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# MoreTrials

**A public campaign to make it much easier to do randomised trials in medicine**

**Created by trialists from Oxford with The James Lind Library, & Sense About Science**

**It started on 1st January, 2016**

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# A paradox exists in medicine


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**This has only happened in the last 20 years, but only in medicine**

**And in medicine 20 years ago we created:**

**ICH-GCP**

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INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

# ICH HARMONISED TRIPARTITE GUIDELINE

# GUIDELINE FOR GOOD CLINICAL PRACTICE
# E6(R1)

Current *Step 4* version

dated 10 June 1996

*(including the Post Step 4 corrections)*

*This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.*

# GUIDELINE FOR GOOD CLINICAL PRACTICE

## INTRODUCTION

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

The objective of this ICH GCP Guideline is to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

The guideline was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organization (WHO).

This guideline should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities.

The principles established in this guideline may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects.

# ICH-GCP is NEITHER an international:

1. **Ethical standard**

2. **Scientific Quality standard**

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**We don't need another ethical standard**

**We already have one!**

**The Declaration of Helsinki**

**Which is universally used and regularly reviewed and updated.**

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# Why has ICH-GCP FAILED as a "scientific quality standard"

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# But, we have a TWOFOLD problem:

# Problem #1

# ICH-GCP

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# Problem #2

# ICH itself

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# MoreTrials

**To REPLACE**
**ICH-Good Clinical Practice (ICH-GCP)**

**with a modern set of principles of how to do a randomised trial well**

**developed by everybody in the trial community**

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# Progress in first year

# Organisations (8) Supporting MoreTrials

EORTC The future of cancer therapy

EUROPEAN SOCIETY OF CARDIOLOGY®

RICERC@ Rete Italiana Comitati Etici, Ricercatori e Cittadini

Alliance for Biomedical Research in Europe

AWMF

British Cardiovascular Society

ANZCA Clinical Trials Network

Deutsches Register Klinischer Studien
German Clinical Trials Register

http://moretrials.net/supporters/

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# More than 200 trialists from 28 countries

http://moretrials.net/supporters/

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ICH HARMONISED GUIDELINE

# INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE

## E6(R2)

Current *Step 2* version

dated 11 June 2015

*At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Steering Committee to the regulatory authorities of the ICH regions (the European Union, Japan, the USA, Health Canada and Switzerland) for internal and external consultation, according to national or regional procedures.*

# Updated open Letter to EMA & ICH: From 5 research organisations and an international consortium of 119 health researchers in 22 countries

***Signatories listed at end:***

To: European Medicines Agency (EMA)
ich@ema.europa.eu

International Council on Harmonisation (ICH)
step2comments@ich.org

26th February, 2016

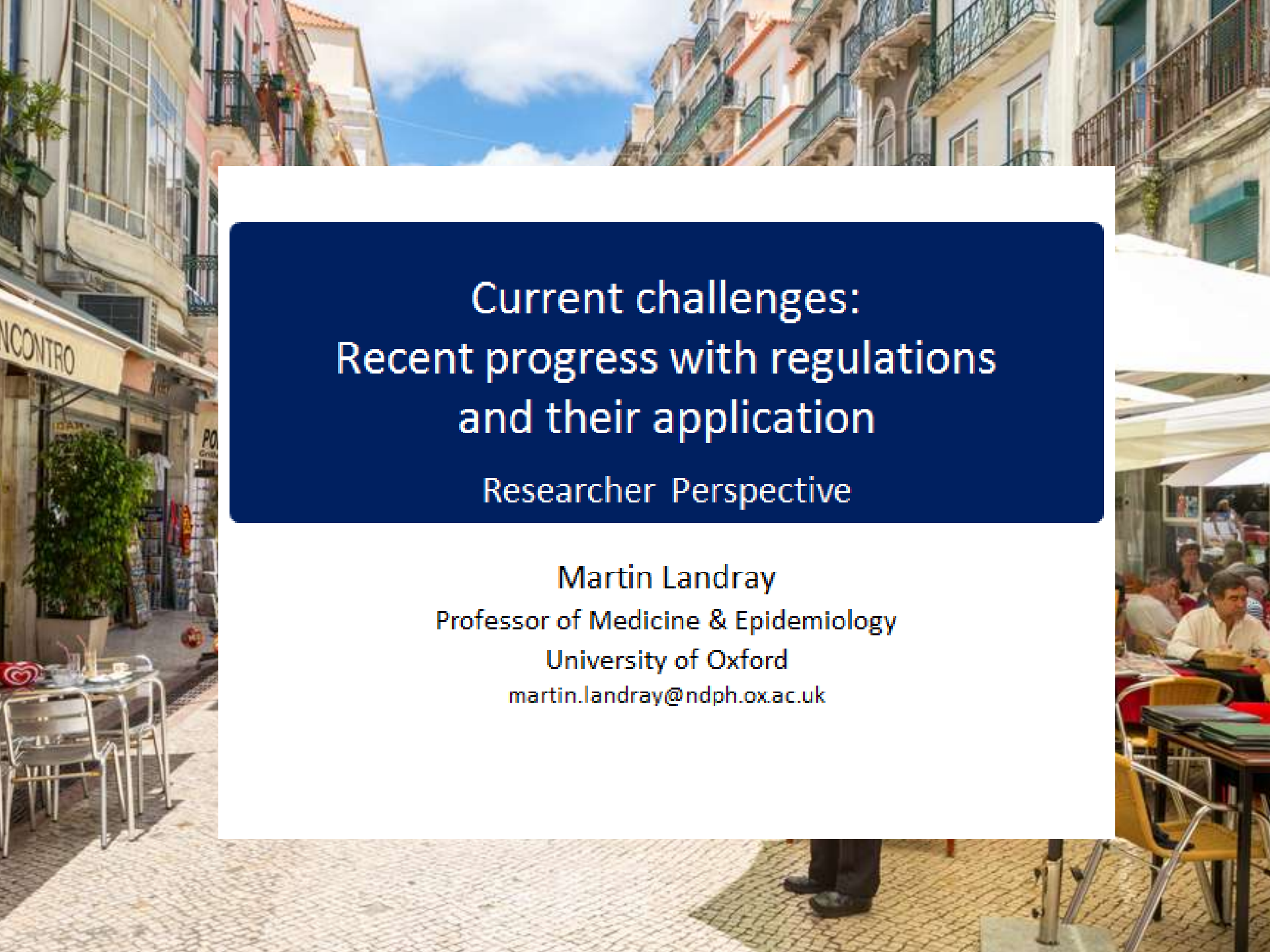
**Co-ordinated response to the consultation by the International Council for Harmonisation (ICH) on its proposed E6 (R2) "Integrated Addendum" to the ICH E6 Guideline for "Good Clinical Practice"**

The new EU Clinical Trial Regulation that was adopted in 2014 is intended to create a regulatory environment in Europe that promotes the conduct of clinical trials (which have declined in number following introduction of the 2001 EC Clinical Trial Directive) while ensuring appropriate protection for clinical trial participants. It refers to the ICH-GCP (International Council for Harmonisation Good Clinical Practice) guideline as a quality standard for clinical trials.

Along with many others, we have previously pointed out the serious problems with the ICH-GCP guideline. In particular, it places undue emphasis on less important aspects of clinical trials (e.g. source data verification) at the expense of those aspects of clinical trials (such as randomisation processes, follow-up completeness, risk-proportionate monitoring, and focused safety reporting) that have important implications not only for the safety of participants in clinical trials, but also for the reliability of the results of clinical trials and the consequent safety of future patients.

Moreover, a lack of flexibility in the ICH-GCP guideline and its interpretation (for example, a failure to recognise properly different levels of risk for participants in different types of trial) has resulted in clinical trial processes that are unnecessarily complex and expensive, as well as seriously hindering the adoption of innovative approaches to their conduct. As a result many clinical trials that should get done are not undertaken, and those that are started quite frequently fail to complete or provide reliable answers. Consequently, in our view, the current ICH-GCP guideline is not a suitable quality standard for the design, conduct, analysis or reporting of clinical trials.

Given these concerns, we welcomed the recent acknowledgement by ICH of the problems with its GCP guideline, and its decision to consult on proposals for change. However, for the reasons set out below, the changes proposed by ICH will do little to improve the regulatory environment for the conduct of clinical trials both in Europe and around the world.



# Current challenges: Recent progress with regulations and their application

## Researcher Perspective

Martin Landray
Professor of Medicine & Epidemiology
University of Oxford
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# Problems still in ICH-GCP update: #1/4

The update to ICH-GCP still focuses on things that don't matter (data checking/admin)

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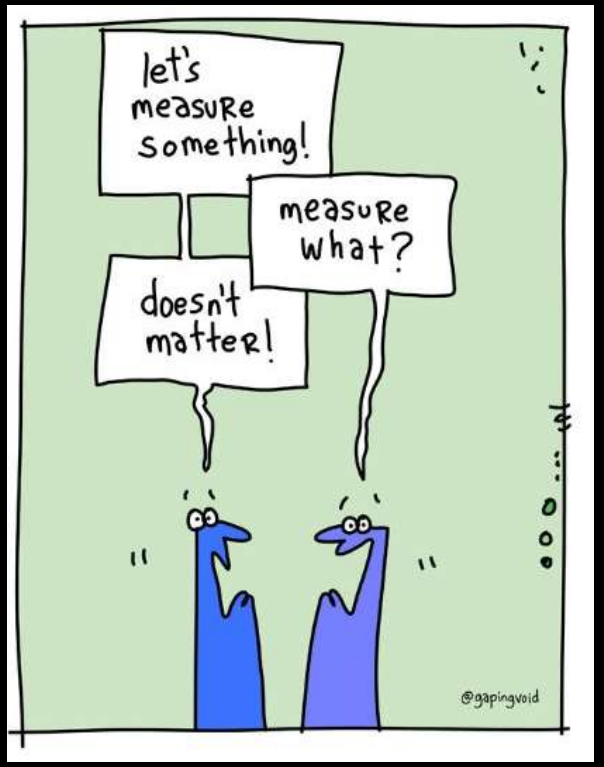


High quality DATA ≠ Reliable RESULT

Reliable RESULT ≠ High quality DATA

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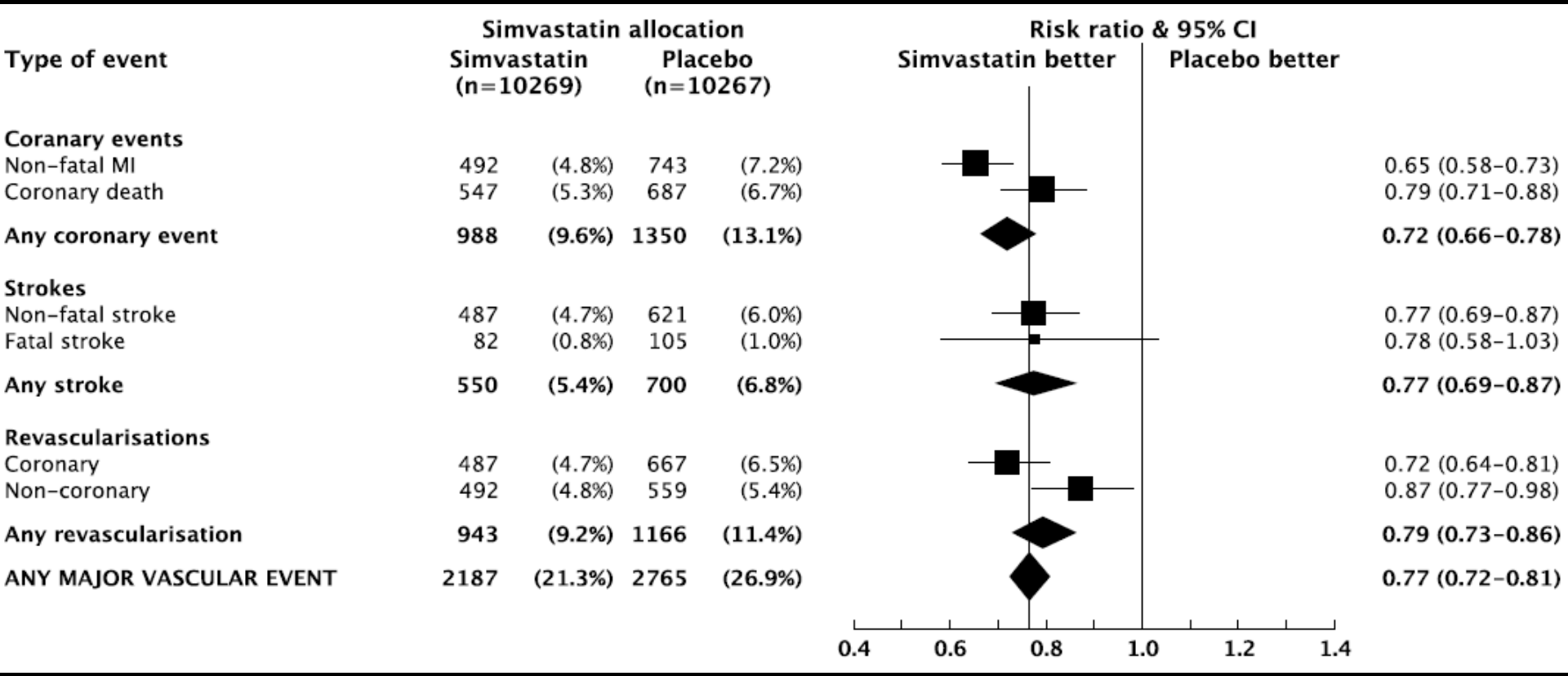

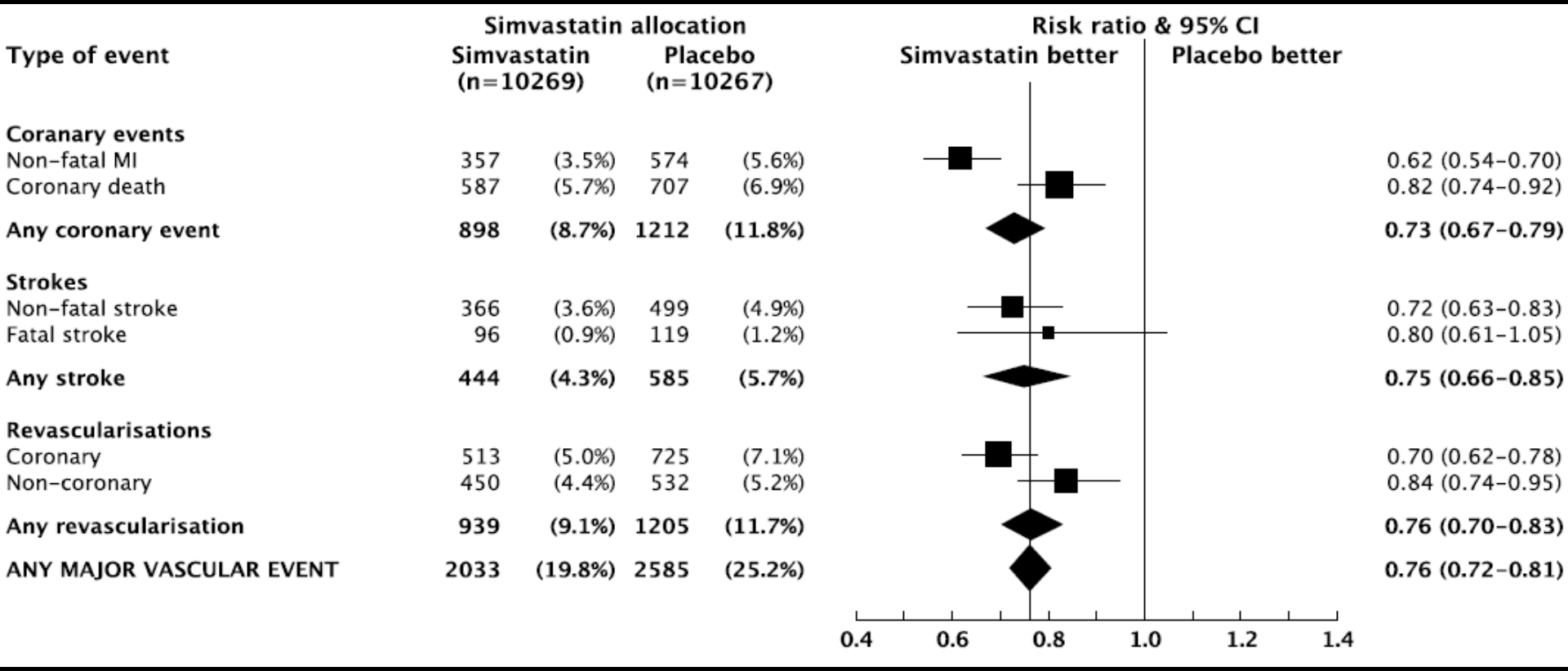

# Problems still in ICH-GCP update: #2/4

The update to ICH-GCP still focuses on things that don't matter and STILL OMITS those few key principles that do matter.

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# Staff Training: It's not painting-by-numbers

"ITT can't be correct, or it would have been included in ICH-GCP"

"ITT and avoiding missing outcomes is not consistent with statements in ICH-GCP about patient withdrawal."


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# Problems still in ICH-GCP update: #3/4

# The update doesn't fix the confusion in key definitions across different trial regulations.

(remember ICH has "harmonisation" in its name)

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# Definition of trial "Sponsor"

**ICH GCP**:
"An individual, company, institution, or organization which takes responsibility for the initiation, management, *and/or* financing of a clinical trial."

**US 21 CFR 312.3**:
"Sponsor means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization."

**EU Clinical Trials Regulation:**
"'Sponsor means an individual, company, institution or organisation which takes responsibility for the initiation, for the management and for setting up the financing of the clinical trial."

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# Problems still in ICH-GCP update: #4/4

ICH insist that their original text "is still correct" so just adding new text as an addendum results in even more confusion.

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# Original text

*"In general there is a need for on-site monitoring before, during, and after the trial: however in exceptional circumstances the sponsor may determine that central monitoring in conjunction with procedures such as investigators' training and meetings, and extensive written guidance can assure appropriate conduct of the trial in accordance with GCP."*

**Original ICH-GCP 5.18.3**

# New text

*"The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials.*
*The flexibility in the extent and nature of monitoring described in this section is intended to permit varied approaches that improve the effectiveness and efficiency of monitoring.*
*A combination of on-site and centralized monitoring activities may be appropriate."*

**Draft Addendum to ICH-GCP 5.18.3**

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ICH
harmonisation for better health

# ASSEMBLY
# AGENDA PAPERS

**9 – 10 November 2016**

**Osaka, Japan**

# What's next in 2017?

## Increase number of researchers & organisations supporting MoreTrials.

## Write a New-GCP.

## Make the campaign a public campaign

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**EC Clinical Trials Regulation (2014):**

*"…ICH guidelines on good clinical practice should be taken appropriately into account for the application of the rules set out in this Regulation, provided that there is no other specific guidance issued by the Commission"*

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# http://moretrials.net/

## ABOUT MORETRIALS

MoreTrials was created by a number of trialists from leading universities around the world,

The James Lind Library, an online library showing the development of fair tests of treatment, and

Sense About Science, a charity that helps people to make sense of scientific and medical claims.

See the list of supporters of the MoreTrials Campaign.

The campaign started in January 2016:

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The mission of ICH is to "achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration, thereby reducing duplication of testing and reporting carried out during the research and development of new medicines."

Created 25 years ago, its membership reflects its mission to harmonise across regions the regulatory approval process for new drugs developed by industry (text reproduced from ICH's website FAQs:

"The ICH Parties are comprised of representatives from the following Regulatory Parties:
– [illegible] represented by the European Commission (EC) and the European Medicines Agency (EMA)
– Japan, the Regulatory Party is the Ministry of Health, Labour and Welfare (MHLW)
– USA, the Regulatory Party is the Food and Drug Administration (FDA)
– Canada, the Regulatory Party is the Health Products and Food Branch (HPFB)
– Switzerland, the Regulatory Party is the Swissmedic

As well as from the following Industry Parties:
– Europe, the European Federation of Pharmaceutical Industries and Associations (EFPIA)

# Thank You!

**or join by emailing me:**
**tim.sprosen@ndph.ox.ac.uk**

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