University of Basel

Department of Clinical Research

University Hospital Basel

Quality Framework for Clinical Trials:

Delphi consensus on a comprehensive framework to Increasing QUality In academic clinical REsearch (INQUIRE)

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SwissTPH Summer Symposium 2018

INQUIRE INcreasing QUality In Clinical REsearch

McMaster University

swiss clinical trial organisation

Disclosures

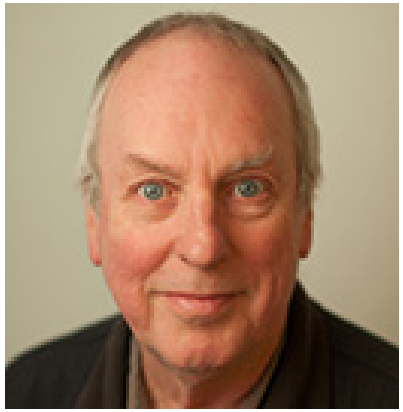
I have no actual or potential conflict of interest in relation to this presentation.

Funding

Universitätsspital Basel

PhD Program Health Sciences

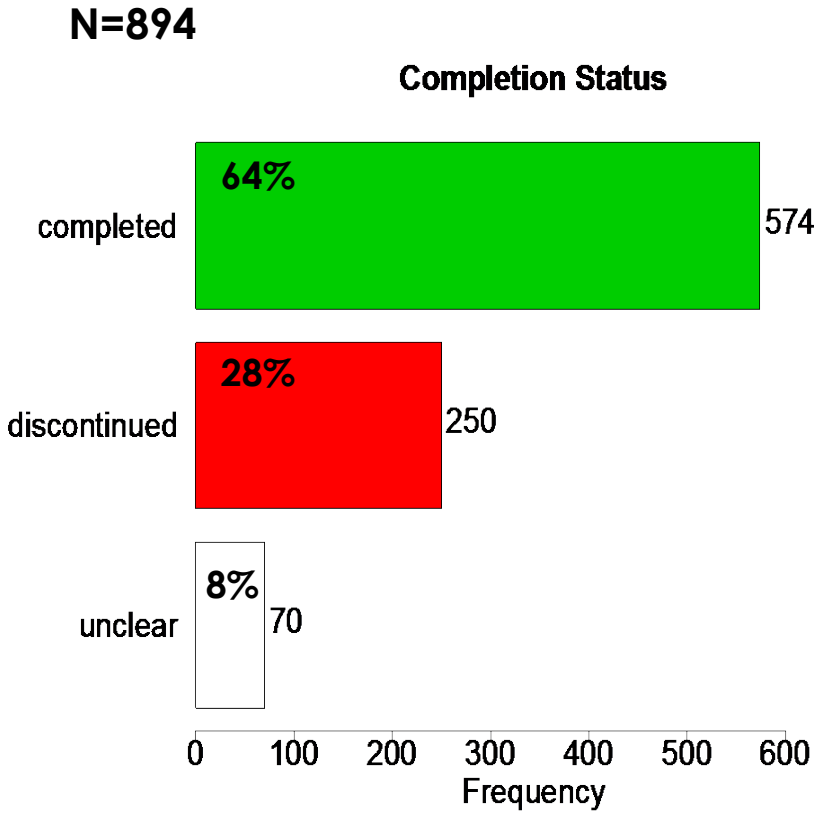
Trigger 2014

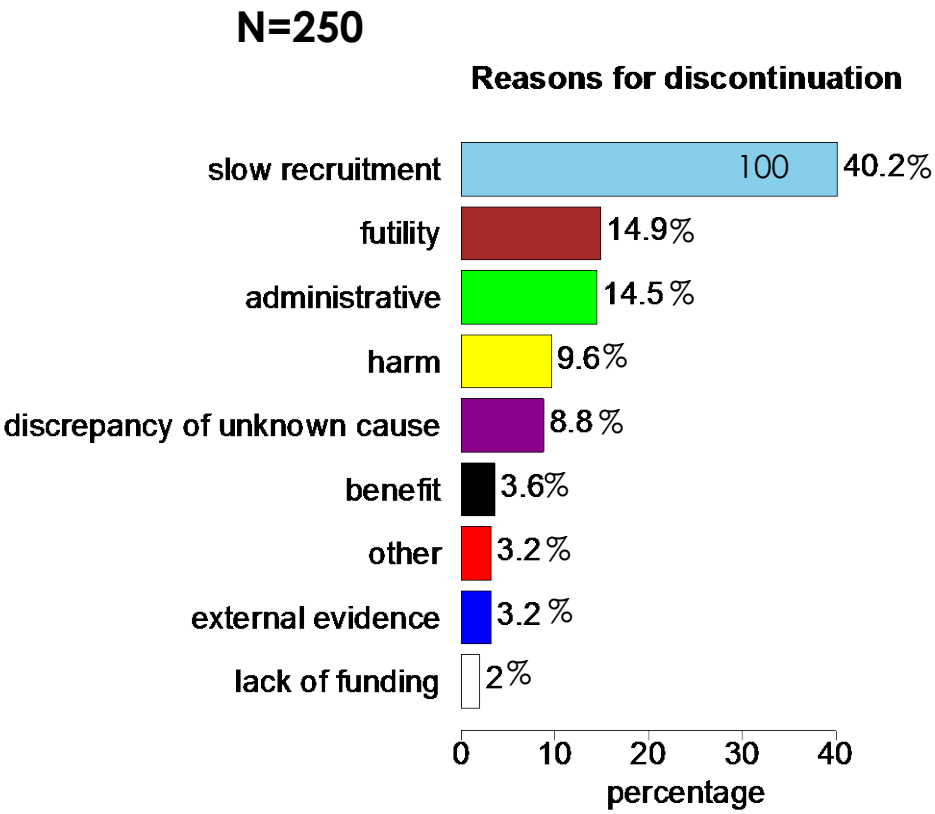


" (…) it is estimated that **85%** of all biomedical research is **waste**." (…)

Many clinical trials are prematurely discontinued…

Most frequent reason: insufficient recruitment

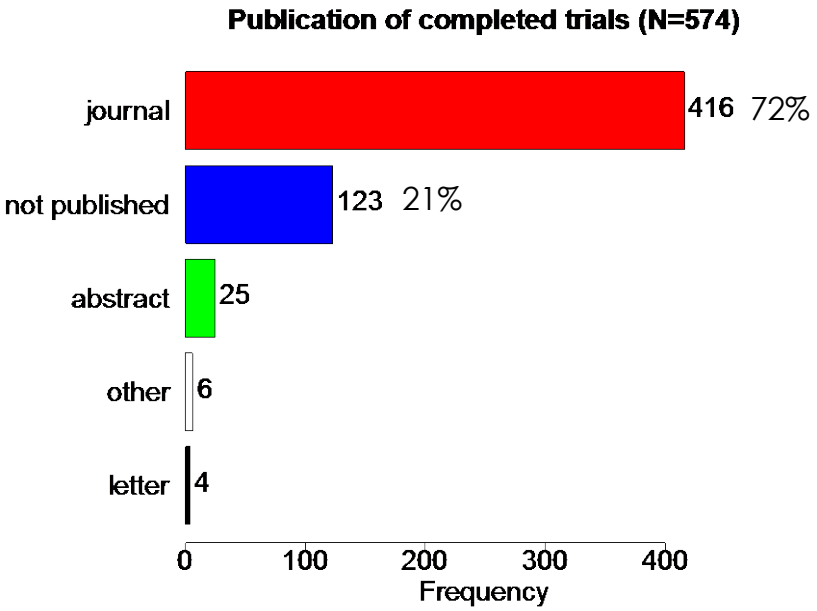


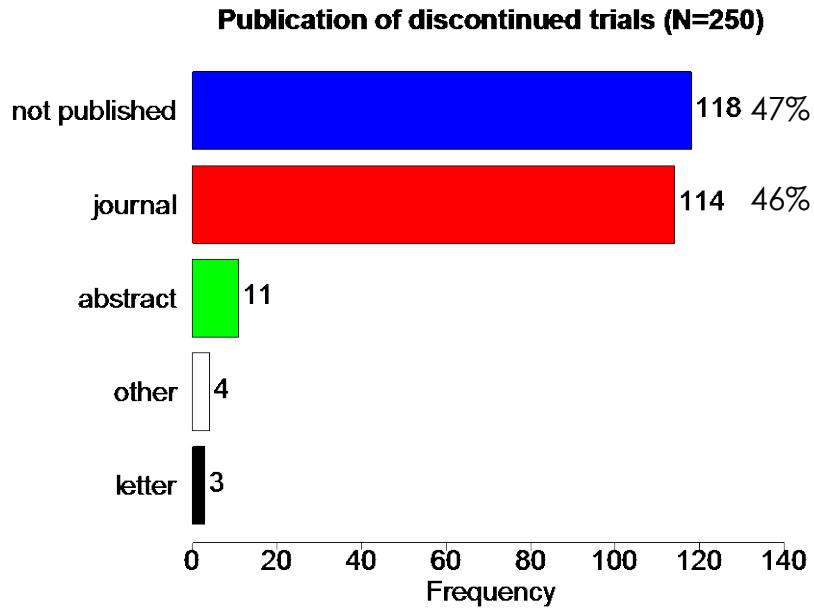


Kasenda et al., JAMA 2014;311:1045-1051

Many clinical trials are not published…

discontinued trials in particular





Kasenda et al., JAMA 2014;311:1045-1051

Who's listening?

Trigger 2016

Review

Increasing value and reducing waste in biomedical research: who's listening?

David Moher, Paul Glasziou, Iain Chalmers, Mona Nasser, Patrick M M Bossuyt, Daniël A Korevaar, Ian D Graham, Philippe Ravaud, Isabelle Boutron

The biomedical research complex has been estimated to consume almost a quarter of a trillion US dollars every year. Unfortunately, evidence suggests that a high proportion of this sum is avoidably wasted. In 2014, *The Lancet* published a series of five reviews showing how dividends from the investment in research might be increased from the relevance and priorities of the questions being asked, to how the research is designed, conducted, and reported. 17 recommendations were addressed to five main stakeholders—funders, regulators, journals, academic institutions, and researchers. This Review provides some initial observations on the possible effects of the Series, which seems to have provoked several important discussions and is on the agendas of several key players. Some examples of individual initiatives show ways to reduce waste and increase value in biomedical research. This momentum will probably move strongly across stakeholder groups, if collaborative relationships evolve between key players; further important work is needed to increase research value. A forthcoming meeting in Edinburgh, UK, will provide an initial forum within which to foster the collaboration needed.

Lancet 2016; 387: 1573–86

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Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada (D Moher PhD, Prof I D Graham PhD); **School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, ON, Ottawa, Canada** (D Moher,

Study aim

To develop a comprehensive framework for the quality of clinical research based on stakeholder consensus – and operationalization in and for the academic setting

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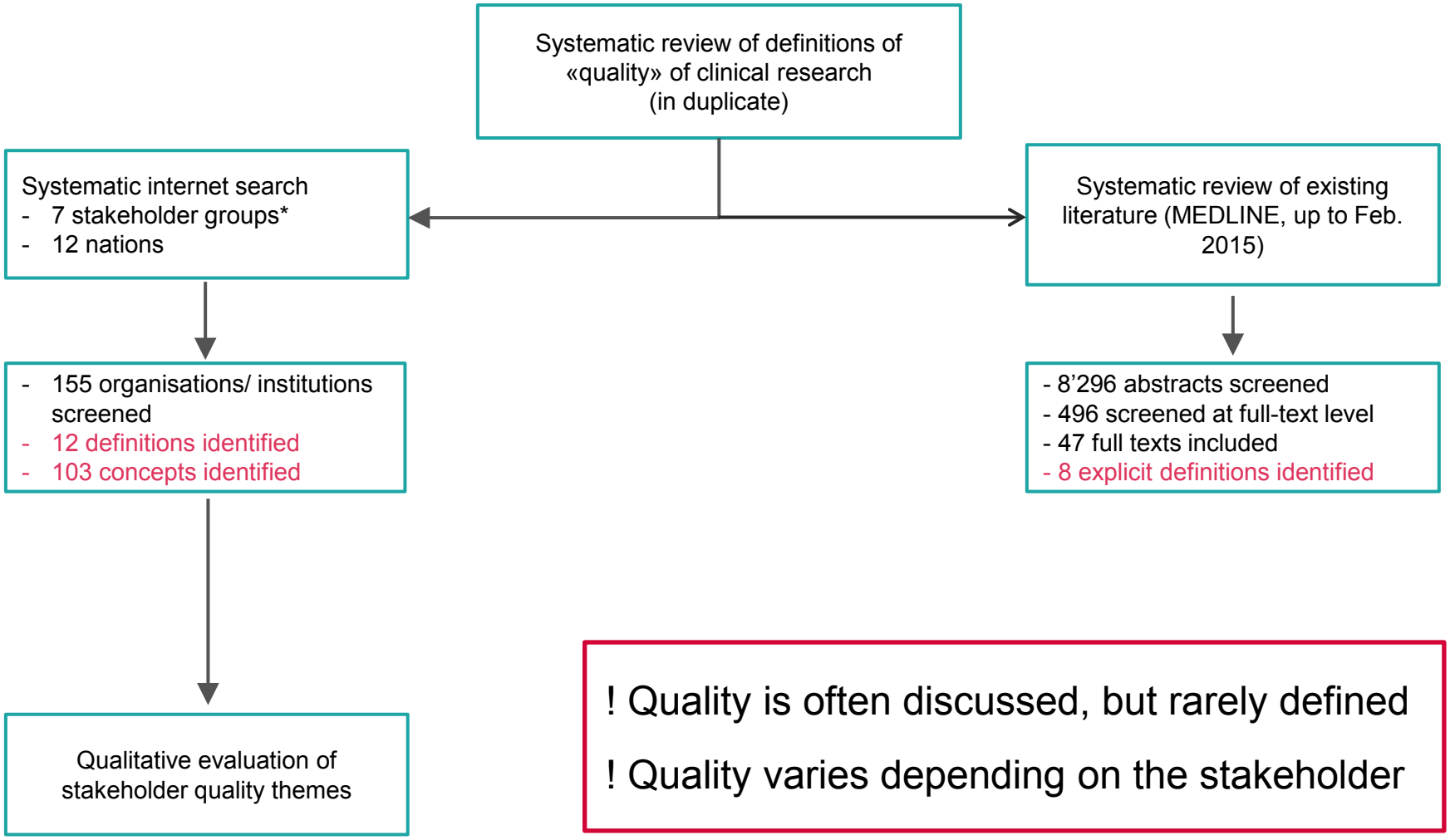
Study design I. Systematic review



* governmental bodies, regulatory agencies, pharmaceutical industry / CROs, academic research initiatives / CTUs, ethics committees, patient organizations, funding agencies

Quality varies depending on the stakeholder

Governmental bodies / Jurisdiction
"Relevant, transparent & ethical"

Regulatory Agencies
"Adherence to guidelines"

Ethics committees / IRBs
"Risk/benefit ratio & subject protection"

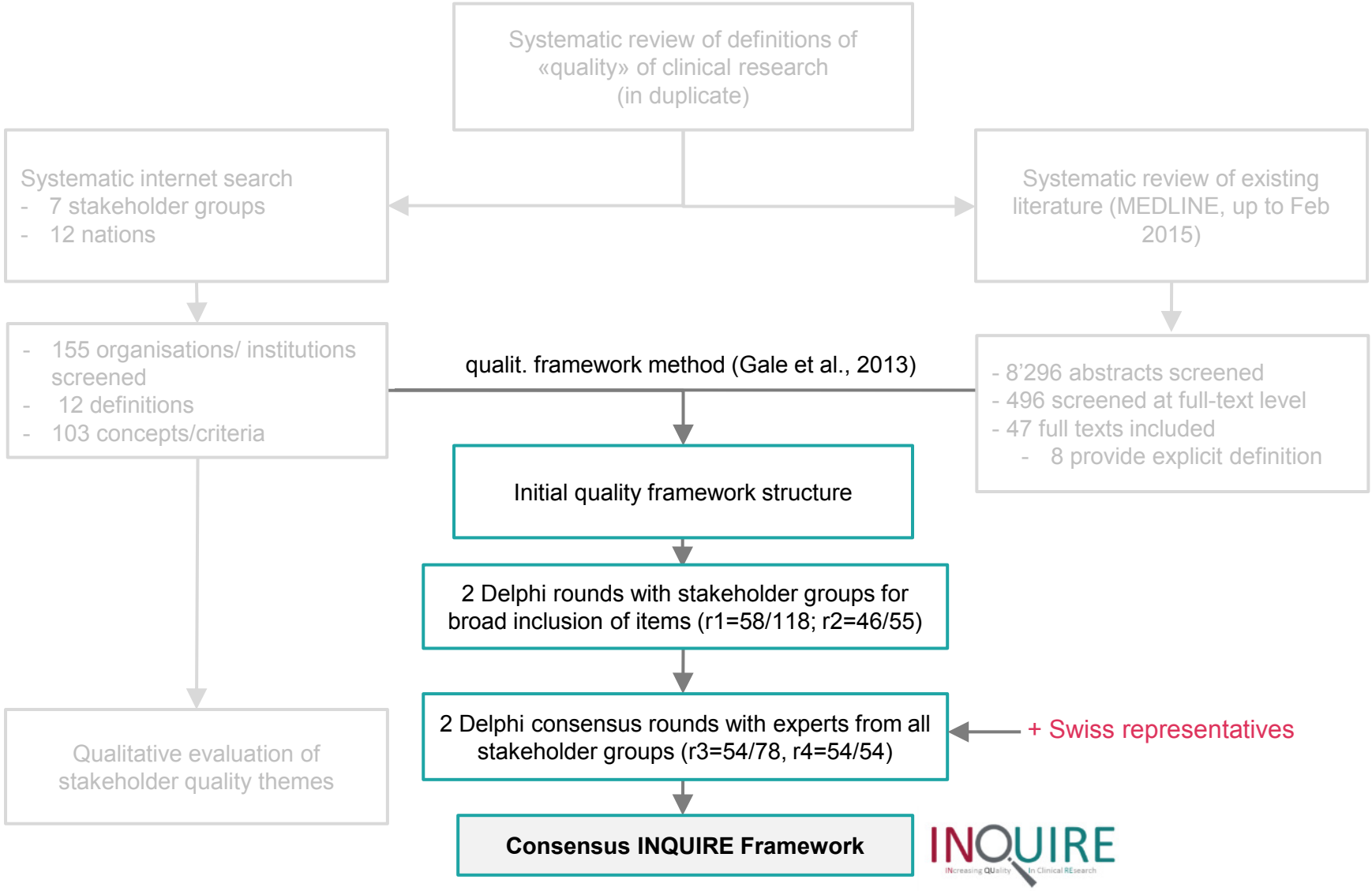
Patients
"Patient involvement & applicability"

Funding Agencies
"Feasible, generalisable & objective"

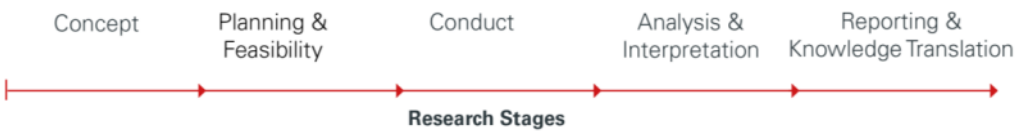
Pharmaceutical Industry / CROs
„High quality data"

Academic Research / Initiatives
"Absence of bias, relevant & transparent"

Study design II. Framework development



Results. INQUIRE Framework



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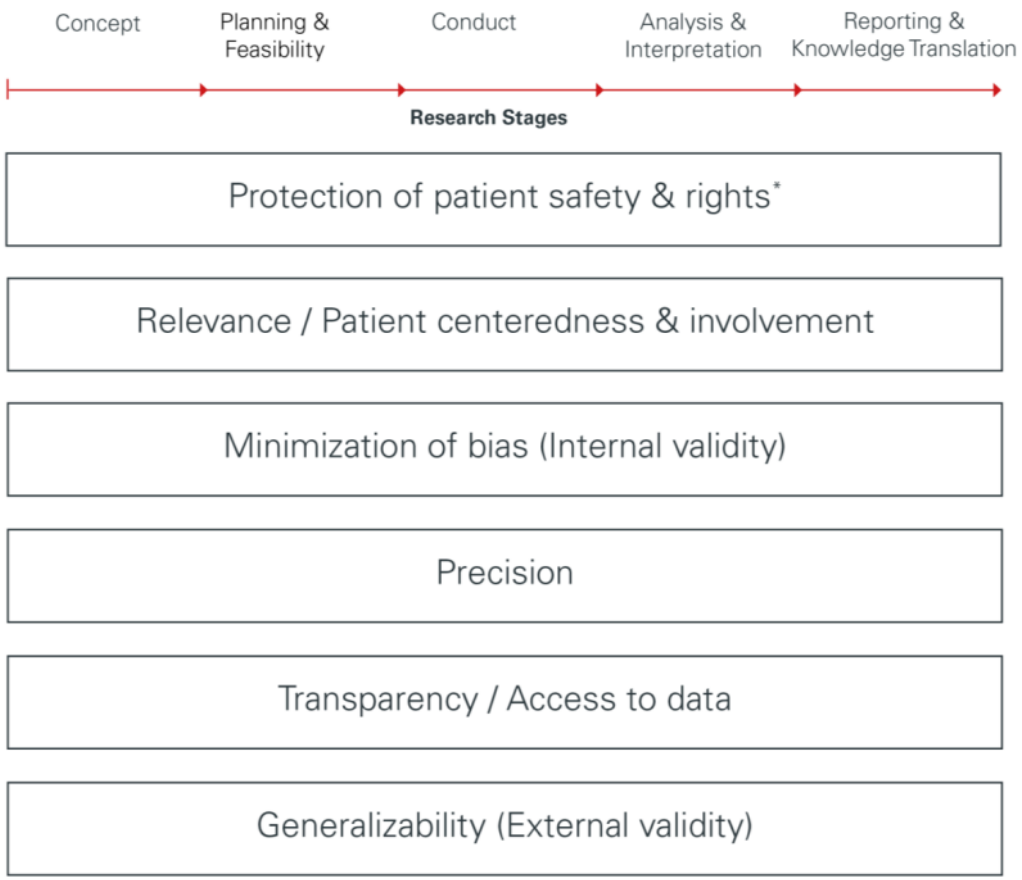

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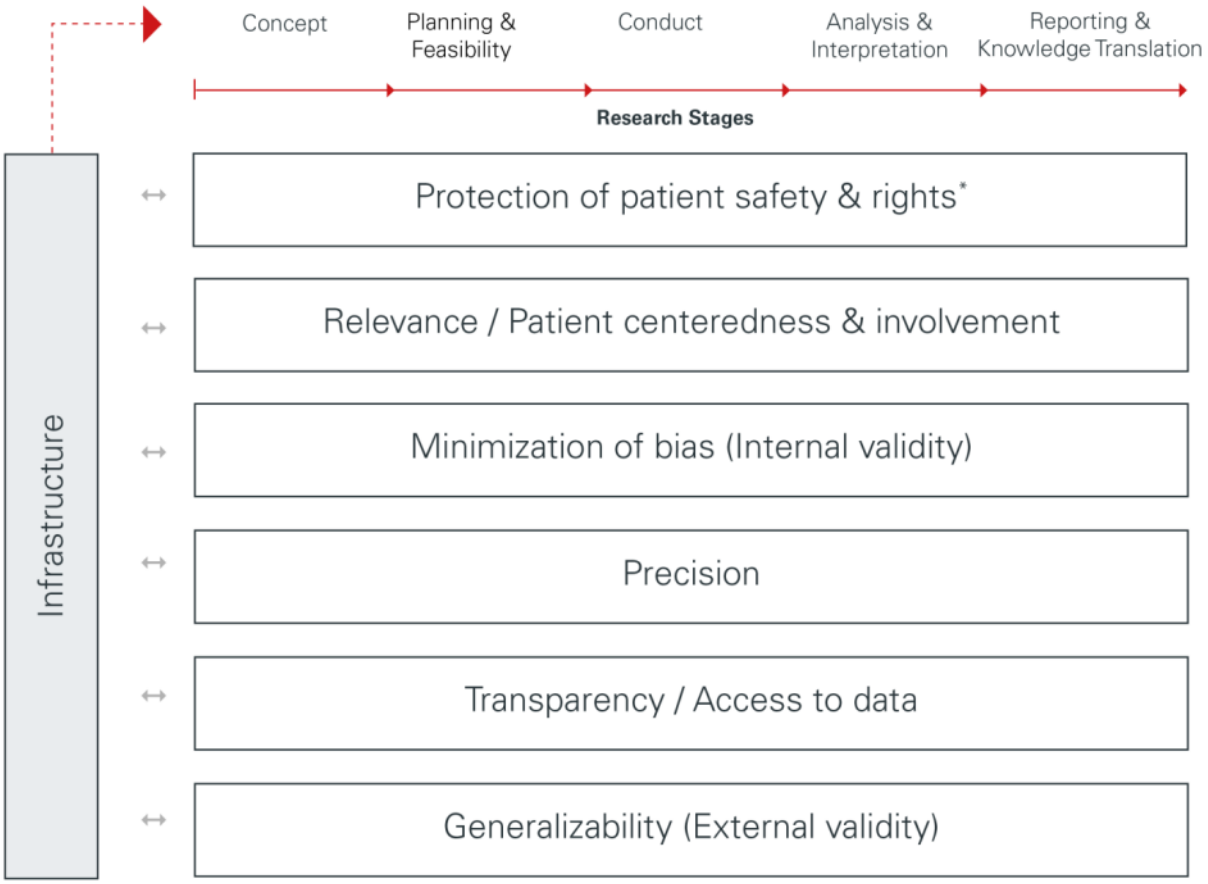

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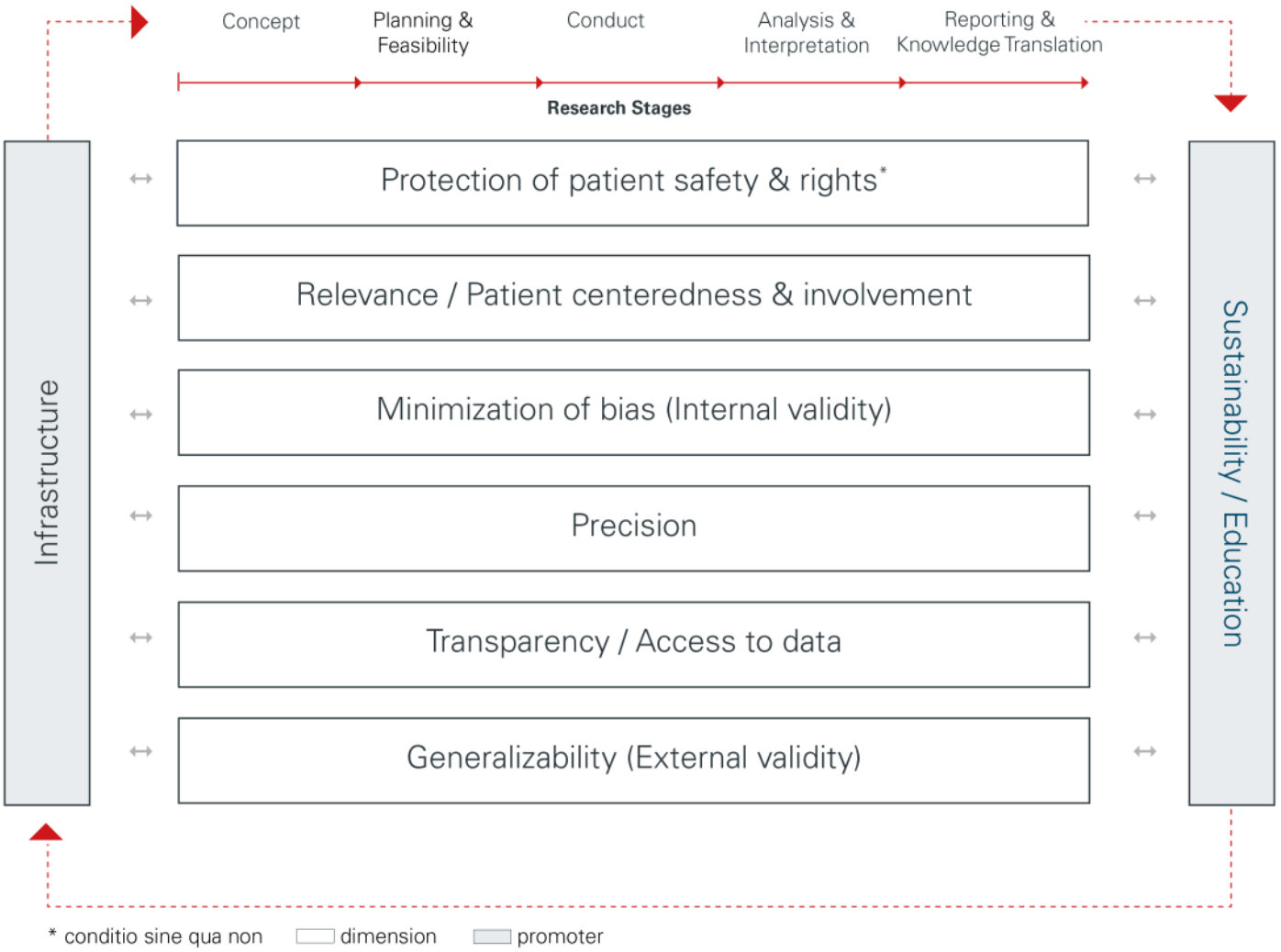
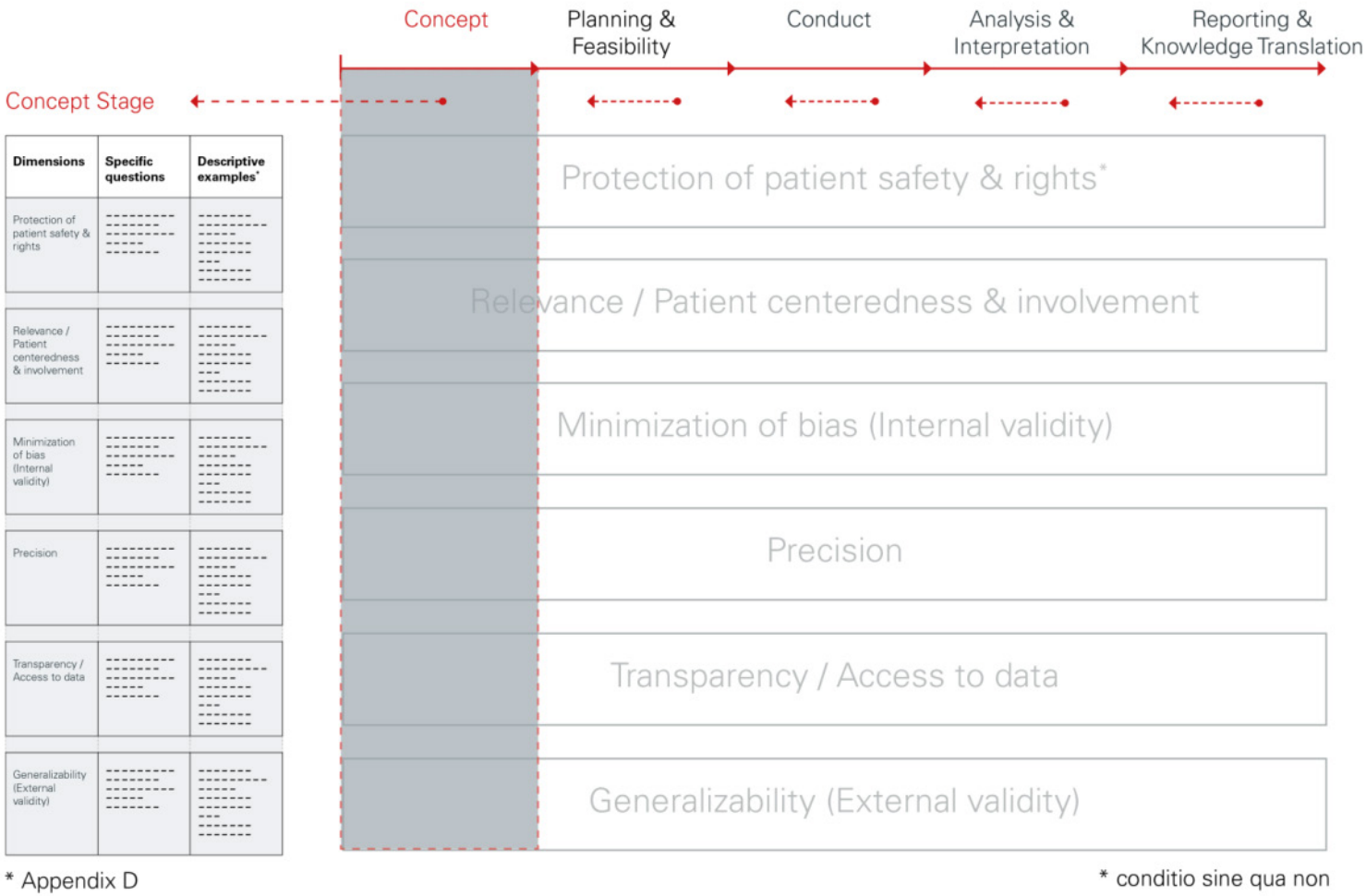
Results. INQUIRE Framework



Results. INQUIRE Operationalization



Study stage

Quality dimensions

Specific quality questions

Study Stage I: Concept **Milestone: Research question including study type defined and viable**	
Dimension	**Main question**
Protection of patient safety & rights	Can the research question be answered in the given setting?
	Does study consider equity appropriately?
	Is the research design adequate for the stage of an investigated technology to ensure patient safety?
	Do the (assumed) short and long term benefits of the study outweigh potential risks associated with the study (consistent with clinical equipoise)?
Relevance / Patient centeredness & involvement	Is significant add-on value to already existing evidence given, taking into consideration burden of disease and anticipated benefit of treatment?
	Are patient representatives/ advocates and their needs and values adequately involved in the development of the research question?
	Are outcome measures patient-relevant?
Minimization of bias (internal validity)	Is the selected study type/design appropriate to minimize bias?
	Are potential sources of bias anticipated, evaluating the magnitude and the likely direction?
	Are outcome measures well-defined, pre-specified, valid, reliable and measured at appropriate times?
Precision	Has estimate of the required sample size been made (for feasibility purposes, see "Protection of patient safety & rights")?

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Study stage

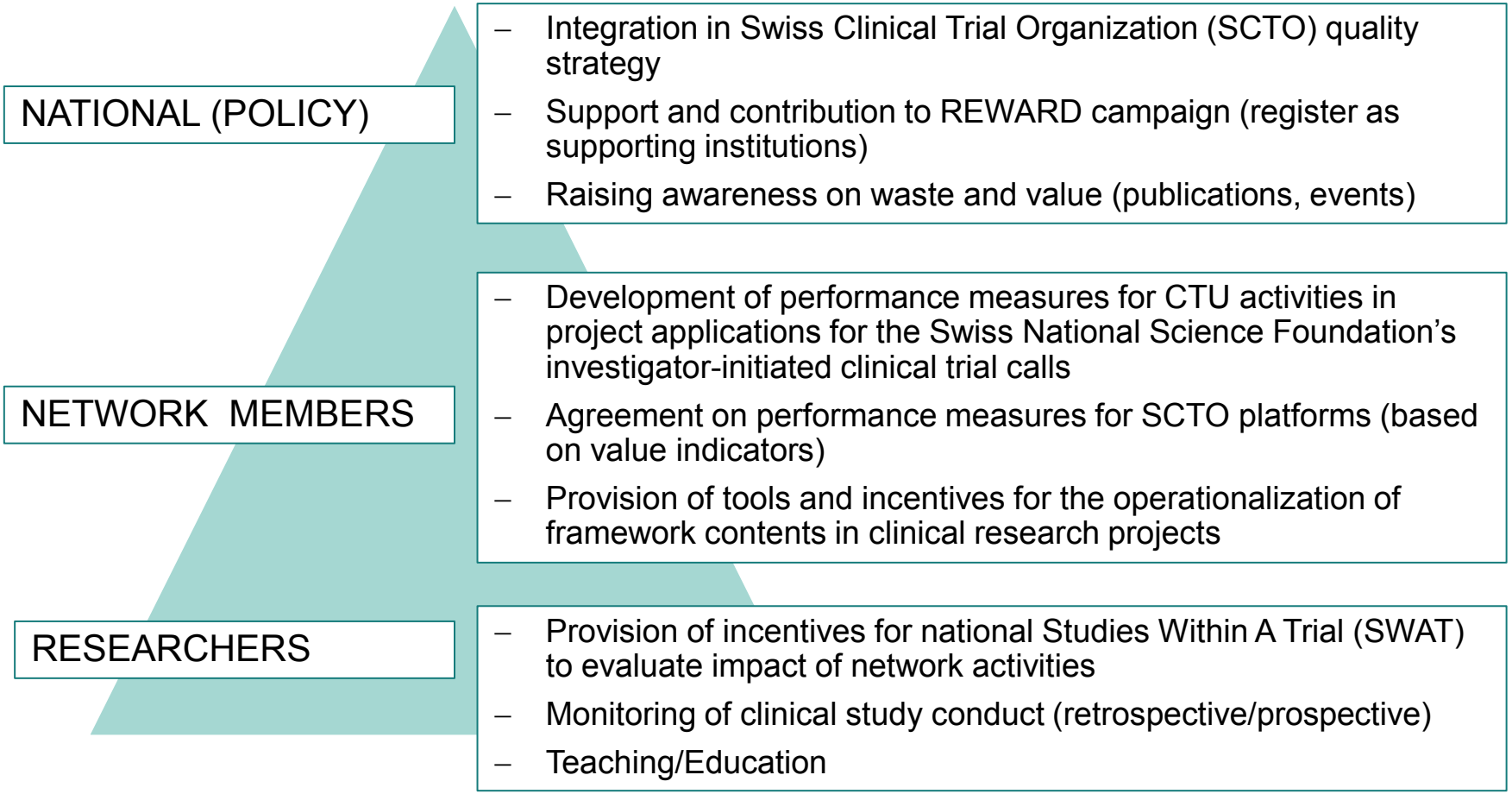
Quality dimensions

Study Stage I: Concept
Milestone: Research question including study type defined and viable

Dimension	Main question	Examples
Protection of patient safety & rights	Can the research question be answered in the given setting?	Based on a rough resource assessment, and potentially available study participants, is it feasible to answer the research question?
		Based on a rough budget estimate, is it feasible to answer the research question with a specified study type?
	Does study consider equity appropriately?	Are participants selected so that :
		vulnerable individuals are neither targeted for risky research nor withheld from research relevant to these populations?
		socially powerful individuals are not favored for potentially beneficial research?
	Is the research design adequate for the stage of an investigated technology to ensure patient safety?	Are sufficient data on toxicity/teratogenicity of an intervention available from animal studies or phase I studies?
	Do the (assumed) short and long term benefits of the study outweigh potential risks associated with the study (consistent with clinical equipoise)?	
Relevance / Patient centeredness & involvement	Is significant add-on value to already existing evidence given, taking into consideration burden of disease and anticipated benefit of treatment?	Are uncertainties in existing evidence identified and discussed in a systematic review?
		Does research:
		Expand or challenge current knowledge?
		Open additional areas for new research activity?
		Justify replication of existing evidence, if applicable?
	Are patient representatives/ advocates and their needs and values adequately involved in the development of the research question?	
	Are outcome measures patient-relevant?	Are outcomes patient-relevant, including quality of life, if applicable, and with judicious use of surrogate endpoints?
Minimization of bias (internal validity)	Is the selected study type/design appropriate to minimize bias?	Is the study randomized or, if not, appropriately controlled for confounding?
	Are potential sources of bias anticipated, evaluating the magnitude and the likely direction?	
	Are outcome measures well-defined, pre-specified, valid, reliable and measured at appropriate times?	Are outcomes: well-defined (upfront)?
		valid (measure what they intend to measure)?
		reliable(stable and consistent when repeatedly measured)?
		sensitive to important change?
		measured at appropriate times?
		standardized across studies (core outcome sets, if applicable)
Precision	Has estimate of the required sample size been made (for feasibility purposes, see "Protection of patient safety & rights")?	

Descriptive examples

Implications. The Swiss academic setting



Conclusions

- Quality of clinical research is often discussed, but rarely defined & focus varies across stakeholders.

- Comprehensive framework on quality based on stakeholder consensus to (1) provide common guidance for researchers
  (2) establish a common goal among stakeholders

- Framework supports stakeholders (predominantly academic institutions) in the assessment of overall research quality at each stage of the research process and for multiple study types

- To effectively increase quality of research in Switzerland further work on the practical implementation / take-up / adaptations for specific settings and purposes are needed

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Thank you
for your attention.

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