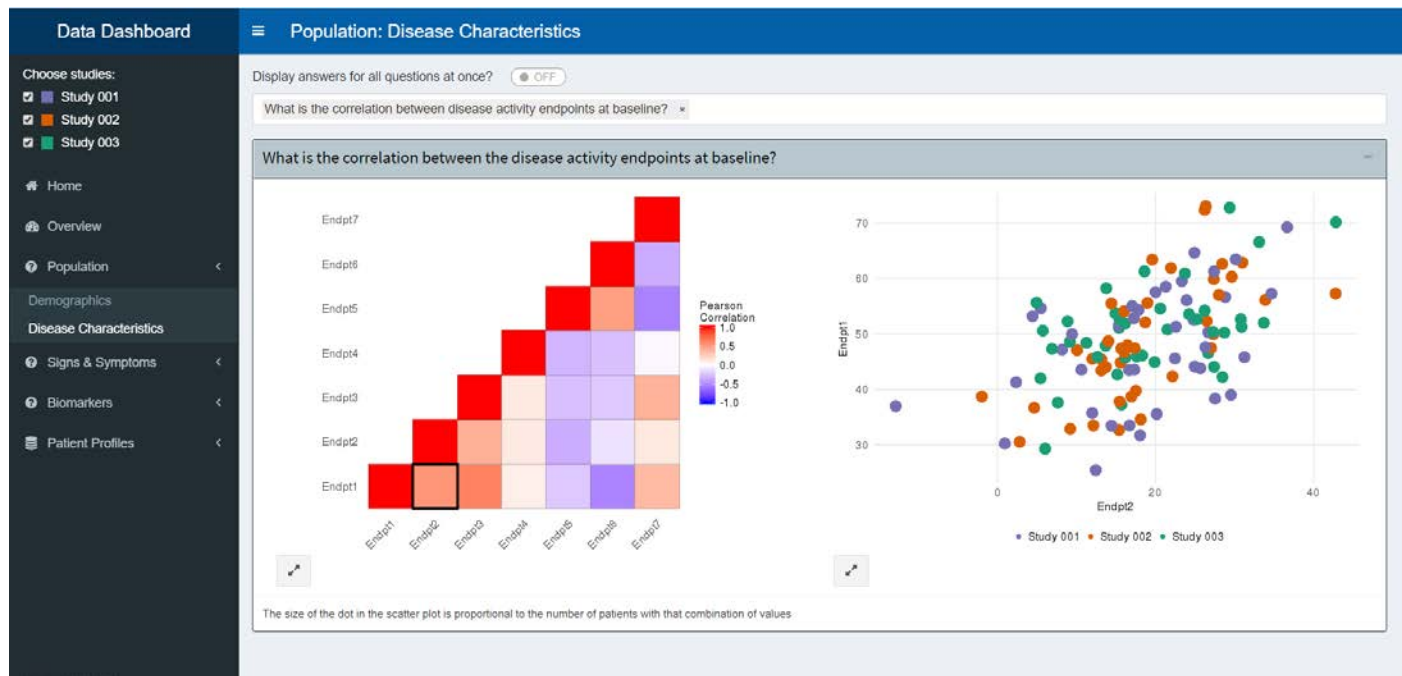
Patient Assessments
What is the distribution of the disease activity endpoint 3 at baseline?
What is the distribution of the individual domains of disease activity endpoint 3 at baseline?
How do the individual domains of disease activity endpoint 3 contribute to the overall score at baseline?
What is the distribution of the disease activity endpoint 4 at baseline?

Others
What disease-related concomitant medication were the patients taking at baseline?
What is the distribution of the disease activity endpoint 5 at baseline?
What is the distribution of the disease activity endpoint 6 & 7 scores at baseline?
Are there clusters of Individuals based on their disease activity at baseline?
What is the correlation between disease activity endpoints at baseline?

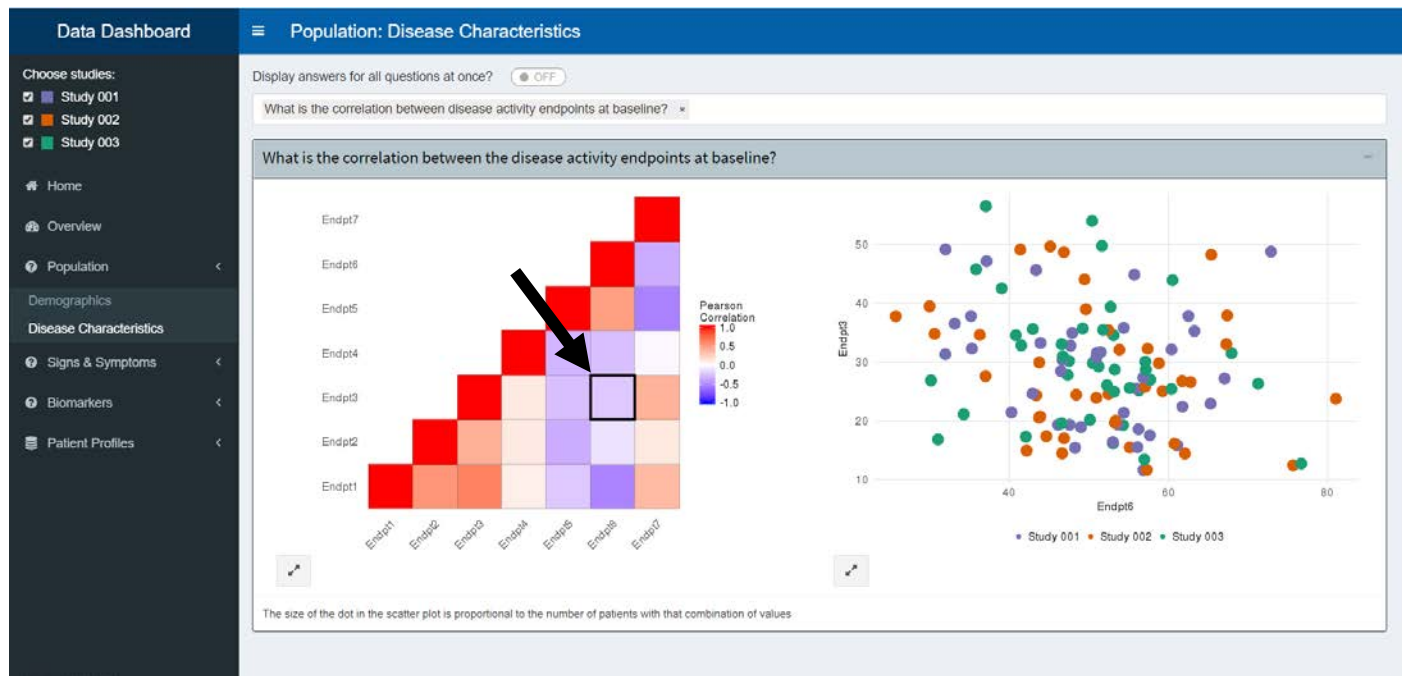
Each Question is Addressed by a Visualisation



Sometimes Multiple Connected Graphs are Required to Answer a Question



Sometimes Multiple Connected Graphs are Required to Answer a Question



Three Applications of QBVs

Replacement for tables, listings and figures in static reports (e.g. CSRs)

Structure for interactive Shiny apps

Framework for exploratory data analyses

Questions As Titles, Really?

Description

- e.g. 'Scatter plot of X versus Y'
- Provides little additional information to your audience

Question

- e.g. 'What is the relationship between X and Y?'
- A good starting point to design the visualization
- Allows the audience to make up their own mind

Answer

- e.g. 'X and Y are positively correlated'
- Tells the audience how you interpret the data
- Best approach for influencing

Questions As Titles, Really?

For titles, choose from one of these two options

Question

- e.g. 'What is the relationship between X and Y?'
- A good starting point to design the visualization
- Allows the audience to make up their own mind

Answer

- e.g. 'X and Y are positively correlated'
- Tells the audience how you interpret the data
- Best approach for influencing

Put Questions Front & Centre in Your Visualisations for Maximal Impact

- Question Based Visualisations can influence by:
 - Aligning teams on the key questions of interest
 - Providing teams with a focussed, clear and concise visualisations to answer these questions

- To make an impact, use QBVs when communicating statistical results