

DOC Data – Advanced Training

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DOC Data – Advanced Training Objectives

After this training, participants will be able to:

1. Understand DRE methodology and how to jointly conduct projects
2. Navigate DOC Data platform and execute analytical methods
3. Use descriptive statistics and visualizations to prepare data for analysis
4. Perform Cohort Analysis, Direct Meta-Analysis, and Bayesian Network Meta-Analysis

DRE - Sanofi Engagement

Doctor Evidence is in the first year of a **multi-year engagement** with Sanofi -- executive sponsors are Ameet Nathwani and Bernard Hamelin

Direct access to DRE
platforms with training and
Single Sign On

Project services for identified
needs (PICO process)

Deliverables to Serve Functions & GBUs

Deliverables

Systematic Literature Reviews

Network Meta Analyses

Landscape Assessments

Safety Analyses

Competitor Label Review

Regulatory Responses

Responsive Communications
(HCP and Payer)

Functions

Medical

Health Economics

Outcomes Research

Patient Centricity

Scientific Communications and
Publications

Clinical Development

Biostatistics

Safety and Epidemiology

GBUs

DCV

Genzyme

GEM

CHC

DRE - Sanofi MSA

There is no additional cost to Sanofi users for any services. All fees are covered under the existing Master Services Agreement.

Our mission is to find, synthesize,
and analyze medical data from
all sources into fit-to-purpose
actionable knowledge.

DRE is a medical evidence company.



What does DRE do?

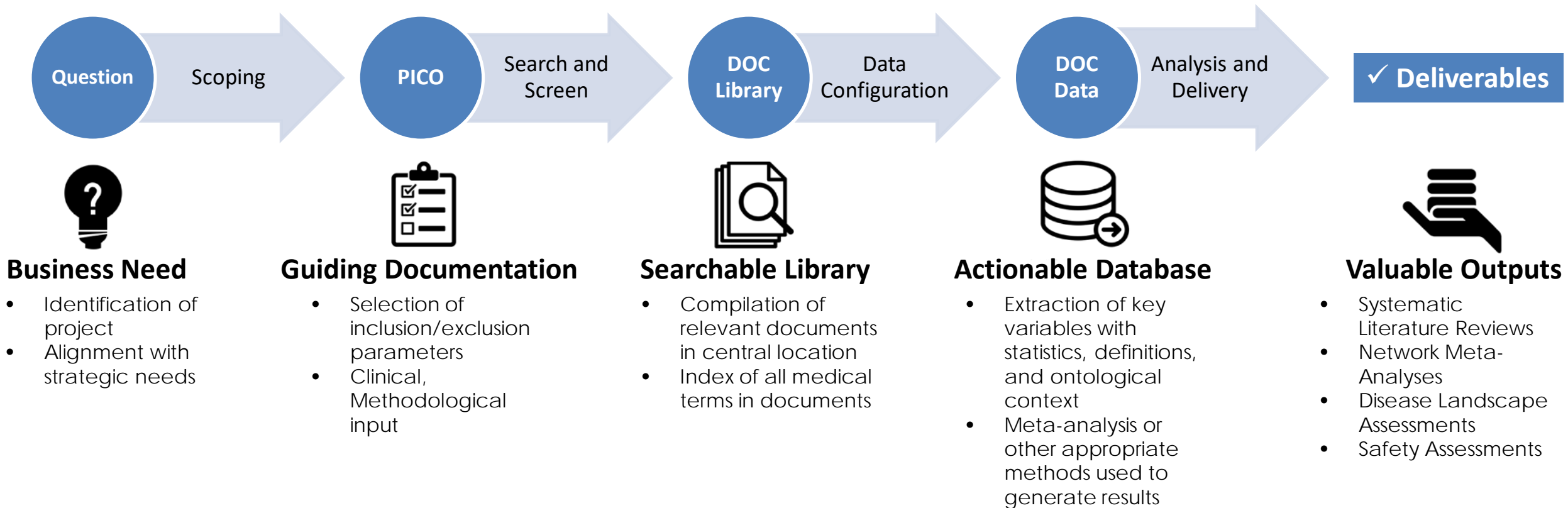
- Identify relevant published literature to answer scientific questions and extract data from these sources using proprietary software technologies
 - Create libraries, curated and searchable
 - Create relational databases suitable for analyses
- Consult with our clients to provide meaningful insights that inform decisions and guide tactics
 - Structured consulting process
 - Frequent and regular touchpoints with our clients
 - Deliverables include written reports, slide decks and publications

Joint DRE-Sanofi Workflow Process

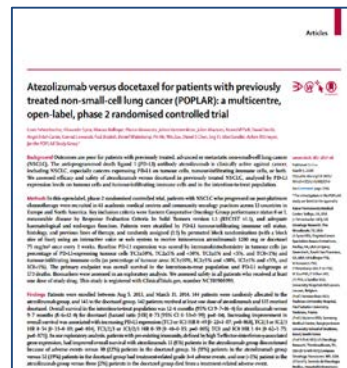
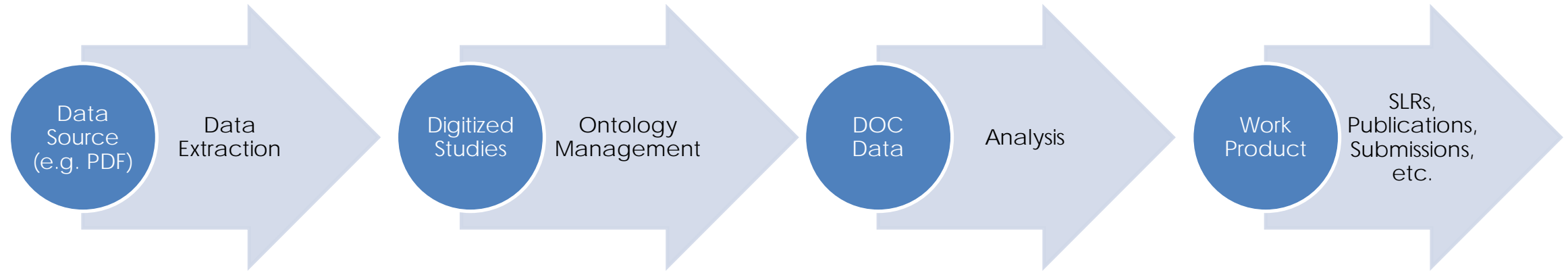
	Business Question	PICO Protocol	Literature Search and Screen	Review of Library Results	Data Configuration	Analysis and Interpretation
DRE Process		Joint collaboration to draft PICO Protocol	DRE conducts literature search and screen into DOC Library	Joint review of search results	DRE conducts data configuration into DOC Data	DRE and/or Sanofi produce analytics
Sanofi Process	Sanofi submits business question					

Workflow Process from Beginning to End

Doctor Evidence Process



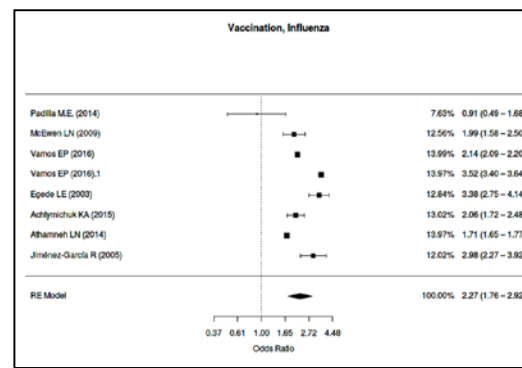
Doctor Evidence – Evidence Synthesis Process



PDF article



Digital Study



Meta-Analysis



Publication

Data Digitization into DOC Data

Articles

Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial

Louis Fehrenbacher, Alexander Spira, Marcus Ballinger, Marcin Kowanzet, Johan Vansteenkiste, Julien Mazieres, Keunchil Park, David Smith, Angel Arta-Cortes, Conrad Lewanski, Fadi Braiteh, Daniel Waterkamp, Pei He, Wei Zou, Daniel S Chen, Jing Yi, Alan Sandler, Achim Rittmeyer, for the POPLAR Study Group*

Background Outcomes are poor for patients with previously treated, advanced or metastatic non-small-cell lung cancer (NSCLC). The anti-programmed death ligand 1 (PD-L1) antibody atezolizumab is clinically active against cancer, including NSCLC, especially cancers expressing PD-L1 on tumour cells, tumour-infiltrating immune cells, or both. We assessed efficacy and safety of atezolizumab versus docetaxel in previously treated NSCLC, analysed by PD-L1 expression levels on tumour cells and tumour-infiltrating immune cells and in the intention-to-treat population.

Methods In this open-label, phase 2 randomised controlled trial, patients with NSCLC who progressed on post-platinum chemotherapy were recruited in 61 academic medical centres and community oncology practices across 13 countries in Europe and North America. Key inclusion criteria were Eastern Cooperative Oncology Group performance status 0 or 1, measurable disease by Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1), and adequate haematological and end-organ function. Patients were stratified by PD-L1 tumour-infiltrating immune cell status, histology, and previous lines of therapy, and randomly assigned (1:1) by permuted block randomisation (with a block size of four) using an interactive voice or web system to receive intravenous atezolizumab 1200 mg or docetaxel 75 mg/m² once every 3 weeks. Baseline PD-L1 expression was scored by immunohistochemistry in tumour cells (as percentage of PD-L1-expressing tumour cells TC3≥50%, TC2≥5% and <50%, TC1≥1% and <5%, and TC0<1%) and tumour-infiltrating immune cells (as percentage of tumour area: IC3≥10%, IC2≥5% and <10%, IC1≥1% and <5%, and IC0<1%). The primary endpoint was overall survival in the intention-to-treat population and PD-L1 subgroups at 173 deaths. Biomarkers were assessed in an exploratory analysis. We assessed safety in all patients who received at least one dose of study drug. This study is registered with ClinicalTrials.gov, number NCT01903993.

Findings Patients were enrolled between Aug 5, 2013, and March 31, 2014. 144 patients were randomly allocated to the atezolizumab group, and 143 to the docetaxel group. 142 patients received at least one dose of atezolizumab and 135 received docetaxel. Overall survival in the intention-to-treat population was 12.6 months (95% CI 9.7–16.4) for atezolizumab versus 9.7 months (8.6–12.0) for docetaxel (hazard ratio [HR] 0.73 [95% CI 0.53–0.99]; $p=0.04$). Increasing improvement in overall survival was associated with increasing PD-L1 expression (TC3 or IC3 HR 0.49 [0.22–1.07]; $p=0.068$), TC2/3 or IC2/3 HR 0.54 [0.33–0.89]; $p=0.014$), TC1/2/3 or IC1/2/3 HR 0.59 [0.40–0.85]; $p=0.005$), TC0 and IC0 HR 1.04 [0.62–1.75]; $p=0.871$). In our exploratory analysis, patients with pre-existing immunity, defined by high T-effector-interferon- γ -associated gene expression, had improved overall survival with atezolizumab. 11 (8%) patients in the atezolizumab group discontinued because of adverse events versus 30 (22%) patients in the docetaxel group. 16 (11%) patients in the atezolizumab group versus 52 (39%) patients in the docetaxel group had treatment-related grade 3–4 adverse events, and one (<1%) patient in the atezolizumab group versus three (2%) patients in the docetaxel group died from a treatment-related adverse event.

Lancet 2016; 387: 1837–46
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See Comment page 1795

*The investigators in the POPLAR study are listed in the appendix
Kaiser Permanente Medical Center, Vallejo, CA, USA (L Fehrenbacher MD); US Oncology Research, The Woodlands, TX, USA (A Spira MD); Virginia Cancer Specialists Research Institute, Fairfax, VA, USA (A Spira); Genentech, South San Francisco, CA, USA (M Ballinger PhD, M Kowanzet PhD, D Waterkamp MD, P He PhD, W Zou PhD, D S Chen MD, J Yi PhD, A Sandler MD); University Hospitals KU Leuven, Leuven, Belgium (Prof J Vansteenkiste MD); Toulouse University Hospital, Paul Sabatier University, Toulouse, France (Prof J Mazieres MD); Samsung Medical Centre, Sungkyunkwan University School of Medicine, Seoul, South Korea (Prof K Park MD); US Oncology Research, The Woodlands, TX, USA (D Smith MD); Compass Oncology, Vancouver, WA, USA (D Smith); Servicio de Oncología Médica, Hospital Universitario

Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial.

Fehrenbacher L, Spira A, Ballinger M, Kowanzet J, Mazieres J, Park K, Smith D, Arta-Cortes A, Lewanski C, Braiteh F, Waterkamp D, He P, Zou W, Chen DS, Yi J, Sandler A, Rittmeyer A

Randomized Controlled Trial | Therapy | Drug

Acronym: POPLAR

Published: 2016 Mar 9

DOI: 10.1016/S0140-6736(16)00587-0

Institution: Unavailable

Reference ID: 1468159

RQ ID: 37677

Abstract

Background: Outcomes are poor for patients with previously treated, advanced or metastatic non-small-cell lung cancer (NSCLC), especially cancers expressing PD-L1 on tumour cells, tumour-infiltrating immune cells, or both. We assessed efficacy and safety of atezolizumab versus docetaxel in previously treated NSCLC, analysed by PD-L1 expression levels on tumour cells and tumour-infiltrating immune cells and in the intention-to-treat population.

Methods: In this open-label, phase 2 randomised controlled trial, patients with NSCLC who progressed on post-platinum chemotherapy were recruited in 61 academic medical centres and community oncology practices across 13 countries in Europe and North America. Key inclusion criteria were Eastern Cooperative Oncology Group performance status 0 or 1, measurable disease by Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1), and adequate haematological and end-organ function. Patients were stratified by PD-L1 tumour-infiltrating immune cell status, histology, and previous lines of therapy, and randomly assigned (1:1) by permuted block randomisation (with a block size of four) using an interactive voice or web system to receive intravenous atezolizumab 1200 mg or docetaxel 75 mg/m² once every 3 weeks. Baseline PD-L1 expression was scored by immunohistochemistry in tumour cells (as percentage of PD-L1-expressing tumour cells TC3≥50%, TC2≥5% and <50%, TC1≥1% and <5%, and TC0<1%) and tumour-infiltrating immune cells (as percentage of tumour area: IC3≥10%, IC2≥5% and <10%, IC1≥1% and <5%, and IC0<1%). The primary endpoint was overall survival in the intention-to-treat population and PD-L1 subgroups at 173 deaths. Biomarkers were assessed in an exploratory analysis. We assessed safety in all patients who received at least one dose of study drug. This study is registered with ClinicalTrials.gov, number NCT01903993.

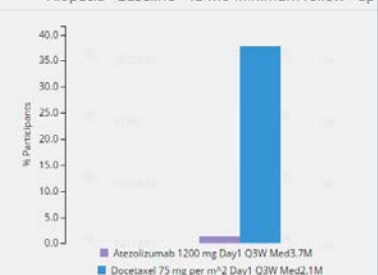
Findings: Patients were enrolled between Aug 5, 2013, and March 31, 2014. 144 patients were randomly allocated to the atezolizumab group, and 143 to the docetaxel group. 142 patients received at least one dose of atezolizumab and 135 received docetaxel. Overall survival in the intention-to-treat population was 12.6 months (95% CI 9.7–16.4) for atezolizumab versus 9.7 months (8.6–12.0) for docetaxel (hazard ratio [HR] 0.73 [95% CI 0.53–0.99]; $p=0.04$). Increasing improvement in overall survival was associated with increasing PD-L1 expression (TC3 or IC3 HR 0.49 [0.22–1.07]; $p=0.068$), TC2/3 or IC2/3 HR 0.54 [0.33–0.89]; $p=0.014$), TC1/2/3 or IC1/2/3 HR 0.59 [0.40–0.85]; $p=0.005$), TC0 and IC0 HR 1.04 [0.62–1.75]; $p=0.871$). In our exploratory analysis, patients with pre-existing immunity, defined by high T-effector-interferon- γ -associated gene expression, had improved overall survival with atezolizumab. 11 (8%) patients in the atezolizumab group discontinued because of adverse events versus 30 (22%) patients in the docetaxel group. 16 (11%) patients in the atezolizumab group versus 52 (39%) patients in the docetaxel group had treatment-related grade 3–4 adverse events, and one (<1%) patient in the atezolizumab group versus three (2%) patients in the docetaxel group died from a treatment-related adverse event.

Interpretation: Atezolizumab significantly improved survival compared with docetaxel in patients with previously treated NSCLC. Immune cells and tumour-infiltrating immune cells, suggesting that PD-L1 expression is predictive for atezolizumab benefit. Atezolizumab was well tolerated.

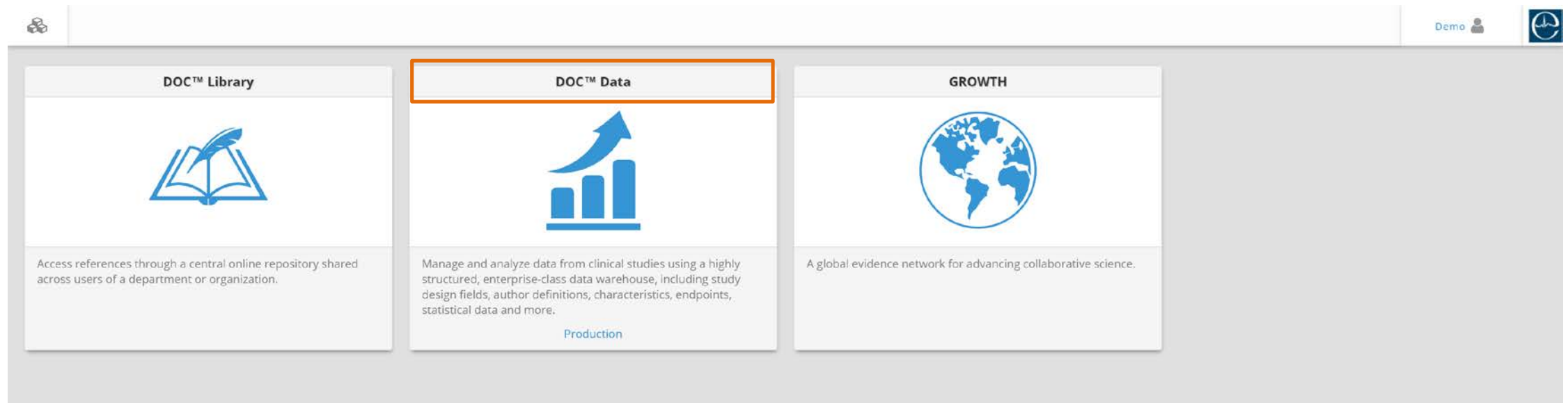
Funding: F Hoffmann–La Roche/Genentech Inc.

Adverse Event		Atezolizumab 1200 mg Day1 Q3W Med3.7M (N = 144)	Docetaxel 75 mg per m ² Day1 Q3W Med2.1M (N = 143)	
Acute Respiratory Distress Syndrome. Treatment-related. Grade = 5	Baseline - 13 mo Minimum follow-up	1 (0.7%)	NR	Int
Adverse Events	Baseline - 13 mo Minimum follow-up	1354	1325	Int
Adverse Events	Baseline - 13 mo Minimum follow-up	136 (96%)	130 (96%)	Int
Adverse Events, Grade 3-4	Baseline - 13 mo Minimum follow-up	57 (40%)	71 (53%)	Int
Adverse Events, Grade = 5	Baseline - 13 mo Minimum follow-up	6 (4%)	5 (4%)	Int
Adverse Events, Leading to Dose Modification or Interruption	Baseline - 13 mo Minimum follow-up	34 (24%)	44 (33%)	Int
Adverse Events, Leading to withdrawal from treatment	Baseline - 13 mo Minimum follow-up	11 (8%)	30 (22%)	Int
Adverse Events, Serious	Baseline - 13 mo Minimum follow-up	50 (35%)		Int
Adverse Events, Treatment-Related	Baseline - 13 mo Minimum follow-up	95 (67%)		Int

Alopecia - Baseline - 13 mo Minimum follow-up



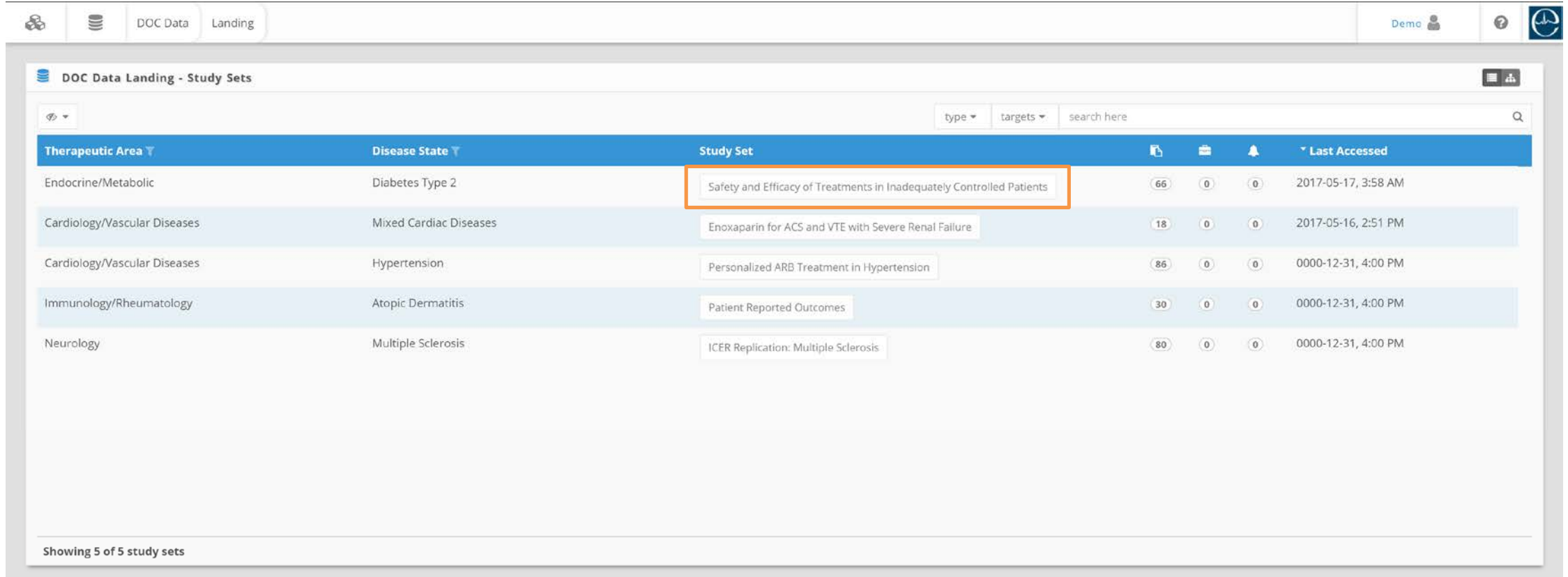
DOC Data Navigation: **ALLOWS YOU TO LAUNCH ANY DOC APPLICATION**



To log in to DOC Data, navigate to <https://sanofi.doctorevidence.com>. Please note that Chrome is the recommended browser.

DOC Data Navigation

LANDING PAGE: **ALLOWS YOU TO LAUNCH ANY STUDY SET**



DOC Data Landing - Study Sets

type targets search here

Therapeutic Area	Disease State	Study Set				Last Accessed
Endocrine/Metabolic	Diabetes Type 2	Safety and Efficacy of Treatments in Inadequately Controlled Patients	66	0	0	2017-05-17, 3:58 AM
Cardiology/Vascular Diseases	Mixed Cardiac Diseases	Enoxaparin for ACS and VTE with Severe Renal Failure	18	0	0	2017-05-16, 2:51 PM
Cardiology/Vascular Diseases	Hypertension	Personalized ARB Treatment in Hypertension	86	0	0	0000-12-31, 4:00 PM
Immunology/Rheumatology	Atopic Dermatitis	Patient Reported Outcomes	30	0	0	0000-12-31, 4:00 PM
Neurology	Multiple Sclerosis	ICER Replication: Multiple Sclerosis	80	0	0	0000-12-31, 4:00 PM

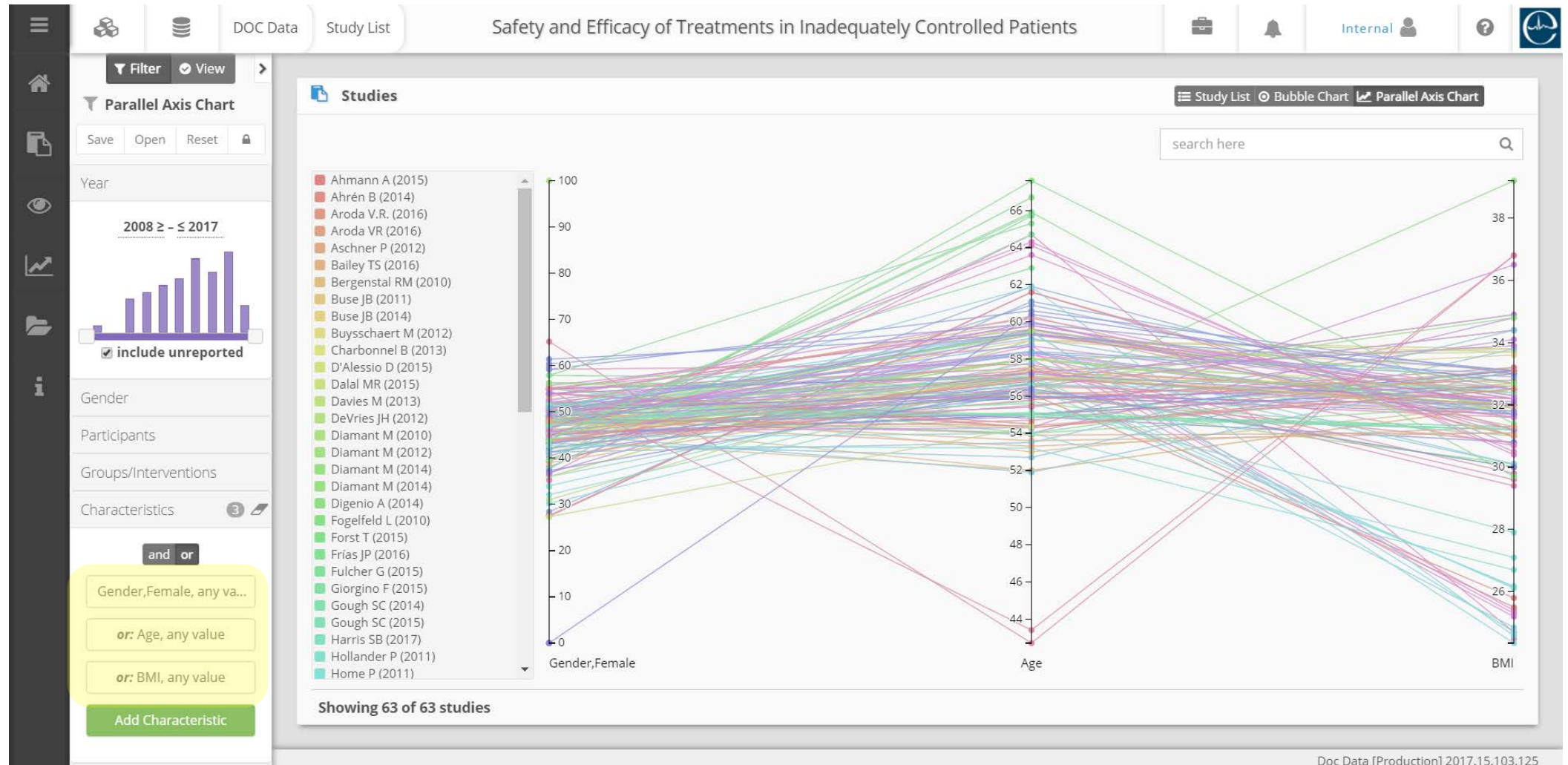
Showing 5 of 5 study sets

Sample Research Question ACTIVITY

- Does Insulin Glargine effectively reduce HbA1c in patients with the following profile?
 - Age, ≥ 50
 - BMI, ≤ 35
 - Race, Caucasian, $\geq 70\%$
 - Gender Female, 40% to 60%

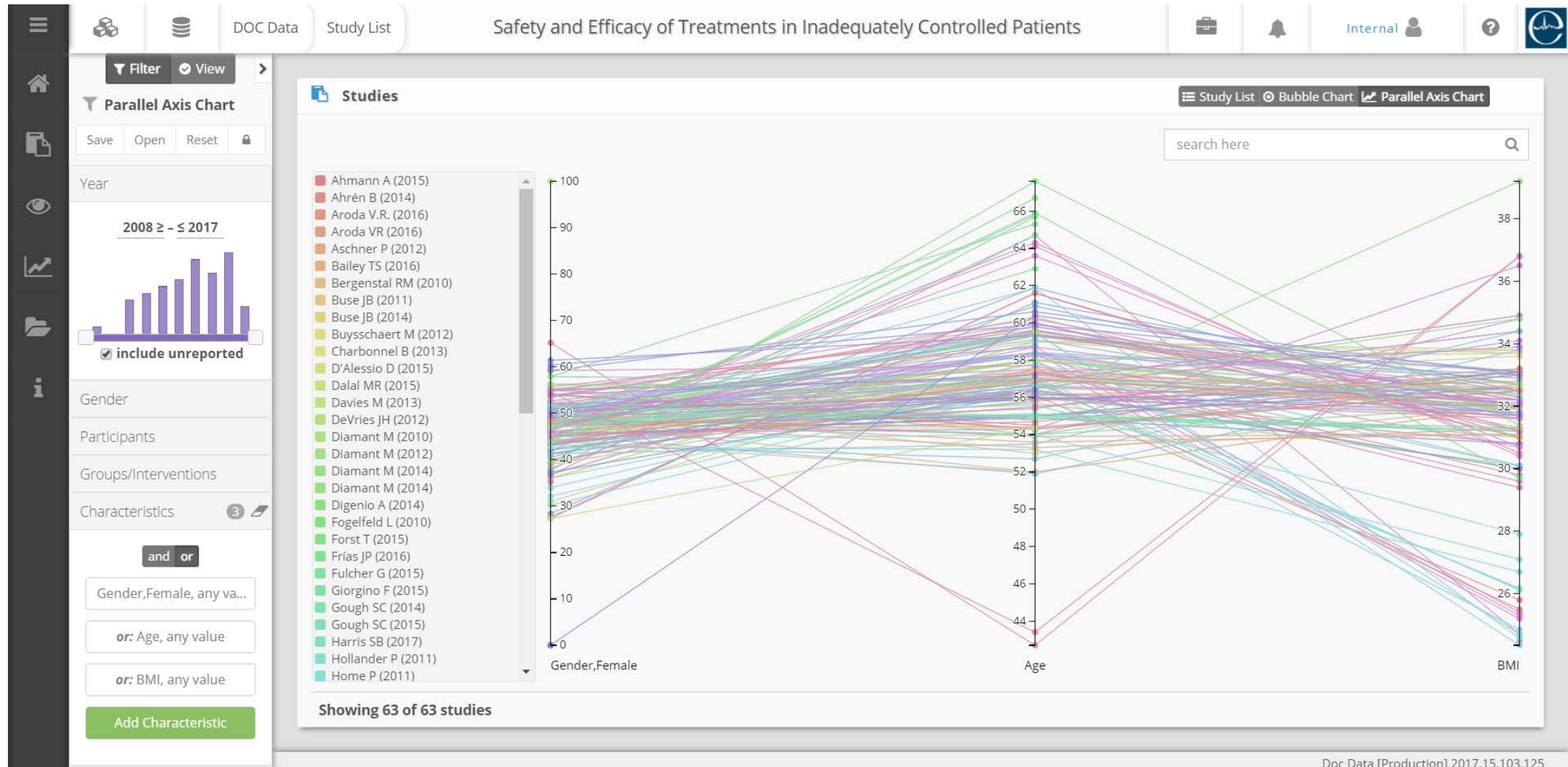
Descriptive Statistics & Visualizations: Using the Parallel Axis Chart

DOC Data – Parallel Axis Chart – Demo



Doc Data [Production] 2017.15.103.125

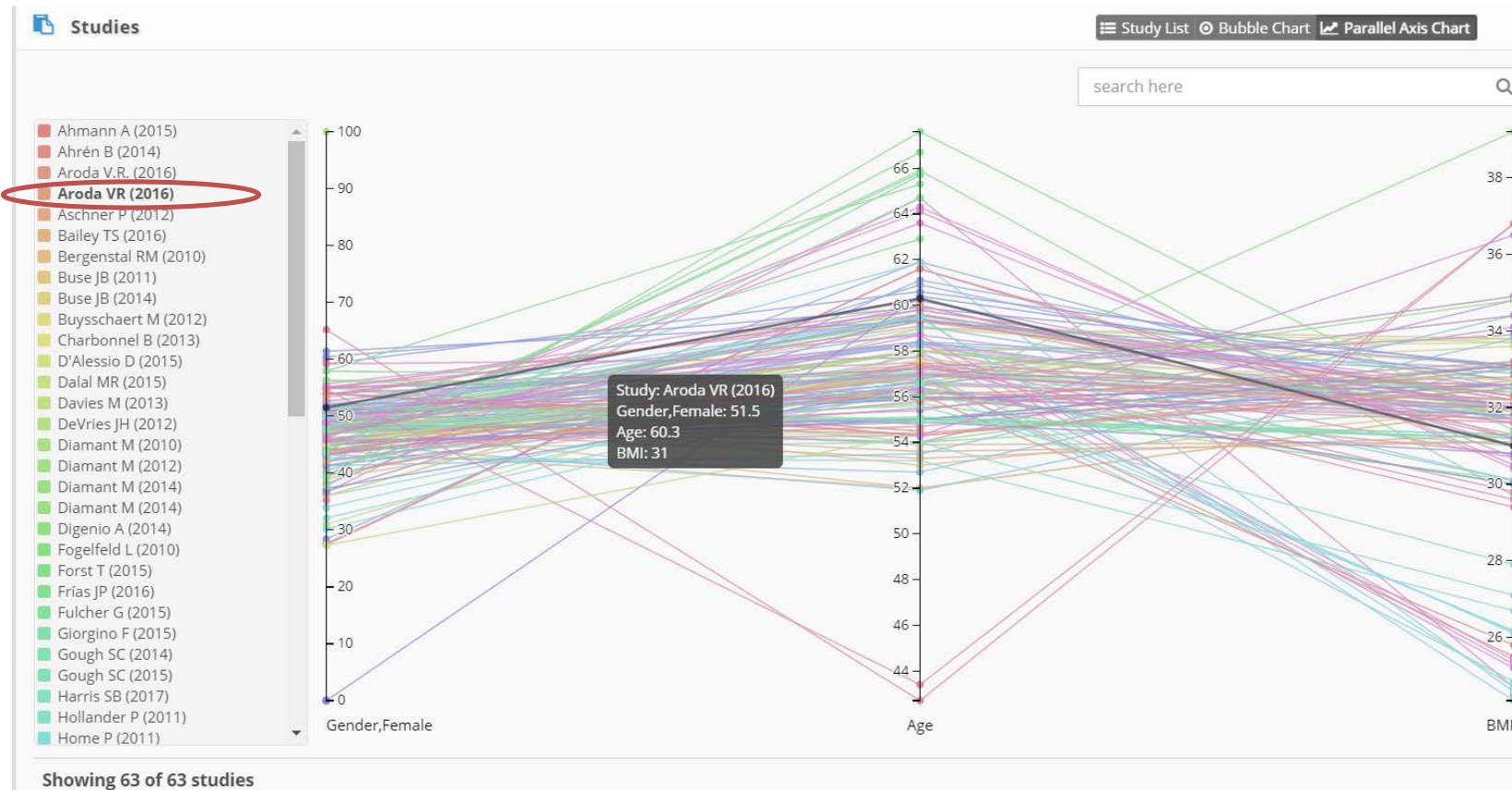
DOC Data – Parallel Axis Chart



This example added [Gender, Female], [Age], and [BMI]

DOC Data – Parallel Axis Chart

Each line represents a study. Hovering over it will bold it across the chart. You can access the study summary by selecting the study on the left bar



Parallel Axis ACTIVITY

1. Select ranges for the following:

- Age, ≥ 50
- BMI, ≤ 35
- Race, Caucasian, $\geq 70\%$
- Gender Female, 40% to 60%

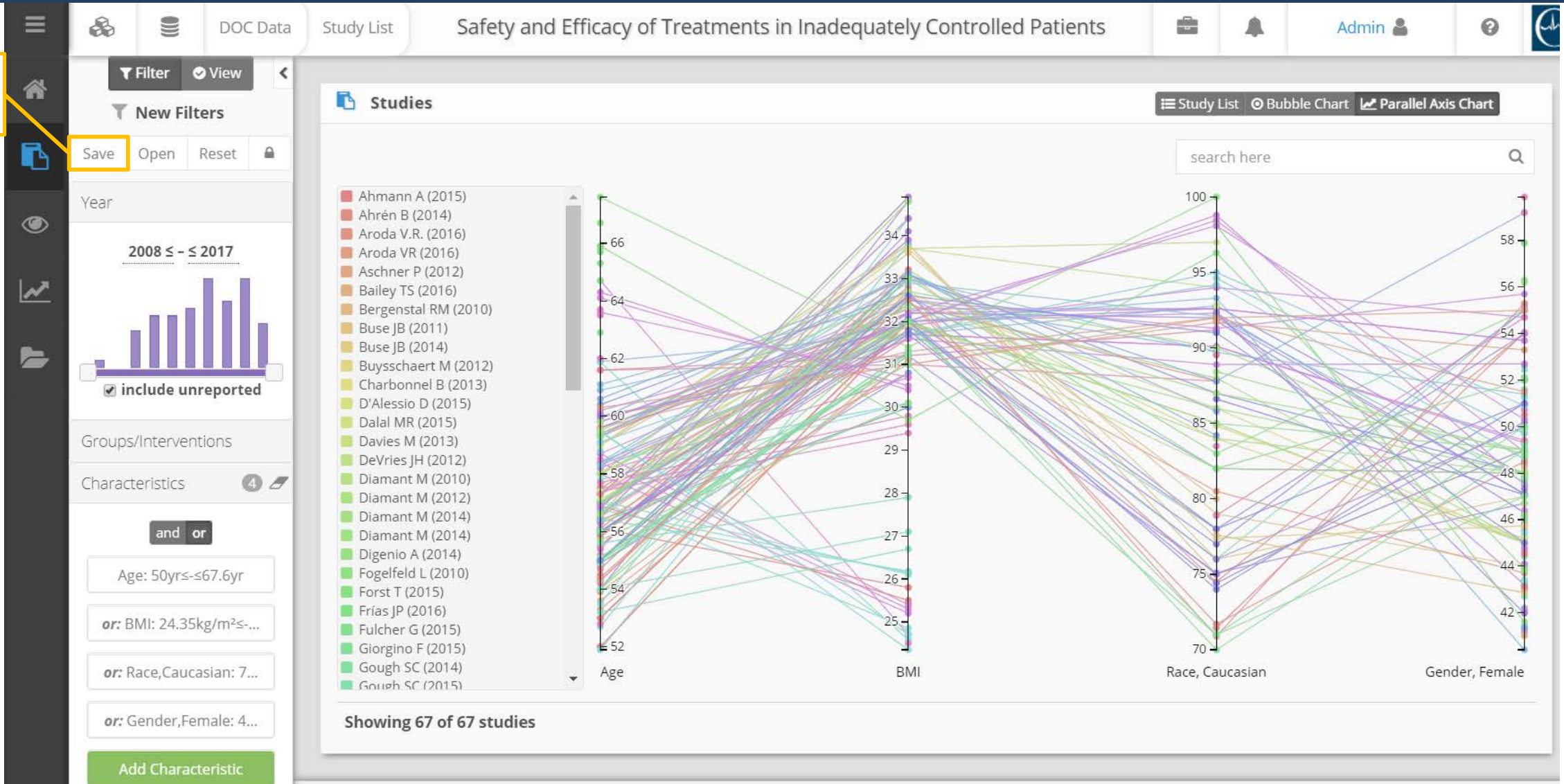
2. Save the filter set as a workflow so that it can be opened in other tools

Clue

59/66 studies Selection: Gender,Female

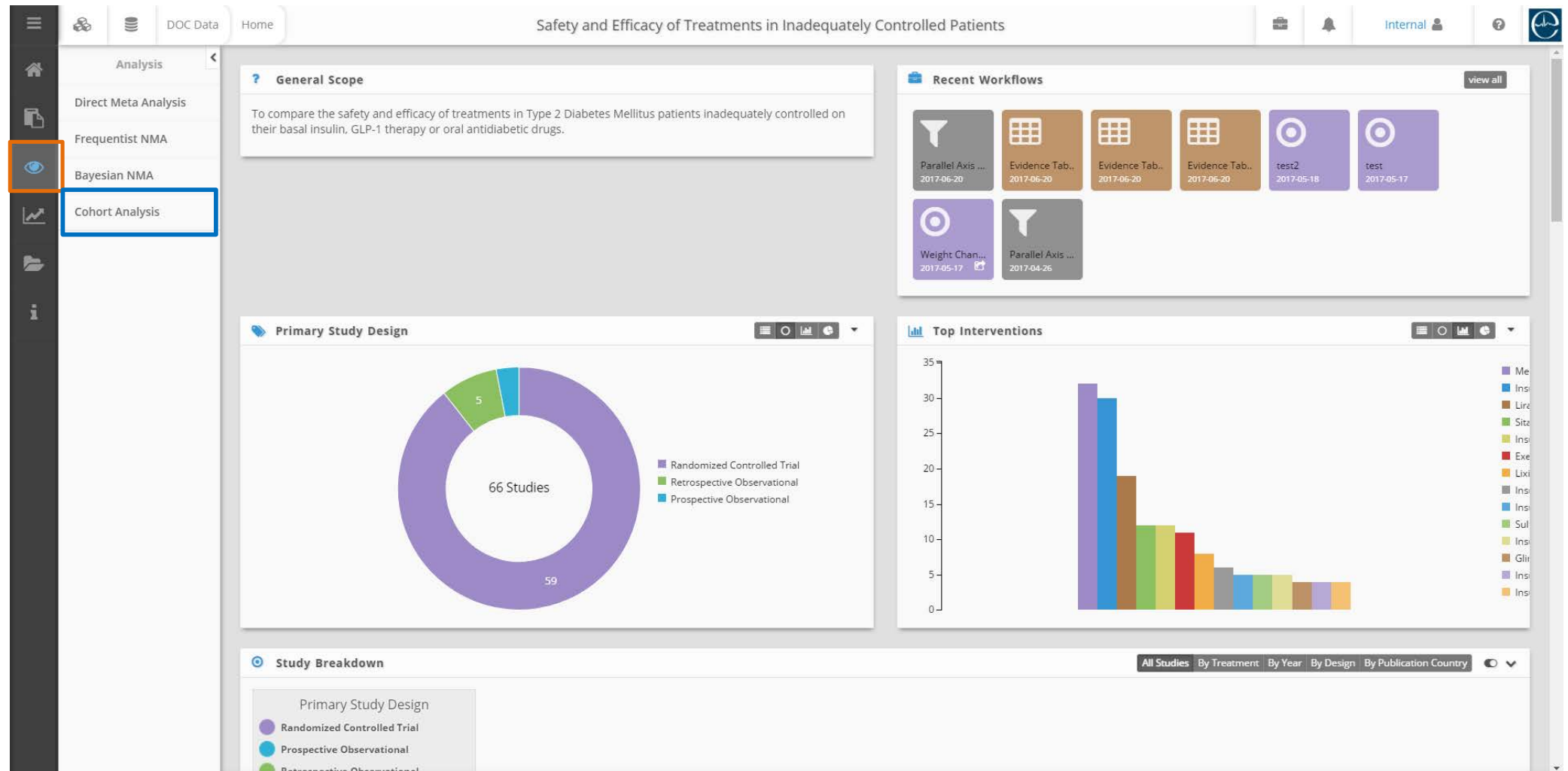
Parallel Axis ACTIVITY – output

Save this patient profile as a filter set



DOC Data: **Cohort Analysis**

Cohort Analysis

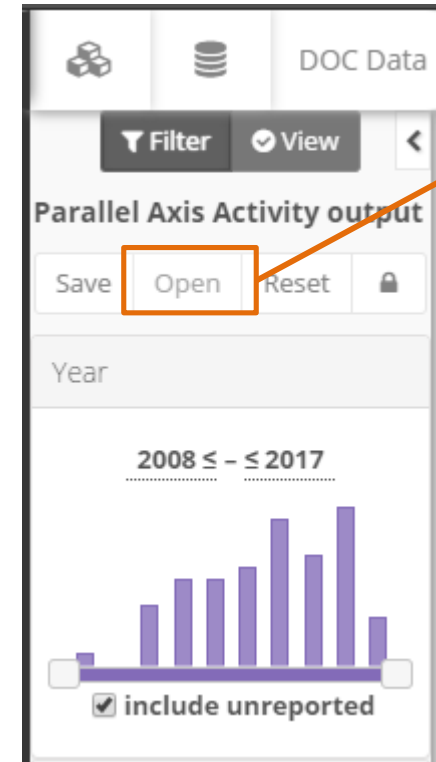


Cohort Analysis ACTIVITY

Does Insulin Glargine reduce HbA1c for patients with following profile?

- Age, ≥ 50
- BMI, ≤ 35
- Race, Caucasian, $\geq 70\%$
- Gender Female, 40% to 60%

Clue



Cohort Analysis – Demo

Does Insulin Glargine Reduce HbA1c?

The screenshot displays the 'Cohort Analysis Wizard' interface within a software application. The main title bar reads 'Safety and Efficacy of Treatments in Inadequately Controlled Patients'. The wizard is currently on the 'Filters' step, with tabs for 'Filters', 'Groups', 'Outcomes', 'Settings', and 'Results'. The 'Filters' section is divided into three main areas: 'Analysis Type', 'Groups', and 'Outcomes'. Under 'Analysis Type', 'Continuous' is selected. Under 'Groups', a green checkmark indicates that additional groups can be added using the filters sidebar. Under 'Outcomes', a green checkmark indicates that additional outcomes can be added using the filters sidebar. On the left sidebar, the 'New Filters' section shows a bar chart for the year range '2008 ≤ - ≤ 2017' and a checkbox for 'include unreported'. Below this, the 'Groups/Interventions' section has a text input 'Insulin Glargine' and an 'Add Group' button. The 'Outcomes' section has a text input 'HbA1c: any value' and an 'Add Outcome' button. At the bottom right, a 'Next' button is visible.

DOC Data Cohort Analysis Safety and Efficacy of Treatments in Inadequately Controlled Patients

Filter View

New Filters

Save Open Reset

Year

2008 ≤ - ≤ 2017

include unreported

Groups/Interventions

and or

Insulin Glargine

Add Group

Characteristics

Outcomes

and or

HbA1c: any value

Add Outcome

Study Level

Study

Participants

Design

Cohort Analysis Wizard:

Configuration Save Open Clear

Filters Groups Outcomes Settings Results

Analysis Type

Continuous Analysis

Groups

Additional groups may be added using the filters sidebar.

Outcomes

Additional outcomes may be added using the filters sidebar.

Next

Cohort Analysis – Groups

Does Insulin Glargine Reduce HbA1c?

The screenshot displays the 'Cohort Analysis Wizard: HbA2c, Change' interface. The top navigation bar shows 'Filters', 'Groups', 'Outcomes', 'Settings', and 'Results'. The 'Groups' tab is active, showing a list of study groups. The sidebar on the left contains filters for 'Year' (2008 ≤ - ≤ 2017), 'Groups/interventions' (1), and 'Outcomes' (1). The main panel lists 37 groups, with 15 selected. The groups are organized into a table with columns for 'Group', 'Number of groups', and 'Randomized Controlled Trial'.

Group	Number of groups	Randomized Controlled Trial
<input type="checkbox"/> Aroda VR (2016)	2 groups	Randomized Controlled Trial
<input type="checkbox"/> Insulin Glargine		
<input type="checkbox"/> iGlarLixi (Metformin)		
<input checked="" type="checkbox"/> Aschner P (2012)	1 group	Randomized Controlled Trial
<input checked="" type="checkbox"/> Insulin Glargine (Metformin)		
<input type="checkbox"/> Buse JB (2011)	2 groups	Randomized Controlled Trial
<input type="checkbox"/> Insulin Glargine		
<input type="checkbox"/> Insulin Glargine (Exenatide)		
<input checked="" type="checkbox"/> D'Alessio D (2015)	2 groups	Randomized Controlled Trial
<input checked="" type="checkbox"/> Insulin Glargine (Metformin/Sulfonylurea)		
<input type="checkbox"/> Liraglutide (Metformin/Sulfonylurea)		
<input checked="" type="checkbox"/> Diamant M (2010)	2 groups	Randomized Controlled Trial
<input type="checkbox"/> Insulin Glargine (Metformin/Sulfonylurea) (Pooled)		

Showing 37 of 37 groups 15 selected

Previous Next

Cohort Analysis – Outcomes

Does Insulin Glargine Reduce HbA1c?

DOC Data Cohort Analysis Safety and Efficacy of Treatments in Inadequately Controlled Patients

Filter View

New Views Save Open Reset

Characteristics and or Add Characteristic

Study Level

Cohort Analysis Wizard: Configuration Save Open Clear

Filters Groups Outcomes Settings Results

CSV Add Custom Data contains fields search here

Study	Outcome	Time	MoA	Full Value	Unit
<input checked="" type="checkbox"/> Aschner P (2012)	HbA1c, Change	Baseline - <=24 Weeks	Intent To Trea...	-1.72 (± 0.06)	%
<input checked="" type="checkbox"/> D'Alessio D (2015)	HbA1c, Change	Baseline - 24 wk	Intent To Treat (ITT)-LOCF; Adjusted	-1.79 (± 0.05)	%
<input checked="" type="checkbox"/> D'Alessio D (2015)	HbA1c, Change	Baseline - 24 wk	Intent To Treat (ITT)-LOCF; Adjusted	-1.94 (± 0.05)	%
<input checked="" type="checkbox"/> Diamant M (2010)	HbA1c, Change	Baseline - 26 wk	Intent To Treat (ITT) Modified	-1.4 (± 0.07)	%
<input type="checkbox"/> Diamant M (2012)	HbA1c, Change	Baseline - 84 wk	Intent To Treat (ITT)	-1 (± 0.1)	%
<input type="checkbox"/> Diamant M (2014)	HbA1c, Change	Baseline - 3 yr	Intent To Treat (ITT) Modified	-0.81 (± 0.07)	%
<input checked="" type="checkbox"/> Giorgino F (2015)	HbA1c, Change	Baseline - 52 wk	Intent To Trea...	-0.63 (± 0.06)	%
<input checked="" type="checkbox"/> Inagaki N (2012)	HbA1c, Change	Baseline - 26 wk	Intent To Trea...	-0.69 (± 0.06)	%
<input checked="" type="checkbox"/> Lingvay I (2016)	HbA1c, Change	Baseline - 26 wk	Intent To Trea...	-1.13 (± 0.98) [95% CI: -1.25 - -1.02]	%

Showing 13 of 13 entries 11 selected

Previous Next

Cohort Analysis – Settings

Does Insulin Glargine Reduce HbA1c?

The screenshot displays the 'Cohort Analysis Wizard' interface. At the top, there's a navigation bar with 'DOC Data' and 'Cohort Analysis' tabs. The main title is 'Safety and Efficacy of Treatments in Inadequately Controlled Patients'. Below this, the 'Cohort Analysis Wizard' section has a breadcrumb trail: 'Filters > Groups > Outcomes > Settings > Results'. The 'Settings' tab is active. It contains two input fields: 'Intervention' with the value 'Insulin Glargine' and 'Outcome' with the value 'HbA1c, Change'. Below these fields is a large empty text area. At the bottom left is a 'Previous' button and at the bottom right is a 'Next' button.

DOC Data Cohort Analysis

Safety and Efficacy of Treatments in Inadequately Controlled Patients

Internal

Cohort Analysis Wizard: Configuration Save Open Clear

Filters > Groups > Outcomes > Settings > Results

Intervention

Generated: Insulin Glargine (Metformin); Insulin Glargine (Biguanide/Thiazolidine Derivative); Insulin Glargine (Metformin/Thiazolidinedione); Insulin Glargine (Metformin/Sulfonylurea); Liraglutide (Metformin/Sulfonylurea); Insulin Glargine (Metformin/Glimepiride)

Insulin Glargine

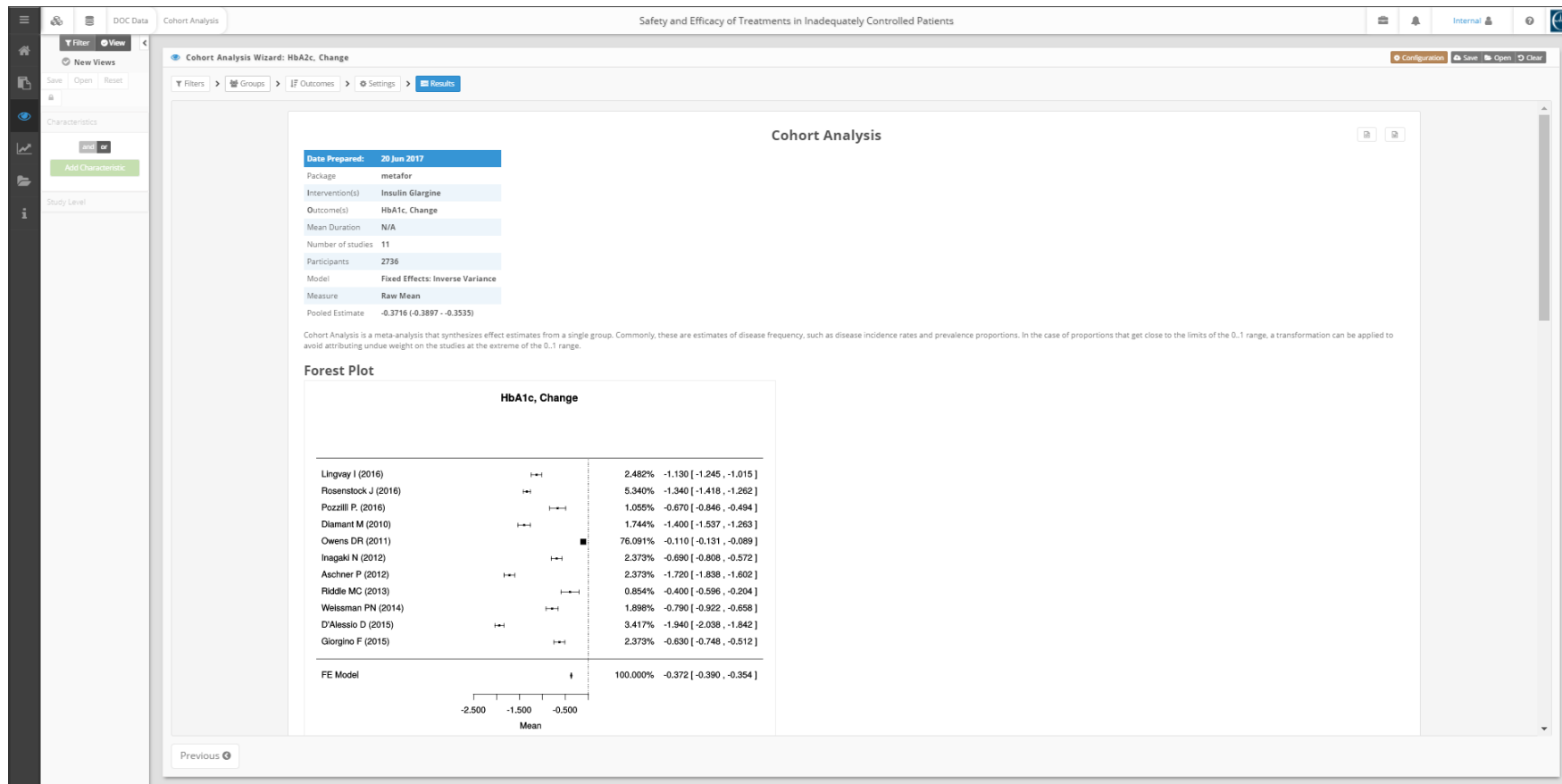
Outcome

HbA1c, Change

Previous Next

Cohort Analysis – Results

Does Insulin Glargine Reduce HbA1c?



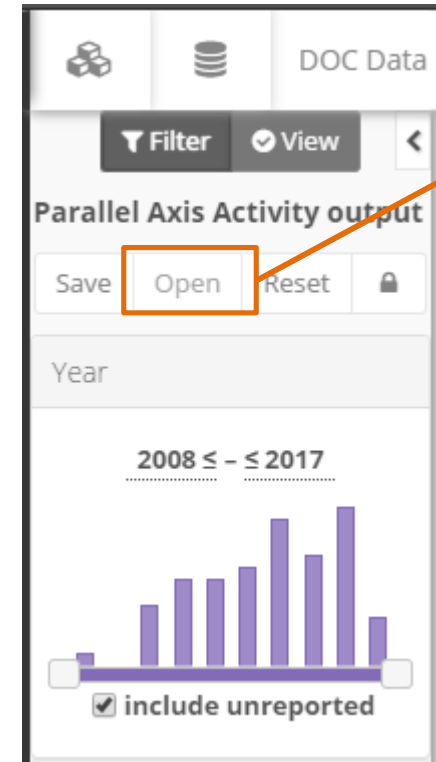
Independent Activity: **Cohort Analysis**

Cohort Analysis INDEPENDENT ACTIVITY

Does Insulin Glargine reduce weight for patients with following profile?

- Age, ≥ 50
- BMI, ≤ 35
- Race, Caucasian, $\geq 70\%$
- Gender Female, 40% to 60%

Clue

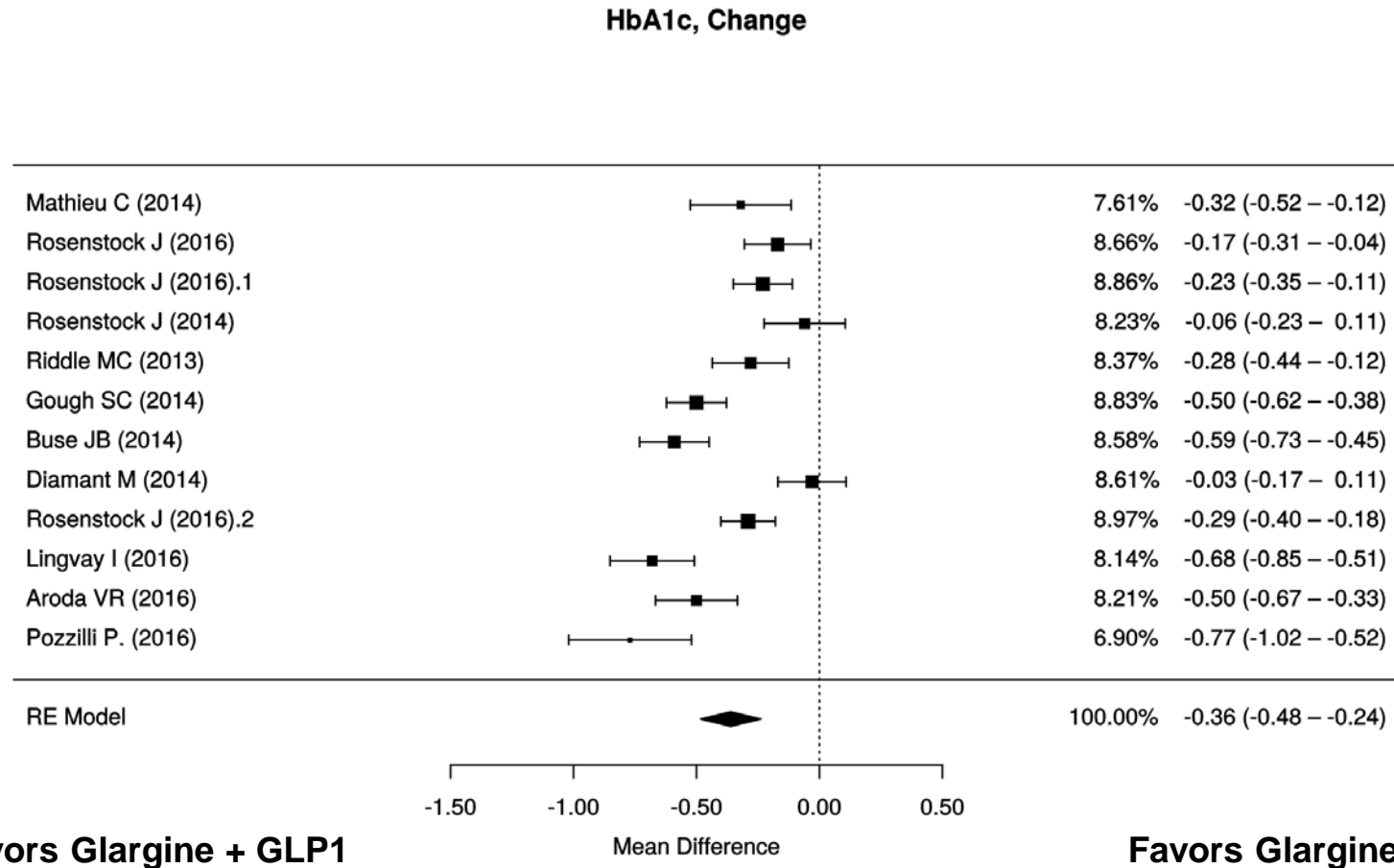


Profile saved in the parallel Axis tool

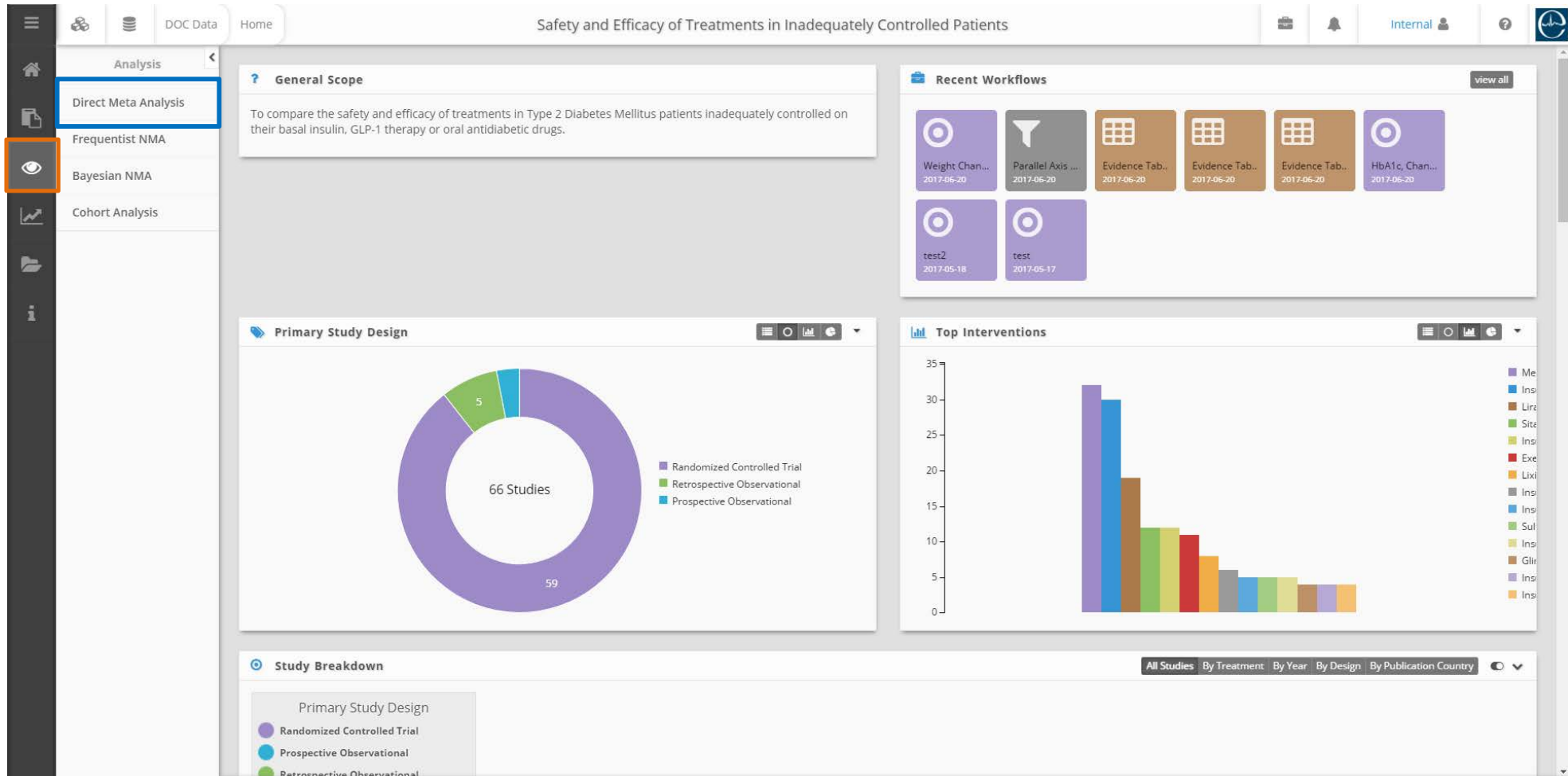
DOC Data: **Direct Meta-Analysis**

Direct Meta-Analysis

Comparative analysis, Glargine+GLP1 vs Glargine for reduction of HbA1c?



Direct Meta-Analysis – Demo



Direct Meta-Analysis – Demo

The screenshot displays the 'Direct Meta-Analysis Wizard' interface. The main title is 'Safety and Efficacy of Treatments in Inadequately Controlled Patients'. The wizard is currently in the 'Filters' step, with tabs for 'Filters', 'Comparisons', 'Outcomes', 'Settings', and 'Results'. The 'Filters' sidebar on the left includes a 'New Filters' section with 'Save', 'Open', and 'Reset' buttons. It also features a 'Year' filter with a bar chart showing data from 2008 to 2017, an 'include unreported' checkbox, and a 'Groups/Interventions' section with 'and/or' buttons and input fields for 'GLP-1 Receptor Agonist' and 'Insulin Analog', followed by an 'Add Group' button. Below this is a 'Characteristics' section with an 'Outcomes' subsection containing an 'and/or' button and an input field for 'HbA1c: any value', followed by an 'Add Outcome' button. The main area of the wizard shows three sections: 'Analysis Type' with a 'Continuous' dropdown and a 'Mean Difference (MD)' selection; 'Groups' with a green checkmark and the text 'Additional groups may be added using the filters sidebar.'; and 'Outcomes' with a green checkmark and the text 'Additional outcomes may be added using the filters sidebar.' A 'Next' button is located at the bottom right of the main area.

DOC Data Direct Meta Analysis Safety and Efficacy of Treatments in Inadequately Controlled Patients

Filter View

New Filters

Save Open Reset

Year

2008 ≤ - ≤ 2017

include unreported

Groups/Interventions

and/or

GLP-1 Receptor Agonist

Insulin Analog

Add Group

Characteristics

Outcomes

and/or

HbA1c: any value

Add Outcome

Study Level

Study

Participants

Meta Analysis Wizard:

Configuration Save Open Clear

Filters Comparisons Outcomes Settings Results

Analysis Type

Continuous Mean Difference (MD)

Groups

Additional groups may be added using the filters sidebar.

Outcomes

Additional outcomes may be added using the filters sidebar.

Next

Direct Meta-Analysis – Demo

The screenshot displays the 'Direct Meta-Analysis' software interface, specifically the 'Meta Analysis Wizard' window. The title bar indicates the analysis is for 'Safety and Efficacy of Treatments in Inadequately Controlled Patients'. The interface is divided into several sections:

- Left Sidebar:** Contains navigation icons and a 'New Filters' section. A bar chart shows the distribution of studies by year (2008 to 2017). Below the chart, there are checkboxes for 'Include unreported' and 'Groups/Interventions'. The 'Characteristics' section includes a table with columns for 'GLP-1 Receptor Agonist' and 'Insulin Analog', with an 'Add Group' button. The 'Outcomes' section includes a table with columns for 'HbA1c: any value' and an 'Add Outcome' button. The 'Study Level' section includes a table with columns for 'Study' and 'Participants'.
- Meta Analysis Wizard:** The main workspace, currently on the 'Comparisons' tab. It features a search bar at the top right. Below the search bar, there is a table with columns for 'Intervention Group' and 'Comparator Group'. The table lists various studies and their corresponding treatments, with checkboxes for selection. A 'Randomized Controlled Trial' label is present next to each row. The bottom of the wizard shows 'Showing 34 of 34 pairs' and a '13 selected' indicator. Navigation buttons 'Previous' and 'Next' are located at the bottom.

Intervention Group	Comparator Group
Aroda V.R. (2016) 1 pair	Insulin Degludec + Liraglutide (Metformin)
Liraglutide (Metformin)	Insulin Degludec + Liraglutide (Metformin)
Aroda VR (2016) 1 pair	Insulin Glargine
iGlarLixi (Metformin)	Insulin Glargine
Buse JB (2011) 1 pair	Insulin Glargine
Insulin Glargine (Exenatide)	Insulin Glargine
Buse JB (2014) 1 pair	Insulin Degludec (Metformin)
iDegLira (Metformin)	Insulin Degludec (Metformin)
D'Alessio D (2015) 1 pair	Insulin Glargine (Metformin/Sulfonylurea)
Liraglutide (Metformin/Sulfonylurea)	Insulin Glargine (Metformin/Sulfonylurea)
Diamant M (2010) 4 pairs	Insulin Glargine (Metformin/Sulfonylurea) (Pooled)
Exenatide 2 mg qw 26wk (++) Metformin +/- Sulfonylurea (Pooled)	Insulin Glargine (Metformin)
Exenatide 2 mg qw 26wk (++) Metformin	Insulin Glargine (Metformin)

Direct Meta-Analysis – Demo

DOC Data Direct Meta Analysis Safety and Efficacy of Treatments in Inadequately Controlled Patients

Meta Analysis Wizard: GLP1 + Insulin vs Insulin HbA1c

Filters > Comparisons > Outcomes > Settings > Results

CSV Add Custom Data Moderator: None

Study	Outcome	Time	MoA	Intervention Full Value	Comparator Full Value	AM	Unit
<input checked="" type="checkbox"/> Diamant M (2014)	4 HbA1c, Change	Baseline - 30 wk	MMRM; Per Protocol(PP)	-1.13 (± 0.05) [95% CI: -1.24 - -1.03]	-1.1 (± 0.05) [95% CI: -1.2 - -1]	MD -0.04 [95% CI: -0.18 - 0.11]	%
<input checked="" type="checkbox"/> Gough SC (2014)	1 HbA1c, Change	Baseline - 26 wk		-1.9 (± 1.1)	-1.4 (± 1)	MD -0.47 [95% CI: -0.58 - -0.36]	%
<input type="checkbox"/> Gough SC (2015)	2 HbA1c, Change	Baseline - 52 wk	Intent To Treat (ITT)-LOCF	-1.84	-1.4	MD -0.46 [95% CI: -0.57 - -0.34]	%

Showing 13 of 13 entries 12 selected

Previous Next

Direct Meta-Analysis – Demo

The screenshot displays the 'Direct Meta-Analysis Wizard' interface. The title bar indicates the topic is 'Safety and Efficacy of Treatments in Inadequately Controlled Patients'. The wizard is currently on the 'Settings' tab, with other tabs being 'Filters', 'Comparisons', 'Outcomes', and 'Results'. The 'Intervention' section lists generated treatments: 'Generated: Liraglutide + Insulin Degludec (Metformin), IDegLira (Metformin), iGlarLixi (Metformin), Insulin Glargine + Exenatide (Metformin), Lixisenatide + Insulin Glargine (Metformin), Albiglutide + Insulin Glargine, Lixisenatide + Insulin Glargine (Metformin/Thiazolidinedione), Dulaglutide + Insulin Glargine (Metformin)'. A text input field contains 'GLP1+Insulin'. The 'Comparator' section lists generated treatments: 'Generated: Insulin Aspart + Insulin Degludec (Metformin), Insulin Degludec (Metformin), Insulin Glargine (Metformin), Insulin Lispro + Insulin Glargine (Metformin), Insulin Glulisine TID + Insulin Glargine (Metformin), Insulin Lispro + Insulin Glargine, Insulin Glargine (Metformin/Thiazolidinedione), Insulin Glargine'. A text input field contains 'Insulin'. The 'Outcome' section has a text input field containing 'HbA1c, Change'. Below this, there are two rows of settings: 'Display Statements' with 'Yes' and 'No' buttons, and 'Person Events' with '100' and '1000' buttons. At the bottom, there are 'Previous' and 'Next' navigation buttons.

Meta Analysis Wizard: GLP1 + Insulin vs Insulin HbA1c

Configuration Save Open Clear

Filters Comparisons Outcomes Settings Results

Intervention

Generated: Liraglutide + Insulin Degludec (Metformin), IDegLira (Metformin), iGlarLixi (Metformin), Insulin Glargine + Exenatide (Metformin), Lixisenatide + Insulin Glargine (Metformin), Albiglutide + Insulin Glargine, Lixisenatide + Insulin Glargine (Metformin/Thiazolidinedione), Dulaglutide + Insulin Glargine (Metformin)

GLP1+Insulin

Comparator

Generated: Insulin Aspart + Insulin Degludec (Metformin), Insulin Degludec (Metformin), Insulin Glargine (Metformin), Insulin Lispro + Insulin Glargine (Metformin), Insulin Glulisine TID + Insulin Glargine (Metformin), Insulin Lispro + Insulin Glargine, Insulin Glargine (Metformin/Thiazolidinedione), Insulin Glargine

Insulin

Outcome

HbA1c, Change

Display Statements Yes No

Person Events 100 1000

Previous Next

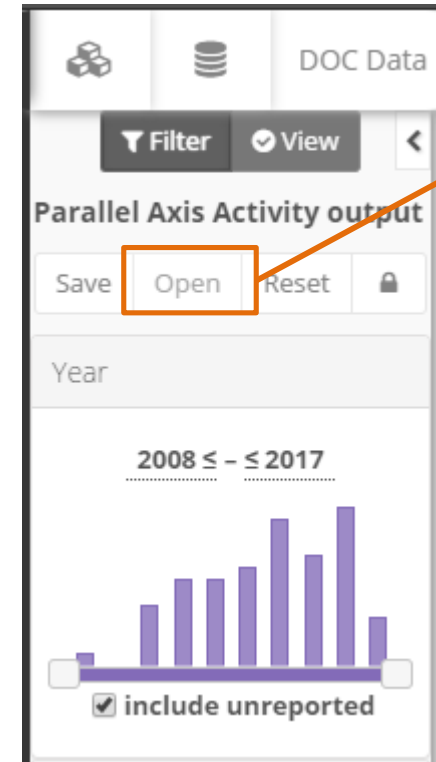
Independent Activity: **Direct Meta-Analysis**

Direct Meta-Analysis INDEPENDENT ACTIVITY

Comparative analysis, Glargine+GLP1 vs Glargine for change in weight?

- Age, ≥ 50
- BMI, ≤ 35
- Race, Caucasian, $\geq 70\%$
- Gender Female, 40% to 60%

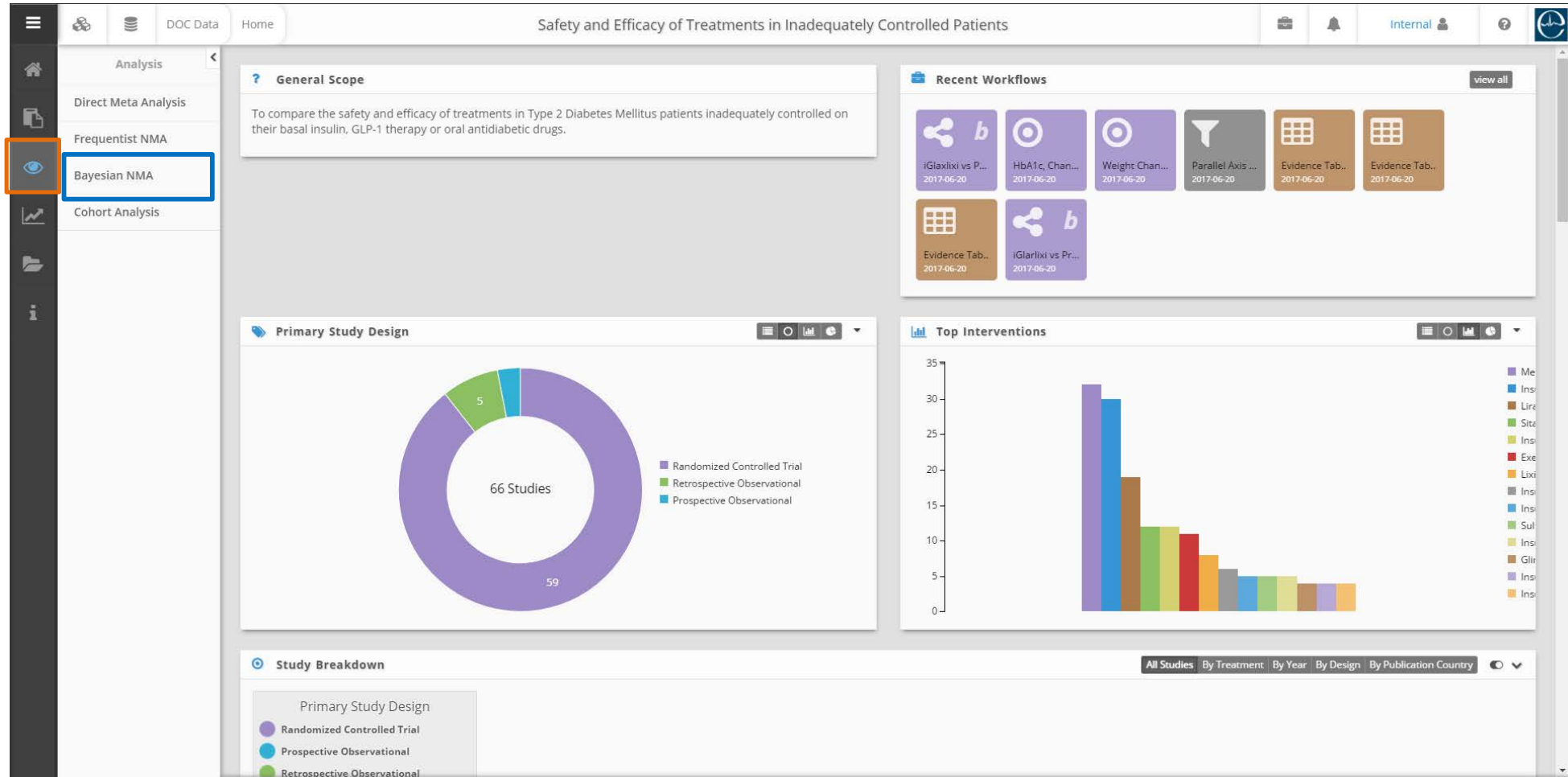
Clue



Profile saved in the parallel Axis tool

DOC Data: Bayesian Network Meta-Analysis

Bayesian NMA – Demo



Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarixi vs Premix, in patients who failed insulin?

The screenshot displays the 'Bayesian Analysis Wizard: iGlarixi vs Premix' interface. The main window is titled 'Safety and Efficacy of Treatments in Inadequately Controlled Patients'. The wizard is currently in the 'Filters' step, with tabs for 'Filters', 'Comparisons', 'Outcomes', 'Network', and 'Results'. The left sidebar contains filters for 'Year' (2008 ≤ - ≤ 2017), 'Groups/Interventions' (with 'and/or' and 'Add Group' buttons), 'Characteristics' (with 'and/or', 'Treatment Failure, Insu...', and 'Add Characteristic' buttons), and 'Outcomes' (with 'and/or', 'HbA1c: any value', and 'Add Outcome' buttons). The main content area shows three sections: 'Analysis Type' (Continuous, Mean Difference (MD)), 'Groups' (with a green checkmark and text 'Additional groups may be added using the filters sidebar'), and 'Outcomes' (with a green checkmark and text 'Additional outcomes may be added using the filters sidebar'). A 'Next' button is located at the bottom right.

Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarlixi vs Premix, in patients who failed insulin?

Safety and Efficacy of Treatments in inadequately controlled Patients

Edit Group Intervention / Comparator

Exclude Subgroups

Intervention

Any Order Exact Order Partial Order

Any Drug Class Zero or more interve... x Detailed Criteria

Any Drug Class Select intervention Detailed Criteria

Groups: Any Group

▼ Comparator

Any Order Exact Order Partial Order

Any Drug Class Select intervention Detailed Criteria

Groups: Any Group

> Exclude

Cancel Reset Save and Add Save Group Filter

Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarlix vs Premix, in patients who failed insulin?

Safety and Efficacy of Treatments in Inadequately Controlled Patients

Add Characteristic Criteria

Field Type Category search by name

Name	Attribute Type	Field Type	Unit	#	
<input type="checkbox"/> > Age #	Standard	Mixed	Mixed	63	
<input type="checkbox"/> > BMI #	Standard	Mixed	Mixed	62	
<input type="checkbox"/> > Treatment Failure #	Standard	Mixed	Mixed	61	
<input type="checkbox"/> > Oral Antidiabetic Treatment	Standard	Binary	%	33	
<input type="checkbox"/> > Metformin	Standard	Binary	%	26	
<input checked="" type="checkbox"/> > Insulin	Standard	Binary	%	25	
<input checked="" type="checkbox"/> > Basal	Standard	Binary	%	24	
<input checked="" type="checkbox"/> > only Basal	Standard	Binary	%	17	
<input checked="" type="checkbox"/> > Glargine	Standard	Binary	%	5	
<input checked="" type="checkbox"/> > or Metformin	Standard	Binary	%	1	

☐ Include unreported values

☒ Include composites ☐ exclude matching studies

Advanced Options

☒ Value

72 ≤ - ≤ 100 %

72

25/63 studies Selection: Treatment Failure,Insulin,Basal or Treatment Failure,In..

Cancel Save and Add Add Characteristic

Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarlix vs Premix, in patients who failed insulin?

Safety and Efficacy of Treatments in Inadequately Controlled Patients

Add Outcome Criteria

Field Type Category

<input type="checkbox"/>	Name	Attribute Type	Field Type	Unit	#	±	i
<input type="checkbox"/>	▼ HbA1c #	Mixed	Continuous	Mixed	25	-	i
<input checked="" type="checkbox"/>	only HbA1c	Change	Continuous	Mixed	24	-	i
<input type="checkbox"/>	only HbA1c	Standard	Continuous	Mixed	19	-	i
<input type="checkbox"/>	> Multiple Imputation	Change	Continuous		1	-	i
<input type="checkbox"/>	> Pattern Mixture Model 1	Change	Continuous		1	-	i
<input type="checkbox"/>	> Pattern Mixture Model 2	Change	Continuous		1	-	i
<input type="checkbox"/>	> Mixed Model	Change	Continuous		1	-	i
<input type="checkbox"/>	> Repeated Measure	Change	Continuous		1	-	i
<input type="checkbox"/>	> Glucose #	Mixed	Continuous	Mixed	22	-	i
<input type="checkbox"/>	> Weight #	Mixed	Continuous	kg	22	-	i
<input type="checkbox"/>	> Insulin #	Mixed	Continuous	Mixed	15		i
<input type="checkbox"/>	> Hypoglycemia #	Standard	Incidence	PPY	5	-	i
<input type="checkbox"/>	> Blood Pressure	Mixed	Continuous	mmHg	4	-	i
<input type="checkbox"/>	> BMI	Mixed	Continuous	kg/m ²	2	-	i
<input type="checkbox"/>	> Heart Rate	Mixed	Continuous	beats/min	2	-	i
<input type="checkbox"/>	> Cholesterol	Mixed	Continuous	mmol/L	1	±	i

☐ Include unreported values

☒ Include composites ☐ exclude matching studies

> Advanced Options

24/26 studies Selection: HbA1c

Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarlix vs Premix, in patients who failed insulin?

Bayesian Analysis Wizard: iGlarlix vs Premix

Configuration Save Open Clear

Filters > Comparisons > Outcomes > Network > Results

CSV contains fields iklar

Intervention Group	Comparator Group
<input checked="" type="checkbox"/> Aroda VR (2016) 1 pair	
<input checked="" type="checkbox"/> Insulin Glargine	<input checked="" type="checkbox"/> iGlarLixi (Metformin)

Randomized Controlled Trial

Bayesian Analysis Wizard: iGlarlix vs Premix

Configuration Save Open Clear

Filters > Comparisons > Outcomes > Network > Results

CSV contains fields o/

Intervention Group	Comparator Group
<input type="checkbox"/> Jin SM (2016) 1 pair	
<input type="checkbox"/> Insulin Glulisine + Insulin Glargine (Pooled)	<input checked="" type="checkbox"/> Insulin Aspart 70/30
<input checked="" type="checkbox"/> Ligthelm RJ (2011) 1 pair	
<input checked="" type="checkbox"/> Biphasic Insulin Aspart 70/30 (Metformin/Thiazolidinediones)	<input checked="" type="checkbox"/> Insulin Glargine (Metformin/Secretagogues/Thiazolidinediones)
<input type="checkbox"/> Rosenstock J (2008) 1 pair	
<input type="checkbox"/> Insulin Lispro + Insulin Glargine	<input checked="" type="checkbox"/> Insulin Lispro 50/50
<input type="checkbox"/> Vora J (2015) 1 pair	
<input type="checkbox"/> Biphasic Insulin Aspart 70/30	<input checked="" type="checkbox"/> Insulin Glargine + Insulin Glulisine

Randomized Controlled Trial

Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarlix vs Premix, in patients who failed insulin?

Bayesian Analysis Wizard: iGlarlix vs Premix

Configuration Save Open Clear

Filters > Comparisons > Outcomes > Network > Results

CSV Add Custom Data

contains fields search here

Study	Outcome	Time	MoA	Intervention Full Value	Comparator Full Value	AM	Unit
<input checked="" type="checkbox"/> Aroda VR (2016)	4 HbA1c, Change	Baseline - 30 wk	Intent To Treat (ITT) Modified	-0.6 (\pm 0.06)	-1.1 (\pm 0.06)	MD -0.5 [95% CI: -0.6 - -0.4] < 0.0001	%
<input checked="" type="checkbox"/> Ligthelm RJ (2011)	1 HbA1c, Change	Baseline - 24 wk	Intent To Trea...	-1.3	-1.2	MD -0.06 [95% CI: -0.32 - 0.2]	%

Bayesian NMA

What is the comparative reduction of HbA1c, with
iGlarlixi vs Premix, in patients who failed insulin?

Bayesian Analysis Wizard: iGlarlixi vs Premix

Configuration Save Open Clear

Filters Comparisons Outcomes Network Results

Network and label treatments

Please provide a short label for each of the treatments. The labels cannot contain special characters or spaces. Treatments with the same label are automatically grouped. Optionally, select a baseline treatment for which to calculate the relative effects.

Make sure all treatments are connected. You can (de)select the treatments by clicking the nodes. The size of the nodes indicates the sample size, the width of the edges the number of comparing studies.

Baseline treatment

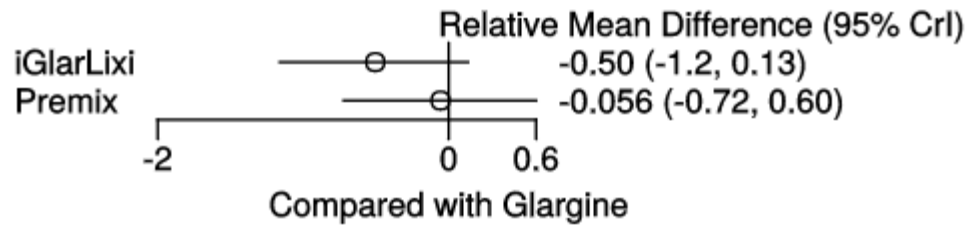
Glargine

Treatment	Label
Biphasic Insulin Aspart 70/30 (Metformin/Thiazolidinediones)	Premix
Insulin Glargine (Metformin/Secretagogues/Thiazolidinediones)	Glargine
iGlarLixi (Metformin)	iGlarLixi

```
graph TD; iGlarLixi --- Glargine; Glargine --- Premix;
```


Bayesian NMA

What is the comparative reduction of HbA1c, with iGlarlixi vs Premix, in patients who failed insulin?



The table below gives the cumulative probabilities of the ranks per treatment

	Rank 1	Rank 2	Rank 3
Glargine	0.022	0.43	1
iGlarLixi	0.86	0.96	1
Premix	0.11	0.6	1

Independent Activity: **Direct Meta-Analysis**

Direct Meta-Analysis

What is the efficacy of Glatiramer Acetate in treatment of Multiple Sclerosis based on a relapse outcome?

- P Patients with Relapsing-Remitting Multiple Sclerosis
- I Glatiramer Acetate
- C Placebo
- O # of patients who have relapses during follow-up

Independent Activity: **Bayesian NMA**

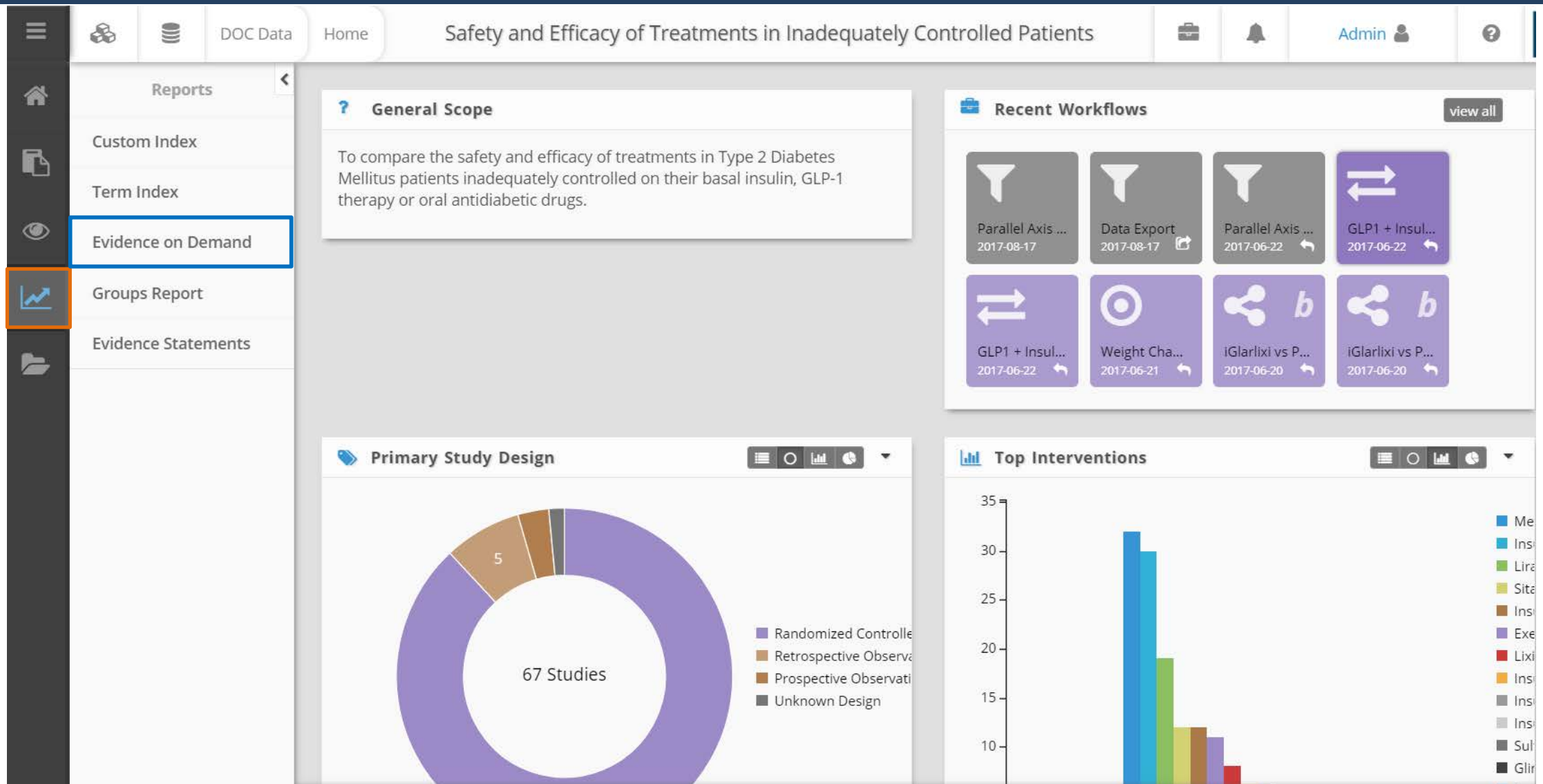
Direct Meta-Analysis

What is the comparative efficacy of non-antibody interventions in treatment of Multiple Sclerosis based on relapse outcome?

- **P:** Patients with Relapsing-Remitting Multiple Sclerosis
- **I:** Non-antibody interventions
 - Dimethyl Fumarate
 - Fingolimod
 - Glatiramer Acetate
 - Interferon Beta 1a
 - Interferon Beta-1b
 - Peginterferon Beta-1a
 - Teriflunomide
- **C:** All Interventions and Placebo
- **O:** # of patients who have relapses during follow-up

DOC Data: Evidence on Demand

Evidence on Demand – Demo



Evidence on Demand – Demo

DOC Data

Evidence on Demand

Safety and Efficacy of Treatments in Inadequately Controlled Patients

Admin

Evidence on Demand

All

Characteristics

Outcomes

Intervention

CSV

Expand All

search here

Unbound Names	Bound Name	Field Type	Collection Status	#	Studies
<div> <div>adverse events, serious</div> <div>Adverse Event, Serious</div> <div>Adverse Events, Serious, >= 1</div> <div>Adverse Events, Serious, > 2 participants</div> <div>Serious adverse event, >= 1</div> <div>Adverse Event, Serious, At least one</div> <div>serious adverse events</div> <div>Adverse Events, Serious, >=1</div> </div>	Adverse Events, Serious	Binary	Uncollected	32	29 Studies
Nausea	Nausea	Binary	Uncollected	31	5 Studies
<div> <div>Study Withdrawal</div> <div>Withdrawal</div> <div>discontinued study</div> <div>Study Withdrawal</div> </div>	Study Withdrawal	Binary	Uncollected	30	13 Studies

Showing 1193 of 1193 entries

DOC Data: Exploring Heterogeneity

Tools for Assessing Heterogeneity

- **Evidence Table Wizard**
- **Data Export Wizard**
- **Parallel Axis Chart**
- **Cohort Analysis**

DOC Data: **Analytic Sensitivity Dashboard**

Analytic Sensitivity Dashboard

See all variations of possible analyses



Sorted by Comparisons & Outcomes,
View graphical representations of studies OR
Click into different analyses to confirm selections and run!


Analytics Report

Group Interventions	Group Comparators	Comparisons	Direct Meta Analyses	Bayesian Analyses	Frequentist Analyses	Cohort Analyses	Studies
> Insulin, Glargine + Insulin, Lispro or Insulin, Aspart or Insulin, Insulin Glulisine	Insulin, Glargine + Insulin, Lispro or Insulin, Aspart or Insulin, Insulin Glulisine	2					
> Insulin, Lispro + Insulin, Glargine	Insulin, Lispro, Mix 50 + Insulin, Lispro, Mix 25	2					
▼ Insulin, Glargine	Non-Glargine Insulin	46					
▼ Cancer			13	13	13	4	8 Studies
Breast			5	5	5	0	6 Studies
Breast			5	5	5	0	3 Studies
Breast			3	3	3	4	2 Studies
> Insulin			0	0	0	7	1 Study


Initiating a Project

Requesting a Customized Library Package

<https://reports.doctorevidence.com/pages/Client/ServiceProject.aspx>

 **Sanofi DRE Service Project Initiation**

Date *



Name *


Department *

Location *

Email *

Phone # *

Requried By Date *



Question *

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DOC Data: Task-Tool Matrix

	Tools ↓	Task →	Understand body of evidence	Explore individual studies	Examine comparative efficacy/ safety	Answer epidemiology question	Explore heterogeneity	Conduct sensitivity analysis	Save & reuse work
	Home page								
	Study List								
	Data Export Tool								
	Evidence Table Wizard								
	Analysis: Direct Meta								
	Analysis: Freq. NMA								
	Analysis: Bayesian NMA								
	Analysis: Cohort								

DOC Data: Task-Tool Matrix

	Tools ↓	Task →	Understand body of evidence	Explore individual studies	Examine comparative efficacy/ safety	Answer epidemiology question	Explore heterogeneity	Conduct sensitivity analysis	Save & reuse work
	Reports: Term Index								
	Reports: EOD								
	Reports: "Other"								
	Evidence Value Statements								
	Workflow Management								
	Study Summary								
	Bubble Chart								
	Parallel Axis Chart								
	Filters								