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Study registration

Tips and tricks

Sven Trelle (Lucia Kacina)
CTU Bern
University of Bern

08.03.2015, CTU Lectures

Selective reporting

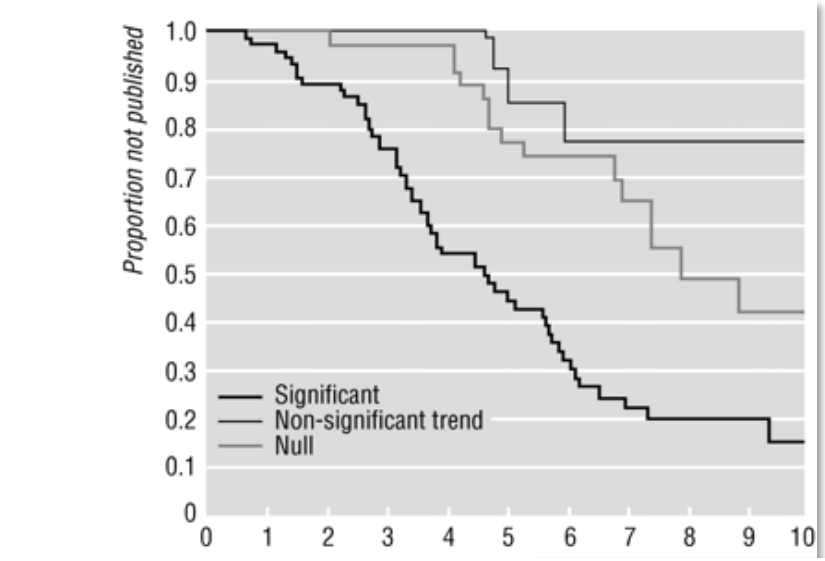
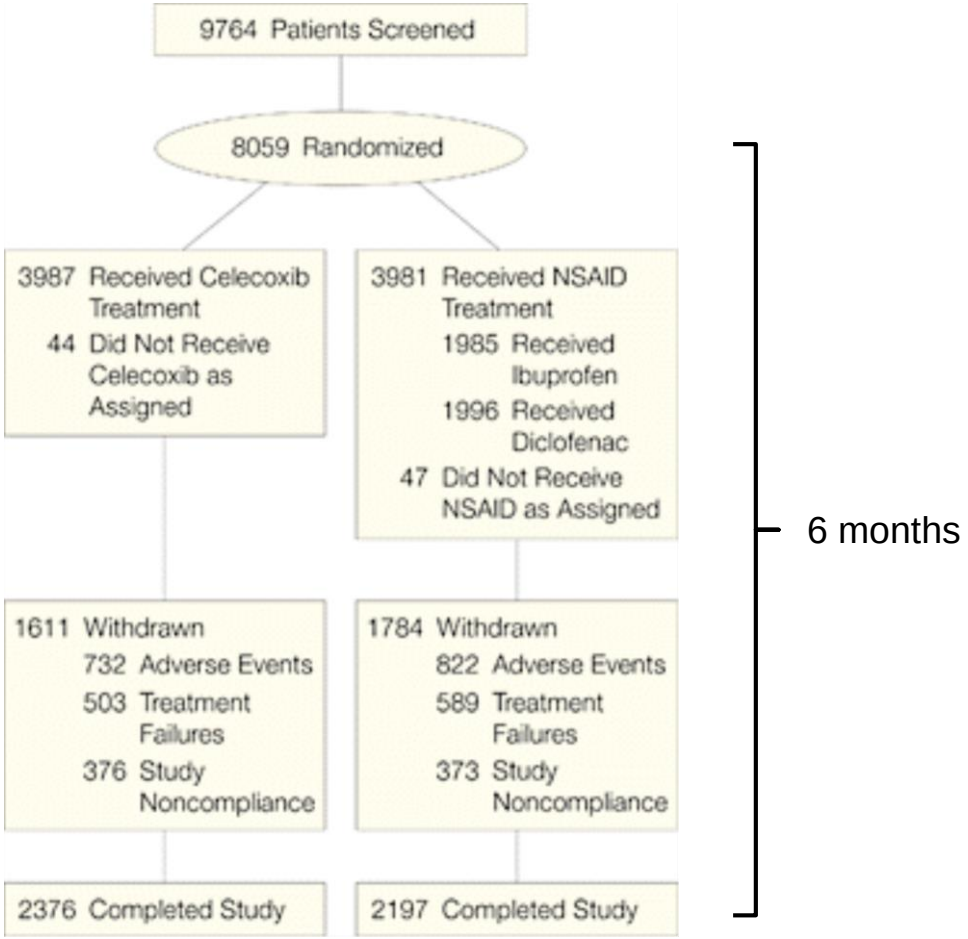


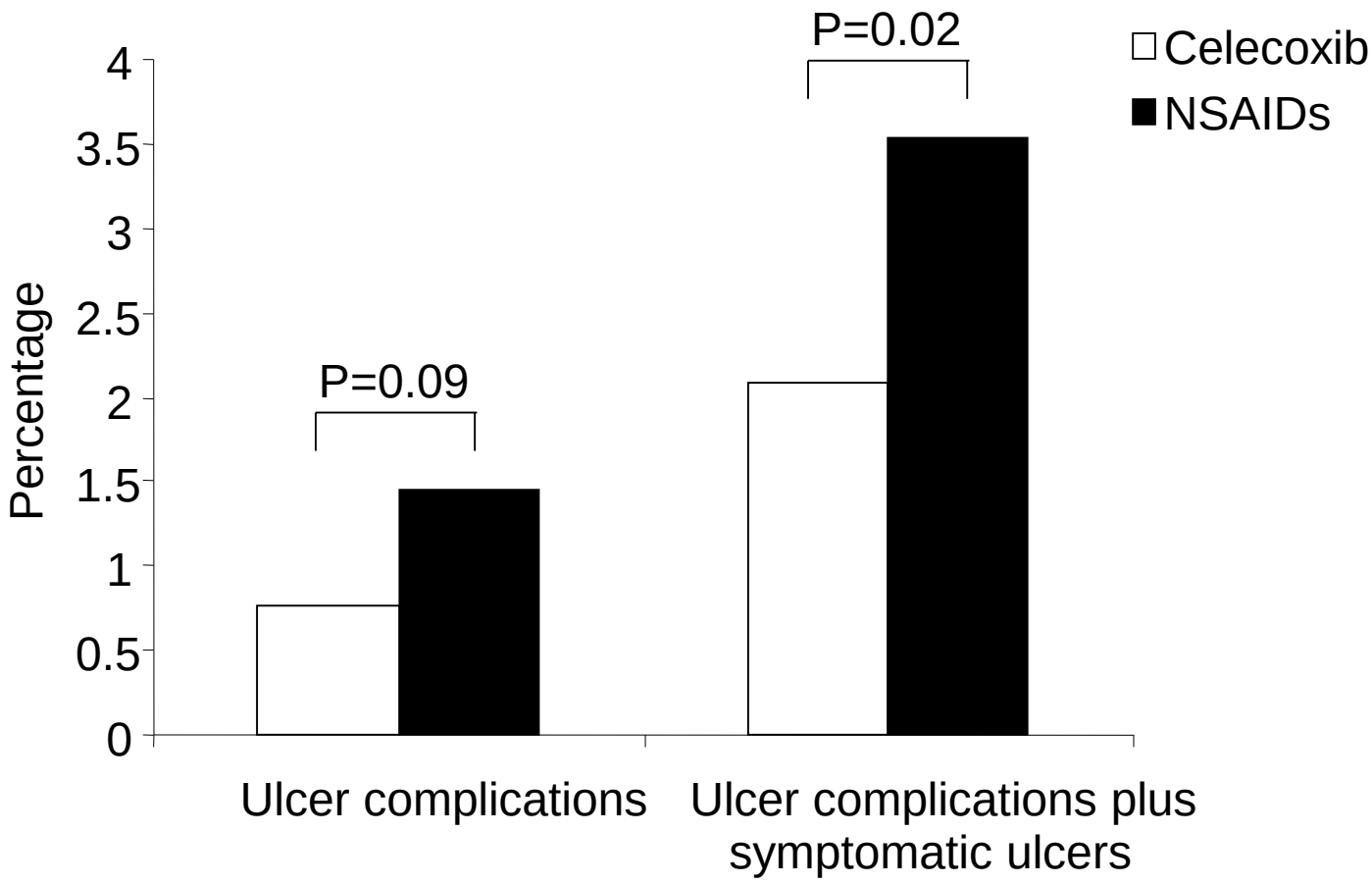
Table 3. Median Proportion of Incompletely Reported Efficacy and Harm Outcomes per Trial, by Study Design

	Incompletely Reported Outcomes per Trial, Median Percentage (10th-90th Percentile Range)			
Trial Design	No. of Trials	Efficacy Outcomes	No. of Trials	Harm Outcomes
All	99	50 (4-100)	72	65 (0-100)
Parallel-group	68	38 (4-78)	57	50 (0-100)
Crossover	29	98 (0-100)	14	100 (0-100)
Other	2	91 (82-100)	1	71 (NA)

Falsification and intransparent post-hoc changes (CLASS)

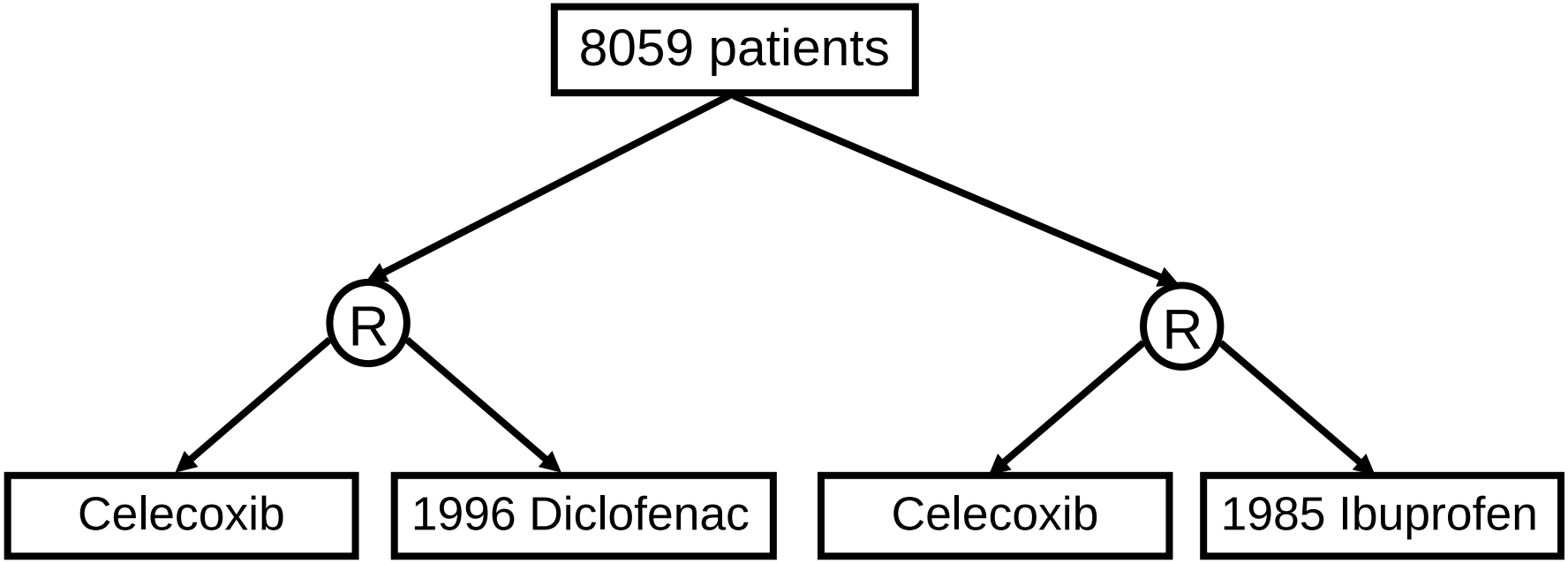


Falsification and intransparent post-hoc changes (CLASS)



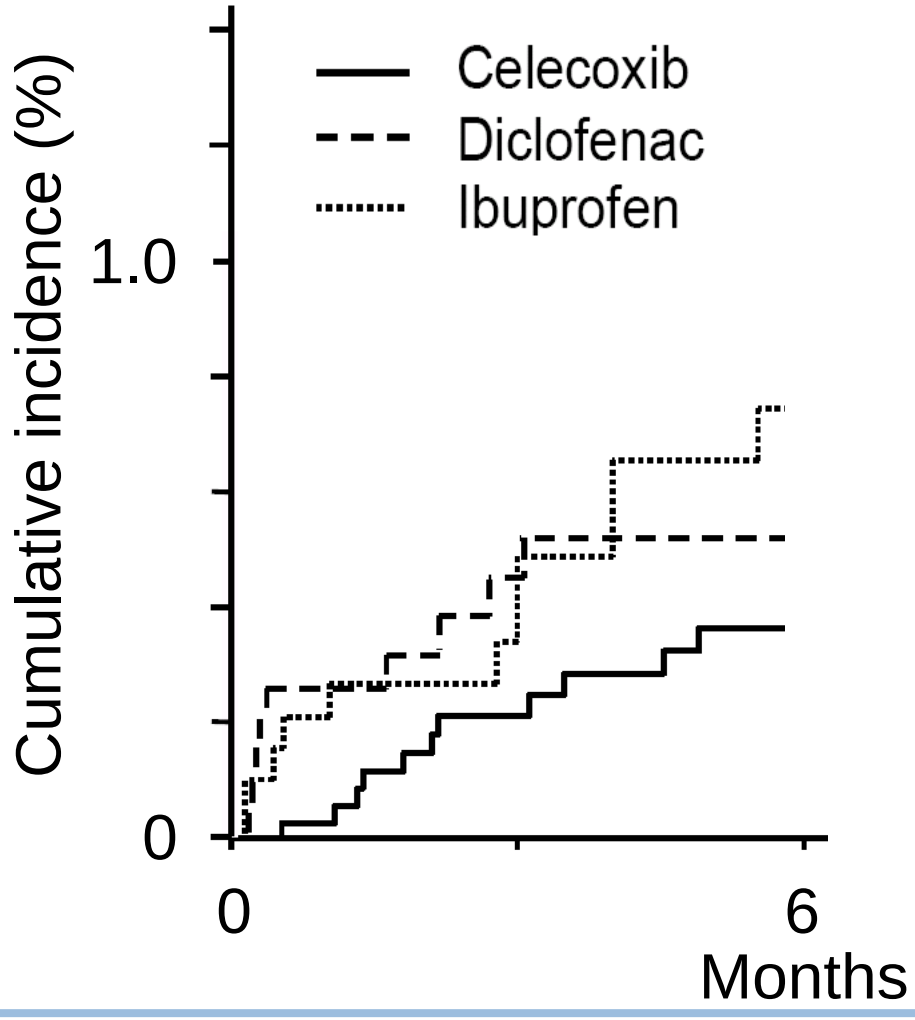
Annual rates extrapolated from 6 months follow-up

CLASS: Reality

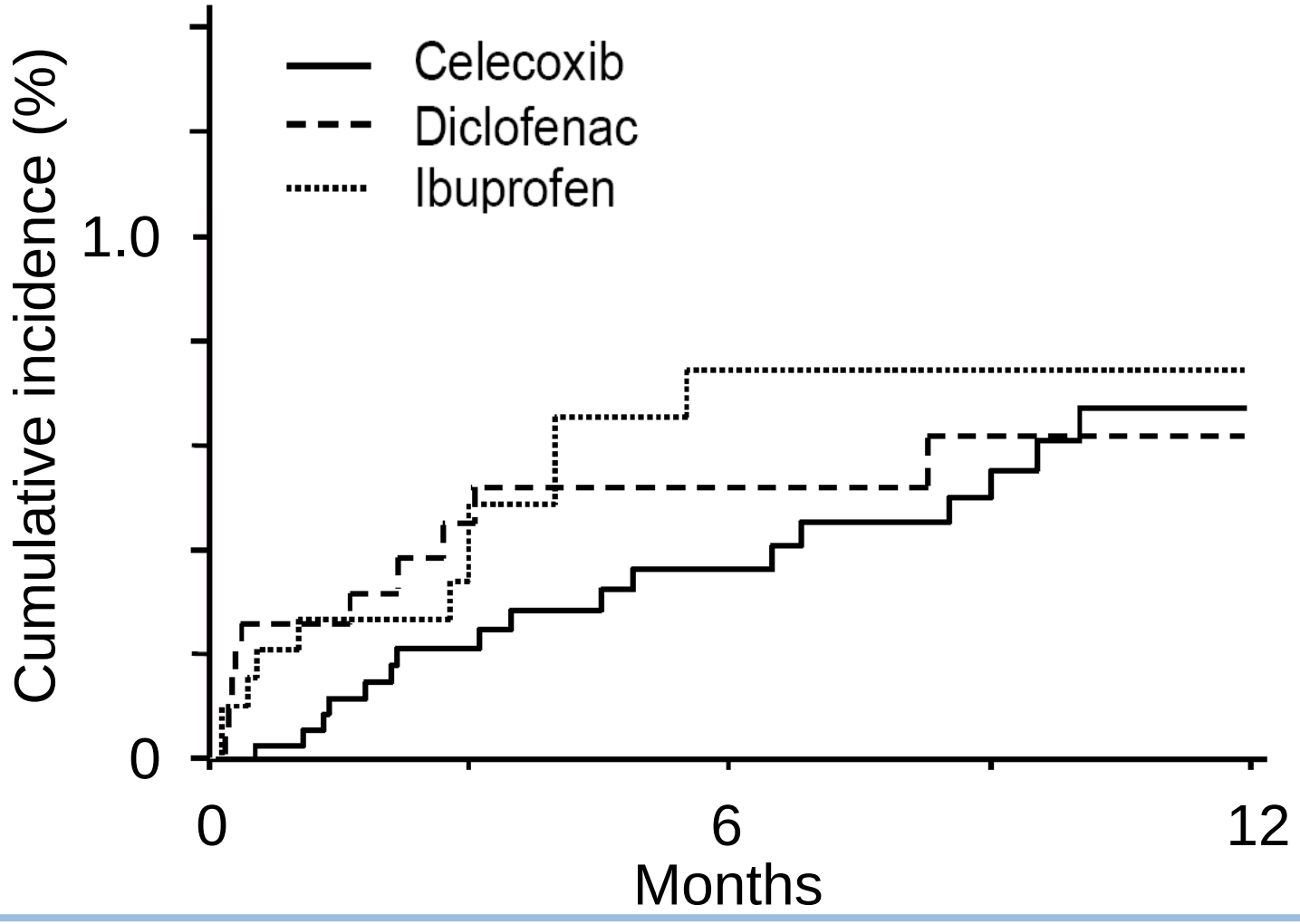


12-16 months duration

CLASS: primary outcome



CLASS: primary outcome



Humanforschungsgesetz

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Art. 56 Registrierung

[1] Bewilligte klinische Versuche müssen in einem öffentlichen Register erfasst werden. Der Bundesrat kann Ausnahmen von der Registrierungspflicht bezeichnen; er orientiert sich dabei an den anerkannten internationalen Regelungen.

[2] Er bezeichnet das Register, informiert über den Zugang zu diesem und legt dessen Inhalt sowie die Meldepflicht und das Meldeverfahren fest. Er beachtet dabei anerkannte internationale Regelungen und berücksichtigt nach Möglichkeit bereits bestehende Register.

[3] Er kann:

a. Organisationen des öffentlichen oder des privaten Rechts mit der Einrichtung und Führung des Registers betrauen;

b. die Veröffentlichung von Ergebnissen registrierter Forschungsprojekte in solchen Registern vorsehen.

Definition klinischer Versuch

Forschungsprojekt mit Personen, d… diese prospektiv einer gesund… …en Intervention zuordnet… …n auf die Gesund… …, die Fu… …zu u…

→ …ene Intervention

… präventive, diagnostische, therapeutische, palliative oder rehabilitative Handlung …

ClinicalTrials.gov

- studyregistration @ctu.unibe.ch
- Protocol Registration and Results System at ClinicalTrials.gov
- Complete: e-mail to CTU Bern
- By CTU Bern
- Draft receipt as pdf for final checks
- E-mail by ClinicalTrials.gov

Basics

- Sponsor is responsible for registration

- Responsible party registers
  - Select «Sponsor» (you as representative of Inselspital)
  - Do not select «Sponsor-Investigator/PI»
- CTU Bern does not regularly check registrations anymore → send us an e-mail if you want us to check something
- Timeframe
  - Release → Publication: 2-5 working days
  - Changes

Errors

- Restricted character set (special characters often do not work)
- Most entry fields have real-time validations
  - NOTE (blue): can be ignored
  - ERRORS (red): cannot be ignored because it will prevent release

Consistency

- Make sure that all dates and study status are consistent
  - Start date
  - Completion
  - Recruiting/Completed …
- Status == Recruiting → at least 1 recruiting site
- «Groups/Arms» == «Interventions»

Completeness (and consistency)

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- Responsibility of the Sponsor(-Investigator)
- Be aware that others might check consistency between later publications and register entries (audit trail!)
  - Peer reviewers, readers, …

Table 3 Overall consistency and discrepancy between protocols and corresponding published reports of academic drug trials by protocol-derived type of study, $N = 95$ protocols

	All trials		Exploratory trials		Confirmatory trials	
	n	% (95 % CI)	*n*	% (95 % CI)*	*n*	% (95 % CI)*
Number of trials	95		42		53	
Overall consistency	37	39 % (29 to 49 %)	21	50 % (35 to 65 %)	16	30 % (18 to 43 %)
Individual discrepancies						
Type of study	22	23 % (15 to 32 %)	6	14 % (4 to 25 %)	16	30 % (18 to 43 %)
Primary objective	19	20 % (12 to 28 %)	12	29 % (15 to 42 %)	7	13 % (4 to 22 %)
Primary endpoint	39	41 % (31 to 51 %)	16	38 % (23 to 53 %)	23	43 % (30 to 57 %)
Hypothesis	- 17	-	-	-	5/37◊	14 % (2 to 25 %)
Sample size calculation	-	-	-	-	17/37◊	46 % (30 to 62 %)

*Prevalence in each subgroup; for example, 21 of 42 exploratory trials (50 %) showed overall consistency
◊Based on the subgroup of 37 trials with a confirmatory protocol and more than one confirmatory published report

Berendt, Trials 2016

Outcomes (general)

- Usually from a patient perspective
  - Death from any cause
  - NOT: Difference in the proportion of deaths
- Use description (freetext)!
- «Safety Issue» == Safety outcomes

Outcomes: be specific!

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- Measurement method, instruments
- Timepoints
  - Fix timepoints (e.g. 3 months) not event-dependent
  - If inevitable, with estimate e.g. «at hospital discharge, expected at 3-7 days»
- Change (repeated measures)

- NOT: Safety; BUT (example): Experiencing at least one serious adverse event

- NOT: Morbidity and mortality; BUT:
  - Either: separate in two outcomes
  - Or: «number of events with events defined as …»

Last but not least

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- Acronym
  - No blanks
- Study officals (Chair, …)
  - All three are synonymous

Outlook (general)

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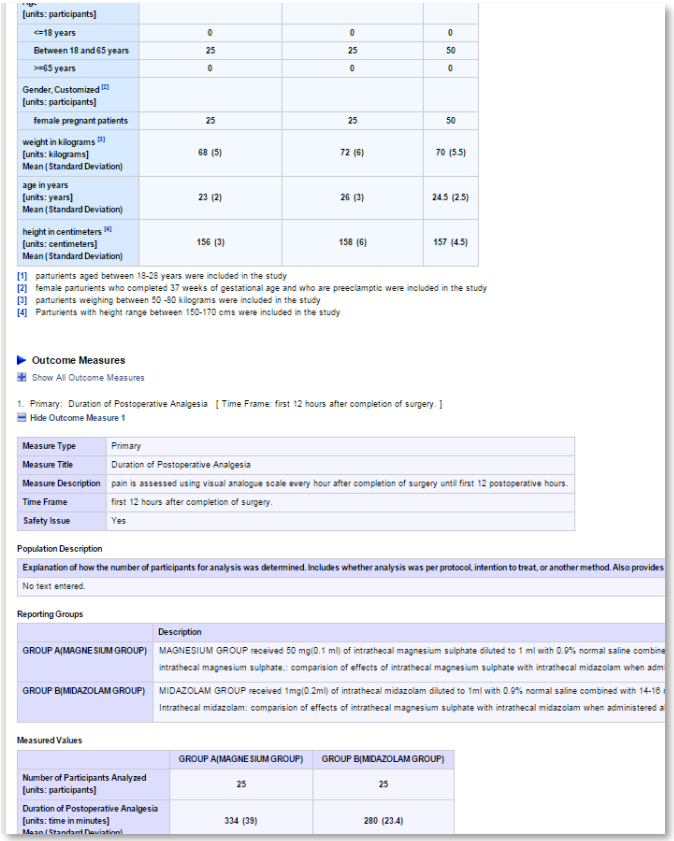
> Results reporting



[units: participants]			
<=18 years	0	0	0
Between 18 and 65 years	25	25	50
>=65 years	0	0	0
Gender, Customized [2] [units: participants]			
female pregnant patients	25	25	50
weight in kilograms [3] [units: kilograms] Mean (Standard Deviation)	68 (5)	72 (6)	70 (5.5)
age in years [units: years] Mean (Standard Deviation)	23 (2)	26 (3)	24.5 (2.5)
height in centimeters [4] [units: centimeters] Mean (Standard Deviation)	156 (3)	158 (6)	157 (4.5)

[1] parturients aged between 18-28 years were included in the study
[2] female parturients who completed 37 weeks of gestational age and who are preeclamptic were included in the study
[3] parturients weighing between 50 -80 kilograms were included in the study
[4] Parturients with height range between 150-170 cms were included in the study

Outcome Measures

Show All Outcome Measures

1. Primary: Duration of Postoperative Analgesia [Time Frame: first 12 hours after completion of surgery.]

Hide Outcome Measure 1

Measure Type	Primary
Measure Title	Duration of Postoperative Analgesia
Measure Description	pain is assessed using visual analogue scale every hour after completion of surgery until first 12 postoperative hours.
Time Frame	first 12 hours after completion of surgery.
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides
No text entered.

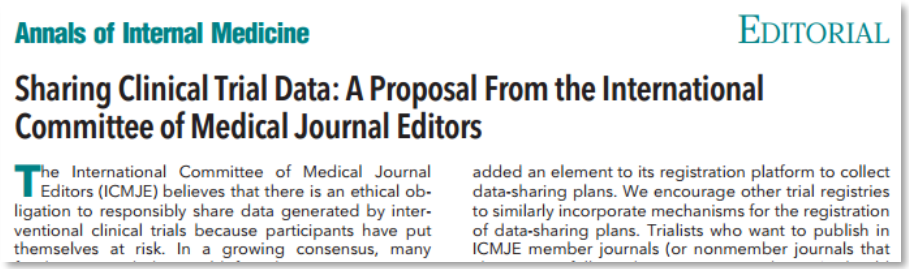
Reporting Groups

	Description
GROUP A(MAGNESIUM GROUP)	MAGNESIUM GROUP received 50 mg(0.1 ml) of intrathecal magnesium sulphate diluted to 1 ml with 0.9% normal saline combine intrathecal magnesium sulphate,: comparision of effects of intrathecal magnesium sulphate with intrathecal midazolam when adm
GROUP B(MIDAZOLAM GROUP)	MIDAZOLAM GROUP received 1mg(0.2ml) of intrathecal midazolam diluted to 1ml with 0.9% normal saline combined with 14-16 Intrathecal midazolam: comparision of effects of intrathecal magnesium sulphate with intrathecal midazolam when administered a

Measured Values

	GROUP A(MAGNESIUM GROUP)	GROUP B(MIDAZOLAM GROUP)
Number of Participants Analyzed [units: participants]	25	25
Duration of Postoperative Analgesia [units: time in minutes] Mean (Standard Deviation)	334 (39)	280 (23.4)

> Sharing trial datasets



Annals of Internal Medicine

EDITORIAL

Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes that there is an ethical obligation to responsibly share data generated by interventional clinical trials because participants have put themselves at risk. In a growing consensus, many

added an element to its registration platform to collect data-sharing plans. We encourage other trial registries to similarly incorporate mechanisms for the registration of data-sharing plans. Trialists who want to publish in ICMJE member journals (or nonmember journals that

Outlook (SNCTP)

- Automatic data transfer from BASEC to kofam.ch
  - Currently, semi-automatic within 30 days
  - Swissethics and FOPH (BAG) are working on an interface
- Timepoint
  - Immediate transfer or
  - Delayed (Phase I trials)
- Conditions for automatic transfer
  1. Name of Primary Registry in BASEC screen #4
  2. External identification number (ID) in BASEC screen #4
  3. Timepoint for transfer specified (see point above)
  4. Ethics committee has (conditional) approval documented in BASEC
  - Automatic reminders will be issued if any of #1-3 is missing
- Transfer will probably require additional authorization
- Final responsibility remains with the Sponsor

BASEC (layout might change)

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Primary Registry

Note: At the time of your initial submission you may not yet have the information to fill in the next two fields. You can add the information later, after receiving the approval from the Ethics Committee (see this FAQ-entry on how to submit updates).

Name of Primary Registry

For information about Primary Registries in the WHO Registry Network, please visit http://www.who.int/ictrp/network/primary/en/.

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External identification number (ID), if available

External identification number (ID) of the trial in the WHO primary registry or clinicaltrials.gov; You received the identification number after registration of your clinical trial in a WHO primary registry or at clinicaltrials.gov.

Registration in SNCTP

Was this project already registered in the SNCTP before the release of this submission portal? *

(Note: for technical reasons you have to fill out the sections above even if you already registered your project through kofam.ch in the past.)

- ○ yes
- ○ no

Agreement on automatic data transfer *

Clinical trials must be registered in the Swiss Clinical Trials Portal SNCTP before the trials are conducted. The relevant data will be automatically transferred into SNCTP, once the trial is approved by the Ethics Committee and, if applicable, by Swissmedic and/or the FOPH.

- ☐ I agree on the automatic transfer of the relevant data into the SNCTP
- ☐ Please wait with the automatic transfer, I will agree on the transfer later *

** Note: Clinical trials in which the medicinal product under investigation is being administered to adult persons for the first time (Phase I clinical trials) must be registered **no later than one year after the completion** of the clinical trial.*

Questions?

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- Lucia Kacina
- studyregistration@ctu.unibe.ch

Next CTU lecture

- 12. April
- Matthias Briel (Basel)
- «Abgebrochene klinische Studien – vermeidbar oder dumm gelaufen?»