

ADDIS: Software for Clinical Trials Data Analysis

using aggregate data within the framework of BR-assessment

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12 October, 2009



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What are we building?

- Build a comprehensive information system
 - That stores efficacy and safety information
 - On a wide variety of drugs
- Enable automated comparisons between drugs
 - Is the drug as *effective* and/or as *safe* as approved drugs?
 - Identify benefits and risks, trade-offs
 - Is the drug suitable for all targeted sub-populations?



Motivation

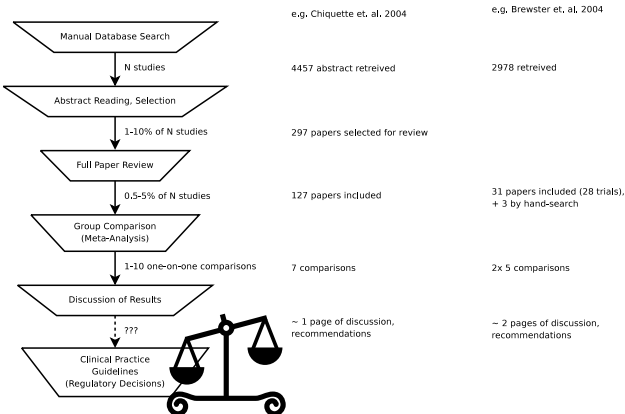
Systematically assessing a new drug application in the **context** of pre-existing evidence is difficult:

- 1 Evidence hard to find, combine
- 2 How to apply evidence is unclear (e.g., efficacy vs safety)
- 3 BR-analysis helps (2), but makes (1) worse

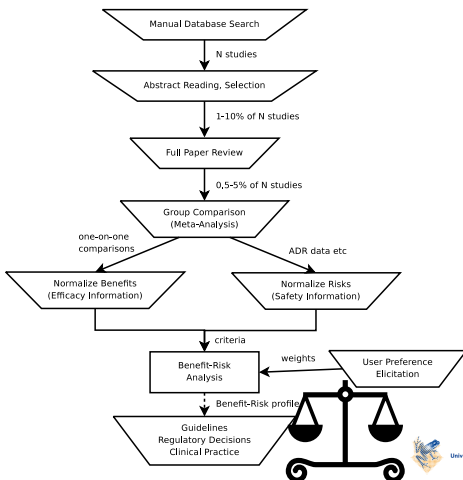
Next slides illustrate workflows.



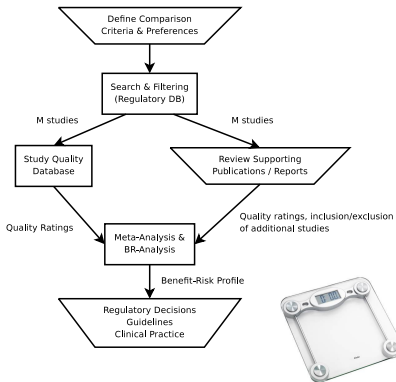
Meta-Analysis: Workflow



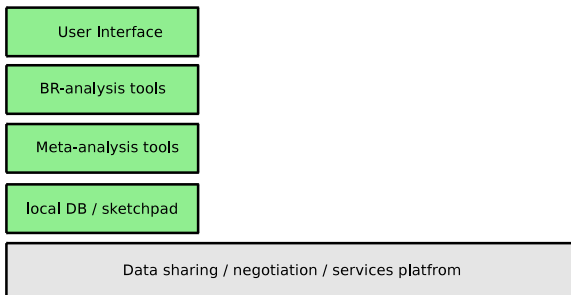
Benefit-Risk Analysis: Workflow



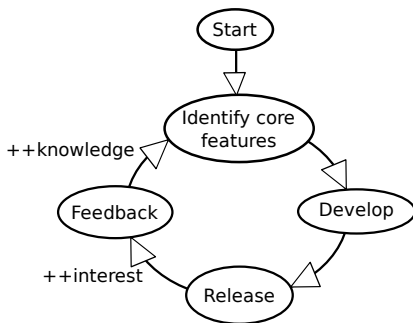
Model-Driven Workflow



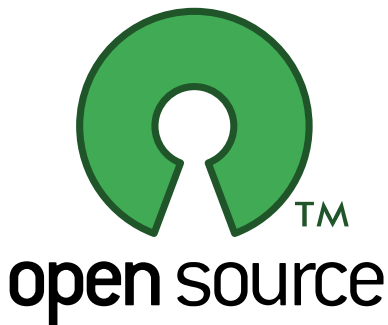
Work So Far: ADDIS v0.2



ADDIS: Agile Software Development



ADDIS v0.2: Open Source Software



Supporting Website: drugis.org

drugis.org

Home News ADDIS Publications About us

Welcome to DrugIS.org

At drugis.org (Drug Information Systems), we are developing prototype software, to discover how ICT may assist or change the way in which pharmaceutical research and regulation is done. We work in an agile way, which means that we aim to deliver valuable, working software early on in the development process. It also means that we do not expect to know now what our software will be able to do in a year's time, but rather that we continuously work with the users of our software to discover their current, and changing, understanding of what is important and valuable.

The Escher Project

Our work is funded by the Dutch **Top Institute Pharma**, specifically through the Escher Project workpackage 3.2. The goal of the Escher project is to "energize pharmaceutical R&D by identifying, evaluating and removing regulatory barriers to bring efficacious and safe medicines to patients in an efficient and timely fashion."

In workpackage 3.2, our goal is to create evidence-based drug information repositories in which drug efficacy and safety questions can be answered in an efficient, transparent and accountable way. Comparisons within and across medicinal products should be made in a more automated and, thus, more efficient way.

Our Commitment: Open Development

Sponsors

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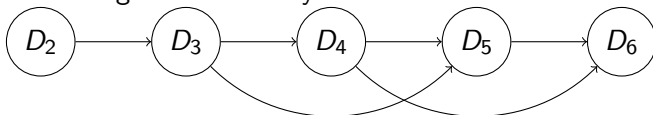
News

- ADDIS v0.2 released**
 The first release of ADDIS, version 0.2, has been released.
 2009-06-30
- drugis.org launched**
 The website drugis.org is launched.
 2009-06-11

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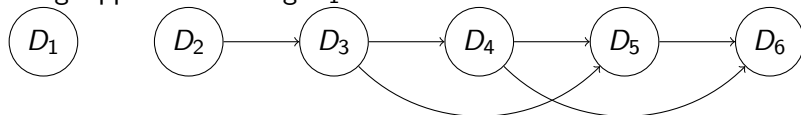
Regulatory Use Case

Known: The following Non-Inferiority relations:



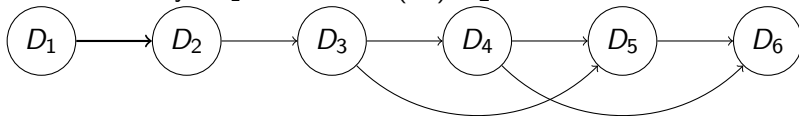
Regulatory Use Case

Drug Application: Drug D_1 .



Regulatory Use Case

Provided study: D_1 not inferior (\rightarrow) D_2 .



How to decide if D_1 is acceptable?



The Easy Case

	D_1	D_2	D_3
S_1	○	○	
S_2		○	○
S_3	○	○	
S_4	○		○

If we want to compare two drugs, say D_1 and D_2 , it is easy:



The Easy Case

	D_1	D_2	D_3
S_1	x	x	
S_2		○	○
S_3	x	x	
S_4	○		○

If we want to compare two drugs, say D_1 and D_2 , it is easy:

- 1 Select the studies that measure both D_1 and D_2



The Easy Case

	D_1	D_2	D_3
S_1	x	x	
S_2		○	○
S_3	x	x	
S_4	○		○

If we want to compare two drugs, say D_1 and D_2 , it is easy:

- 1 Select the studies that measure both D_1 and D_2
- 2 Pool efficacy data from these studies to get an effect estimate



Problem: Indirect Comparison?

	D_1	D_2	D_3
S_1	○	○	
S_2		○	○
S_3		○	○

Can we compare D_1 to D_3 ?



Problem: Comparing > 2 Drugs

	D_1	D_2	D_3
S_1	○	○	
S_2		○	○
S_3	○	○	
S_4	○		○

If we want to compare $D_1 \dots D_3$:



Problem: Comparing > 2 Drugs

	D_1	D_2	D_3
S_1	x	x	
S_2		x	x
S_3	x	x	
S_4	x		x

If we want to compare $D_1 \dots D_3$:

- 1 Select the studies that measure at least two of $D_1 \dots D_3$



Problem: Comparing > 2 Drugs

	D_1	D_2	D_3
S_1	x	x	
S_2		x	x
S_3	x	x	
S_4	x		x

If we want to compare $D_1 \dots D_3$:

- 1 Select the studies that measure at least two of $D_1 \dots D_3$
- 2 How do we combine this data?



The (immediate) future of ADDIS

- ADDIS v0.4 to be released 01-01-2010
- Two additional programmers starting 15-10-2009
- Focus on toolkit for meta-analysis
- Research looking further ahead
 - To more advanced applications/features



Conclusions

- Using RCT data through evidence synthesis difficult:
 - Lack of structured (meta-)data on studies
 - Lack of automated tools
- ADDIS will provide
 - A way to store studies in a machine-readable way
 - Automated tools for meta-analysis and BR-analysis
- My research will likely focus on *new approaches to evidence synthesis for drug benefit-risk assessment*

