ADDIS - uz pierādījumiem balstītu veselības aprūpes lēmumu pieņemšanas atbalsta sistēma

Kārlis Zālīte

Groningenas Universitātes Medicīnas centrs

#STATISTIKAI100

ADDIS - uz pierādījumiem balstītu veselības aprūpes lēmumu pieņemšanas atbalsta sistēma

Kārlis Zālīte, PhD

ADDIS?

- Aggregate Data Drug Information System
- ADDIS 1 (2009-2013)
  - Programmatūra lēmumu pieņemšanas atbalstam
  - Saikne starp klīniskajiem pētījumiem un lēmumiem
  - Pārsvarā domāta regulatoriem
- ADDIS 2 (2014-..)
  - Tīmekļa lietotne
  - Datu apmaiņa un cita papildus funkcionalitāte
- Atklātā pirmkoda programmatūra

addis.drugis.org | github.com/drugis

Mērķi

- Veicināt labāko metožu un prakšu izmantošanu
- Novērst atkārtošanos, iegūstot datus
- Viecināt caurskatāmību, atkārtojamību un koplietošanu

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Regulatoru darbībā

Mērķi

- Veicināt labāko metožu un prakšu izmantošanu
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Regulatoru darbībā

Veselības politikas veidošanā

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- Veicināt labāko metožu un prakšu izmantošanu
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Regulatoru darbībā

Veselības politikas veidošanā

Veselības aprūpes pakalpojumu sniedzējiem un pacientiem

Piemērs - zāļu reģistrācijas process

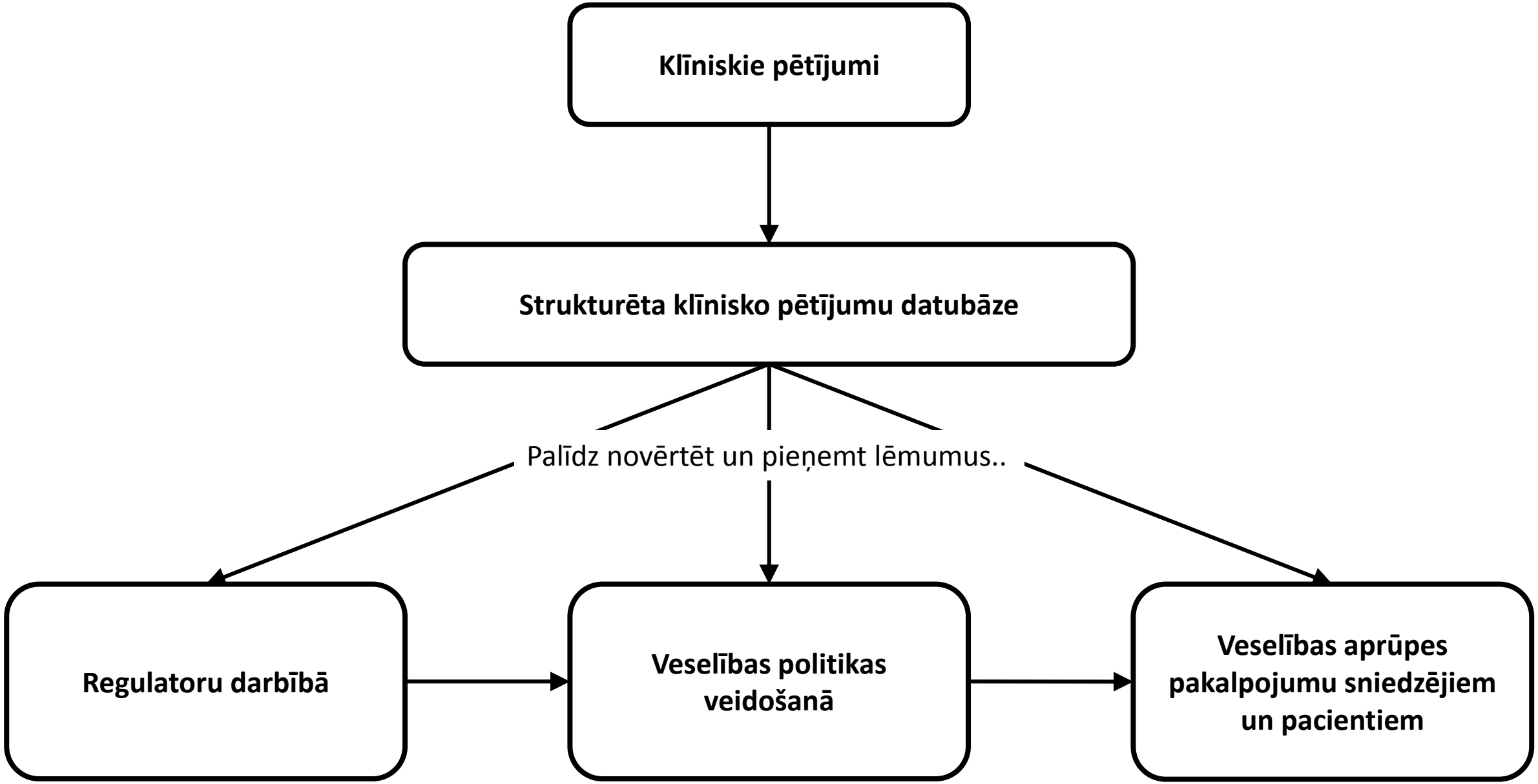
«A fair regulatory process requires accountability for reasonableness, i.e., publicity about the reasons and rationales that play a part in decisions»

(Daniels N, BMJ, 2000)

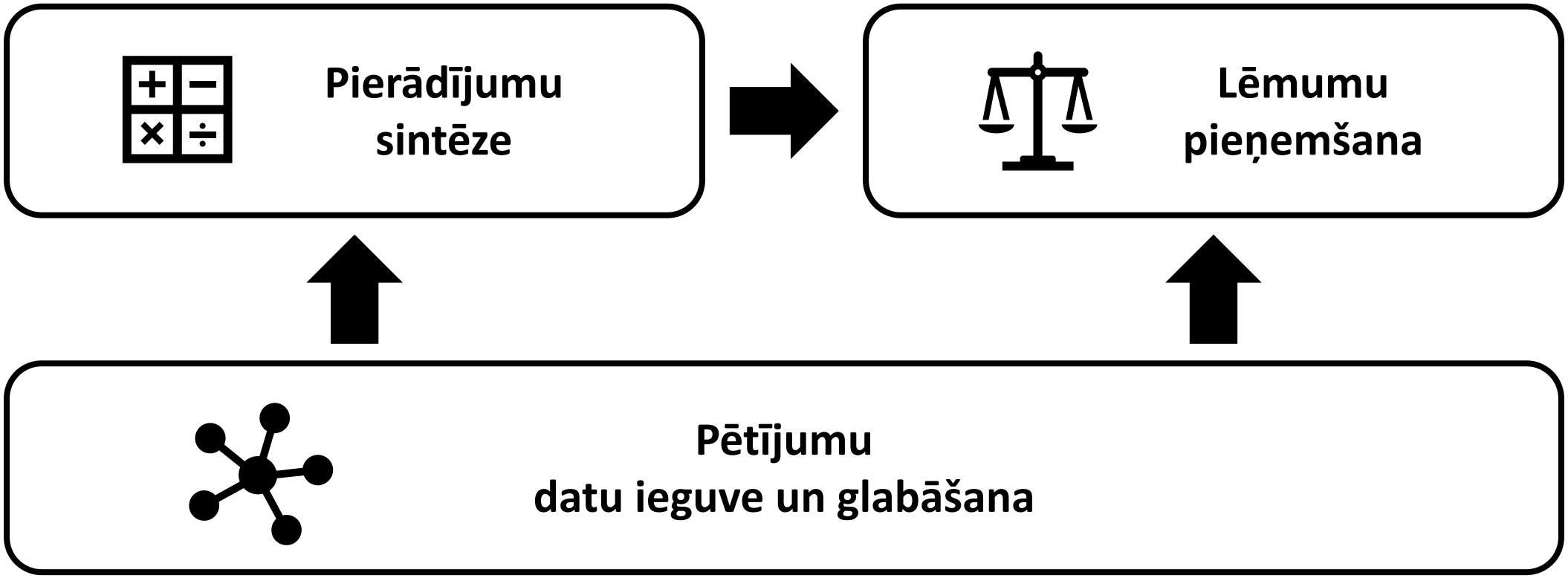
Piemērs - zāļu reģistrācijas process

«…it is seldom that preferences used in these decisions (i.e., acceptable trade-offs among the different benefits, risks, and other decision criteria) are adequately quantified and communicated, if at all.»

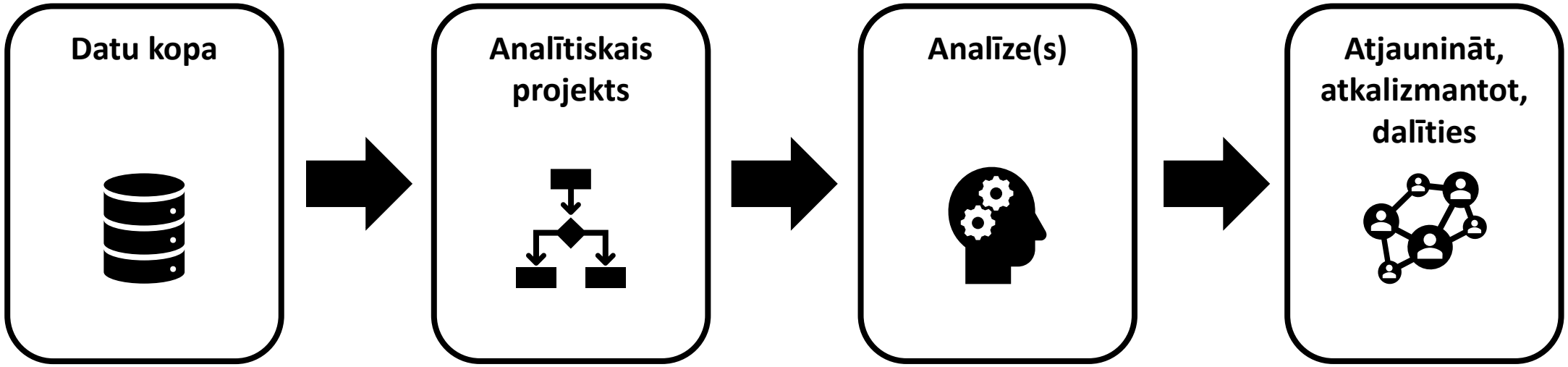
(Tervonen et al., Clin Pharmacol Ther, 2019)


Klīniskie pētījumi
Strukturēta klīnisko pētījumu datubāze
Palīdz novērtēt un pieņemt lēmumus..
Regulatoru darbībā
Veselības politikas veidošanā
Veselības aprūpes pakalpojumu sniedzējiem un pacientiem

ADDIS


Pierādījumu sintēze
Lēmumu pieņemšana
Pētījumu datu ieguve un glabāšana

Analītiskais process



Datu kopa -> projekts

Datu kopa

- Pētījumu datu repozitorijs
- Strukturēti semantiski dati un mērījumi
- Audita iespējas, pastāvīgas datu kopas versijas
- Datu atkalizmantošana un iespēja piekļūt citu lietotāju datiem
- Pieejami pārskati (D80)
- Iespēja harmonizēt mainīgos pētījumu starpā
- Ielase no clinicaltrials.gov, EudraCT, publikācijām

Analītiskais projekts

Balstoties uz datu kopas konceptiem, iespēja izvēlēties:

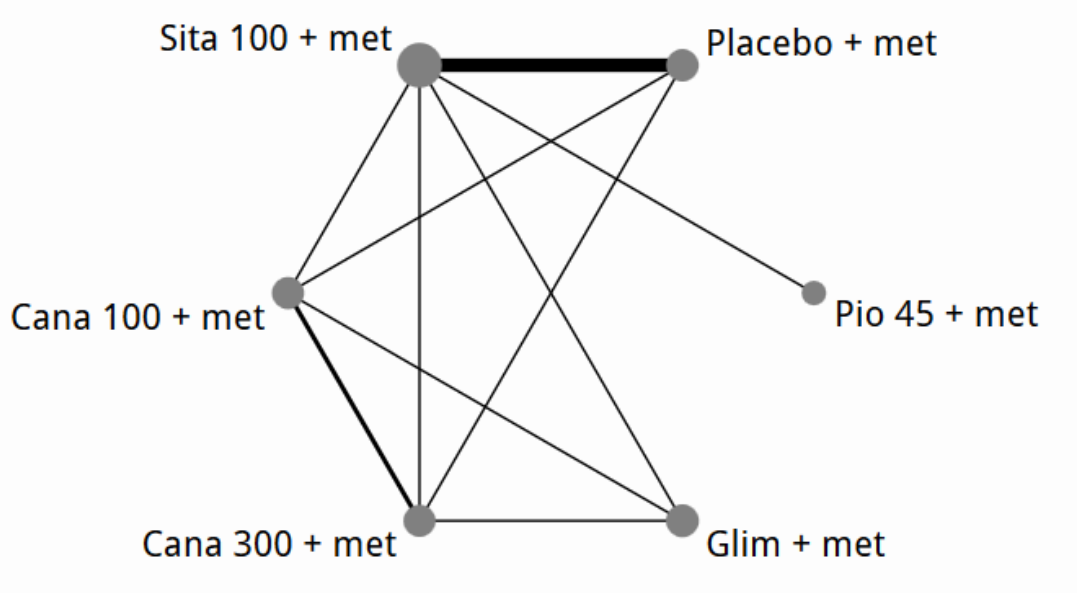
- Iznākumus
- Kovariātus
- Procedūras (atkarībā no devas, kompleksā ar citām procedūrām, u.c.)

Balsoties uz veiktajām izvēlēm, tālāk iespējams veikt:

- Network meta-analyses
- Network meta-regressions
- Ieguvumu-risku analīzes

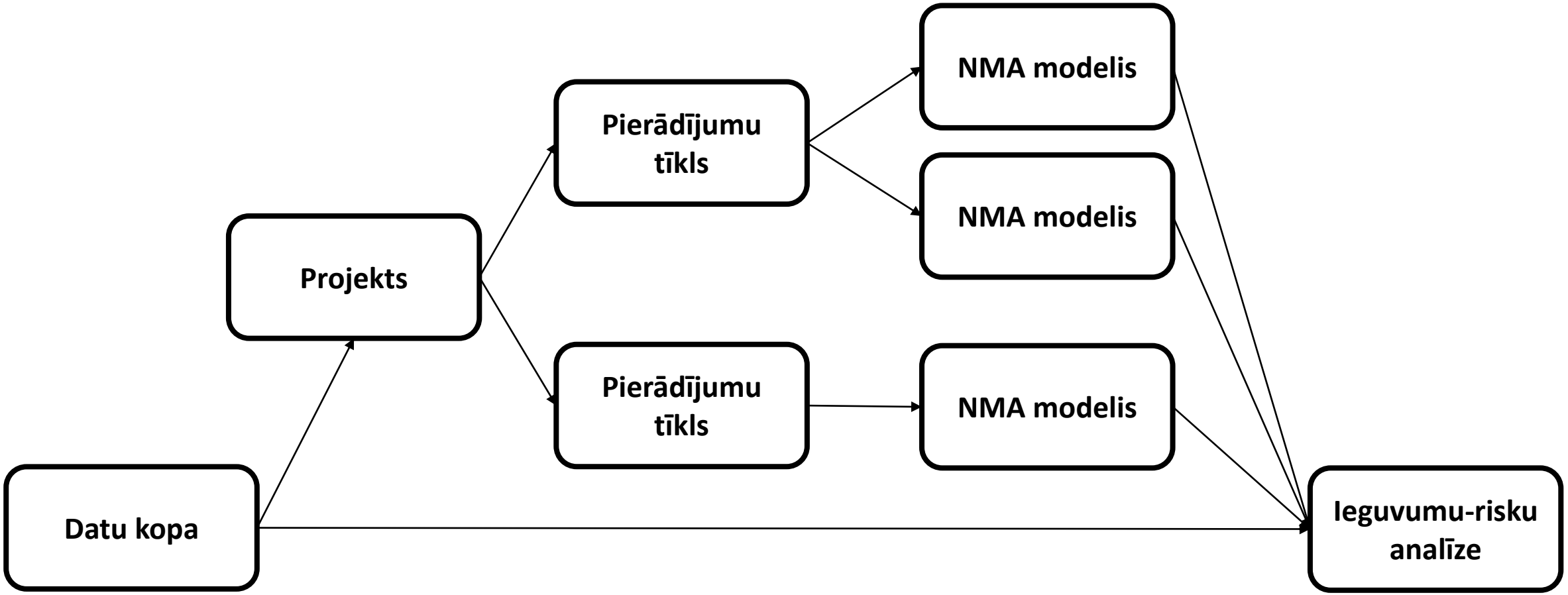
Analītiskā komponente

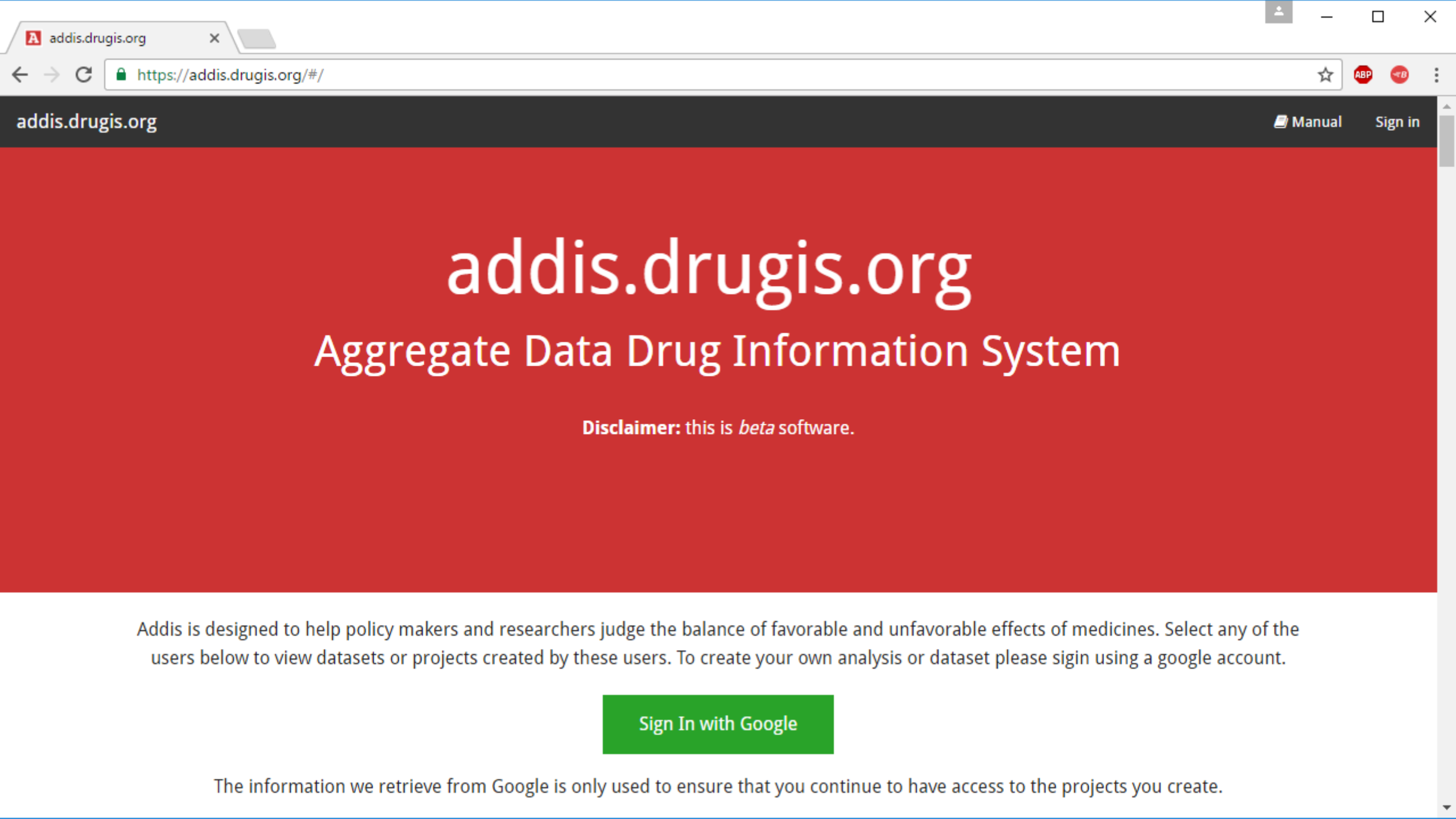
- Pierādījumu sintēze
- Ieguvumu-riska analīze
- Pārskatu veidošana
- Pieeja R modeļiem



Atjaunināt, atkalizmantot, dalīties

- Atjaunināt
  - Pievienot jaunus pētījumus datu kopai
  - Automātiski atjaunināt analīzes un modeļus
- Atkalizmantot
  - Kopēt analīzes
  - Pievienot modeļus
  - Izmantot rezultātus, lai veiktu citas analīzes
- Dalīties
  - Visas datu kopas, analīzes un modeļi pastāvīgi pieejami tiešsaistē
  - Iespēja veidot pārskatus


Datu kopa
Projekts
Pierādījumu tīkls
Pierādījumu tīkls
NMA modelis
NMA modelis
NMA modelis
Ieguvumu-risku analīze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Manual
Sign in
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Aggregate Data Drug Information System
Disclaimer: this is beta software.
Addis is designed to help policy makers and researchers judge the balance of favorable and unfavorable effects of medicines. Select any of the users below to view datasets or projects created by these users. To create your own analysis or dataset please sigin using a google account.
Sign In with Google
The information we retrieve from Google is only used to ensure that you continue to have access to the projects you create.

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https://addis.drugis.org/#/users/3/datasets

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Manual

Gert van Valkenhoef

Datasets | Projects | Search Studies

Featured Datasets

hide

Hansen (2005) anti-depressants review

This dataset contains 43 studies included in the Hansen et al. (2005) systematic review of 2nd generation anti-depressants (PMID 16172440). The studies include 10 anti-depressants and placebo, and compare them on efficacy and side effects. This is an excellent dataset to try out pair-wise meta-analysis, network meta-analysis, and benefit-risk analysis in ADDIS. For our

View Dataset | Create project

EMA assessment of Edarbi for hypertension

The main mono-therapy studies that supported the application of Edarbi (Azilsartan medoxomil) to the EMA for hypertension. Comparators include placebo, Olmesartan, and Ramipril. We identified the manufacturer's study IDs from the EMA EPAR and found the studies on ClinicalTrials.gov. The studies were imported automatically and corrected where needed (using

View Dataset | Create project

Datasets

Other users

Datasets

+ Add new dataset

Hansen (2005) anti-depressants review

create project

This dataset contains 43 studies included in the Hansen et al. (2005) systematic review of 2nd generation anti-depressants (PMID 16172440). The studies include 10 anti-depressants and placebo, and compare them on efficacy and side effects. This is an excellent dataset to try out pair-wise meta-analysis, network meta-analysis, and benefit-risk analysis in ADDIS. For our benefit-risk analysis based on this dataset, see PMID 22197518.

EMA assessment of Edarbi for hypertension

create project

The main mono-therapy studies that supported the application of Edarbi (Azilsartan medoxomil) to the EMA for hypertension. Comparators include placebo, Olmesartan, and Ramipril. We identified the manufacturer's study IDs from the EMA EPAR and found the studies on ClinicalTrials.gov. The studies were imported automatically and corrected where needed (using ADDIS 1.x).

Other users

- Abraham Nunes
- ad foobar
- Adriani Nikolakopoulou
- Aijing Shang
- Alexey Soshnin
- Alfi Yasmina
- Amichai Perlman
- Andrew Benson
- Aneta Obloza
- Areti - Angeliki Veroniki
- Ashraf Nabhan

Ahrén et al, 2004

Twelve- and 52-Week Efficacy of the Dipeptidyl Peptidase IV Inhibitor LAF237 in Metformin-Treated Patients With Type 2 Diabetes

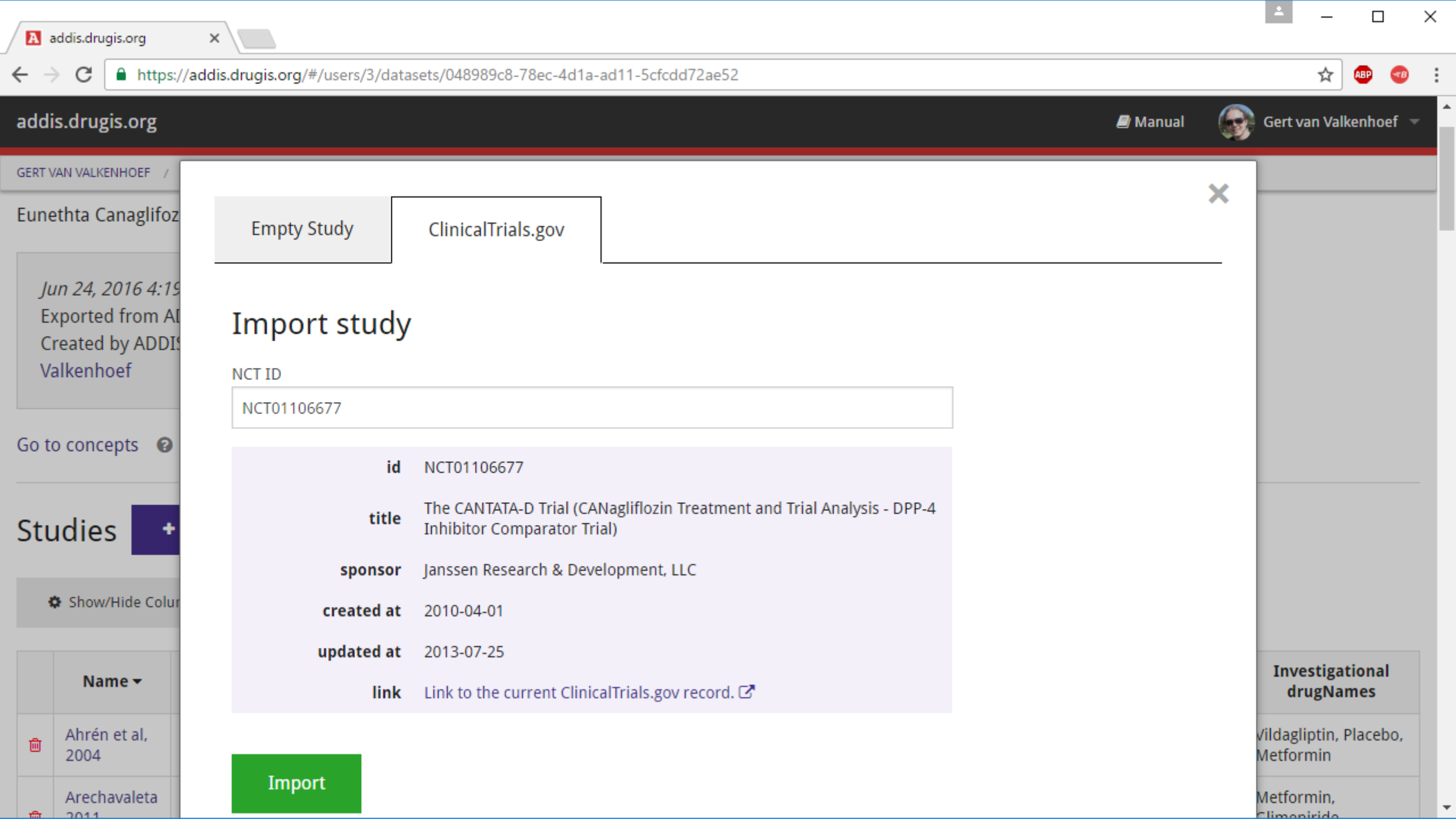
Nov 15, 2016 5:01:14 PM
Ahrén et al, 2004 DONE
Created by mona afra

✔ This is the current version
Dataset history
Study History
Copy study

DESIGN

Study Information

Group allocation: **Randomized**
Blinding: **Double blind**
Status: **Completed**
Number of centers: **unknown**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addis.drugis.org
Manual
Gert van Valkenhoef
GERT VAN VALKENHOEF /
Eunethta Canaglifoz
Jun 24, 2016 4:19
Exported from AI
Created by ADDIS
Valkenhoef
Go to concepts
Studies
Show/Hide Colur
Name
Ahrén et al, 2004
Arechavaleta
Investigational drugNames
Vildagliptin, Placebo, Metformin
Metformin,
Empty Study
ClinicalTrials.gov
Import study
NCT ID
NCT01106677
id NCT01106677
title The CANTATA-D Trial (CANagliflozin Treatment and Trial Analysis - DPP-4 Inhibitor Comparator Trial)
sponsor Janssen Research & Development, LLC
created at 2010-04-01
updated at 2013-07-25
link Link to the current ClinicalTrials.gov record.
Import

Study history

Created by mona afra (Nov 15, 2016 5:01:14 PM)

Ahrén et al, 2004 DONE

Created by mona afra (Nov 15, 2016 4:59:49 PM)

Done

Created by mona afra (Nov 15, 2016 4:55:07 PM)

12 weeks added

Created by ADDIS 1.x Export on behalf of mona afra (Jul 15, 2016 12:45:42 PM)

Exported from ADDIS 1.x

Drugs

Study Concept	Dataset Concept	
Vildagliptin	Vildagliptin	remove
Placebo	Placebo	remove
Metformin	Metformin	remove

Baseline characteristics

Study Concept	Dataset Concept	
Age	Age	remove
BMI	BMI	remove
Duration of diabetes	Duration of diabetes	remove
Duration of previous MET treatment	Duration of previous MET treatment	remove

Glim
Met + Cana 100
Met + Dapa 10
Met + Dapa 5
NOPE1
NOPE2
Sita 100
Lira 1.2
Met + Lira 1.2
Met + Vilda 100
Lira 1.8
Met + Sita

Simple intervention | Dose-restricted drug | Combination intervention | Intervention class

Semantic intervention

Canagliflozin

Name

Cana 300

Motivation

High-dose formulation of Canagliflozin

Dose type

(•) Fixed only ( ) Titrated only ( ) Both

Lower bound [x] Exactly (=) 300 milligram/day

Upper bound [ ]

Add intervention

Drugs

Study Concept	Dataset Concept	
Vildagliptin	Vildagliptin	remove
Placebo	Placebo	remove
Metformin	Metformin	remove

Baseline characteristics

Study Concept	Dataset Concept	
Age	Age	remove
BMI	BMI	remove
Duration of diabetes	Duration of diabetes	remove
Duration of previous MET treatment	Duration of previous MET treatment	remove

Selected Outcome

HbA1c change (lower is better)

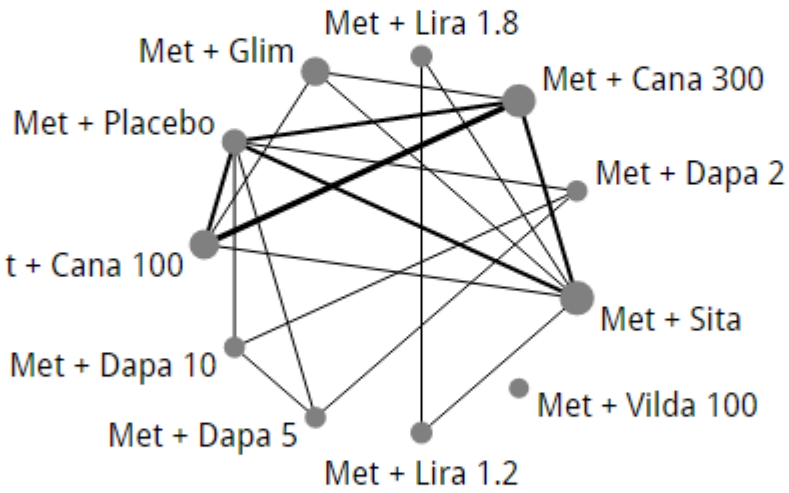
Included interventions

- [ ] Saxa 5
- [ ] Glim
- [x] Met + Cana 100
- [x] Met + Dapa 10
- [x] Met + Dapa 5
- [ ] NOPE1
- [ ] NOPE2
- [ ] Sita 100
- [ ] Lira 1.2
- [x] Met + Lira 1.2
- [x] Met + Vilda 100

Included covariates

No covariates have been defined.

Network graph



The network graph shows the evidence network for all selected interventions. The size of an intervention's circle reflects the total number of participants for that intervention. Lines signify that interventions are connected through at least one study, with thicker lines indicating more connecting studies.

Criterion and alternative selection

Settings

Criterion	Description	Units	Daclizumab	IFN β-1a	Strength of evidence / Uncertainties	References
Favorable effects						
ARR	Annualised relapse rate	Annual rate	0.249 (0.215, 0.283)	0.422 (0.374, 0.470)		Study 205MS301
MRI lesions	Number of new/newly enlargin...		2.16 (1.941, 2.380)	3.84 (3.45, 4.23)		Study 205MS301
Disability	% of subjects ≥ 1.0-point increa...	%	7.0 (5.4, 8.6)	8.0 (6.2, 9.8)	**Unc:** Data on disability was the least robust of endpoints	Study 205MS301
PRO	% of subjects ≥ 7.5-point worse...	%	17.0 (14.6, 19.4)	20.0 (17.4, 22.6)	**Unc:** PRO data also with great variability, significant uncertainty	Study 205MS301
Unfavorable effects						
Hep. AE	Hepatic Events (SMQ)	%	16.0 (13.6, 18.4)	14.0 (11.8, 16.2)	**Unc:** Most serious hepatic events occured with DAC HYP	Study 205MS301
Cut. AE	All cutaneous events	%	37.0 (33.9, 40.1)	19.0 (16.5, 21.5)	**Unc:** Serious cutaneous <1% IFN beta vs. 2% DAC HYP	Study 205MS301
Inf. AE	Infections	%	65.0 (61.9, 68.1)	57.0 (53.8, 60.2)		Study 205MS301
GI AE	Gastrointestinal events	%	31.0 (28.0, 34.0)	24.0 (21.2, 26.8)	**Unc:** Serious GI <1% IFN beta vs. 1% DAC HYP	Study 205MS301
Fatal events (distribution)	Fatal event (liver, infection)	%	0.400 (0.100, 0.900)	0.200 (0.020, 0.600)		

Criterion	Description	Units	Daclizumab	IFN β-1a	Strength of evidence / Uncertainties	References
Favorable effects						
ARR	Annualised relapse rate	Annual rate	0.249 0.215, 0.283	0.422 0.374, 0.470	**SoE:** A similar effect was found for the number of new/newly enlarging MRI T2 lesions (2.16 for DAC HYP vs 3.84 for IFN beta)	Study 205MS301
Unfavorable effects						
Hep. AE	Hepatic Events (SMQ)	%	16 13.6, 18.4	14 11.8, 16.2	**Unc:** Most serious hepatic events occured with DAC HYP	Study 205MS301
Cut. AE	All cutaneous events	%	37 33.9, 40.1	19 16.5, 21.5	**Unc:** Serious cutaneous <1% IFN beta vs. 2% DAC HYP	Study 205MS301
Inf. AE	Infections	%	65 61.9, 68.1	57 53.8, 60.2		Study 205MS301

Zinbrytha DEMO

Settings

Overview | Problem definition | Preferences | Deterministic results | SMAA results

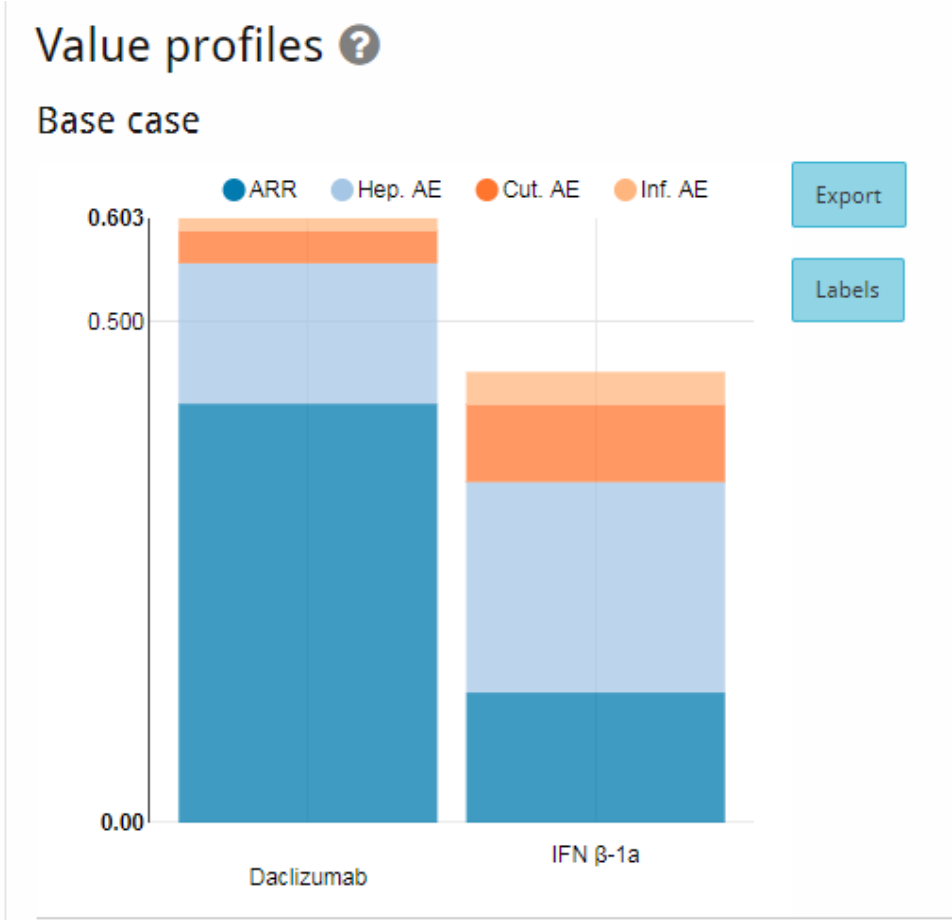
Precise swing weighting (2/2)

Criterion	Description	Unit	Worst	Best	Importance
ARR	Annualised relapse rate	Annual rate	0.5	0.2	100%
Hep. AE	Hepatic Events (SMQ)	%	20	10	70%
Cut. AE	All cutaneous events	%	50	10	20%
Inf. AE	Infections	%	70	50	10%

You've indicated that improving ARR from 0.5 Annual rate to 0.2 Annual rate is the most important (i.e. it has 100% importance). Now indicate the relative importance (in %) to this improvement of each other criterion's improvement using the sliders below.

decreasing ARR from 0.5 Annual rate to 0.2 Annual rate	1% 100%
decreasing Hep. AE from 20 % to 10 %	1% 70% 100%
decreasing Cut. AE from 50 % to 10 %	1% 20% 100%
decreasing Inf. AE from 70 % to 50 %	1% 10% 100%

Cancel | Previous | Save


Value profiles
Base case
ARR
Hep. AE
Cut. AE
Inf. AE
Export
Labels
0.603
0.500
0.00
Daclizumab
IFN β-1a

Lietotāji

- Interese no nacionālajām un ES iestādēm
  - Liela interese par ieguvumu un risku analīzi (arī ārpus veselības aprūpes)
  - Doma par ADDIS kā ‘patiesuma’ avotu šķiet pievilcīga
- Demo projekti vairākos farmakoloģijas uzņēmumos
  - Seko līdzi, kādus lēmumus pieņems oficiālās iestādes..

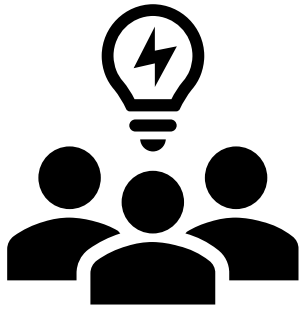
Publiski pieejama sistēma

github.org/drugis

addis.drugis.org

mcda.drugis.org

gemtc.drugis.org



Paldies kolēģiem..

Hans Hillige

Douwe Postmus

Tommi Tervonen

Daan Reid

Joris de Keijser

un auditorijai!

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d.reid [at] umcg.nl