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**Isla S Mackenzie**
**On behalf of SCOT investigators**

# The Standard Care versus Celecoxib Outcome Trial

# Declarations of interest

**University of Dundee was the study sponsor.**

**Funding was an investigator initiated research grant from Pfizer.**

**TMM has provided consultancy on NSAIDs to Novartis, Pfizer, NiCox & Astra Zeneca**

# Background

- Selective cyclooxygenase-2 inhibitors (COX-2) and non-selective non-steroidal anti-inflammatory drugs (nsNSAIDs) have been associated with adverse cardiovascular effects.
- SCOT compared the cardiovascular safety of celecoxib with nsNSAID therapy in the setting of European healthcare systems.
- SCOT was initially an EMA commitment.

# Method: Patients

- Aged ≥ 60 years with osteoarthritis or rheumatoid arthritis
- Free from established cardiovascular disease
- Taking chronic prescribed nsNSAIDs in primary care

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# Pragmatic Trial

- Search Primary Care Practices
- Invite all suitable subjects
- Randomise eligible
- GPs prescribed treatment
- Usual care thereafter
- Follow up by Record-Linkage
  - Hospitalisations & Deaths

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# End Points

- **Primary**
  - **Hospitalisation for non-fatal MI, non-fatal stroke or cardiovascular death**
- **Main Secondary**
  - **Hospitalisation or death from ulcer related upper gastrointestinal complications (bleeding, perforation or obstruction)**
- **Other Secondary**
  - **Heart failure, mortality, renal failure, critical limb ischaemia; pulmonary embolism.**

# Power

- Powered for non-inferiority to exclude 40% increase in CV events with celecoxib v nsNSAIDs
- Required 277 events on treatment

# End Point Detection & Adjudication

- By Record-Linkage to computerised hospitalisation data & deaths and/or Reported by investigators
- Original hospital & GP case records retrieved copied & abstracted
- Independent end point committees

# Committees

- **Cardiovascular Endpoint Committee:**
  - **John McMurray (Chair), Pardeep Jhund, Mark Petrie, Michael MacDonald.**
- **Gastrointestinal Endpoint Committee:**
  - **James Scheiman (Chair), John Dillon, Jane Moeller, Angel Lanas.**
- **Independent Data Monitoring Committee:**
  - **Kim Fox (Chair), Gordon Murray, Frank Murray.**

# Results

- >9,400 patients screened
- 7,297 patients randomised
- Mean FU ~ 3.2 years (max 6.3)
- 9 regional centers
- 706 primary care practices
- UK, Denmark & The Netherlands

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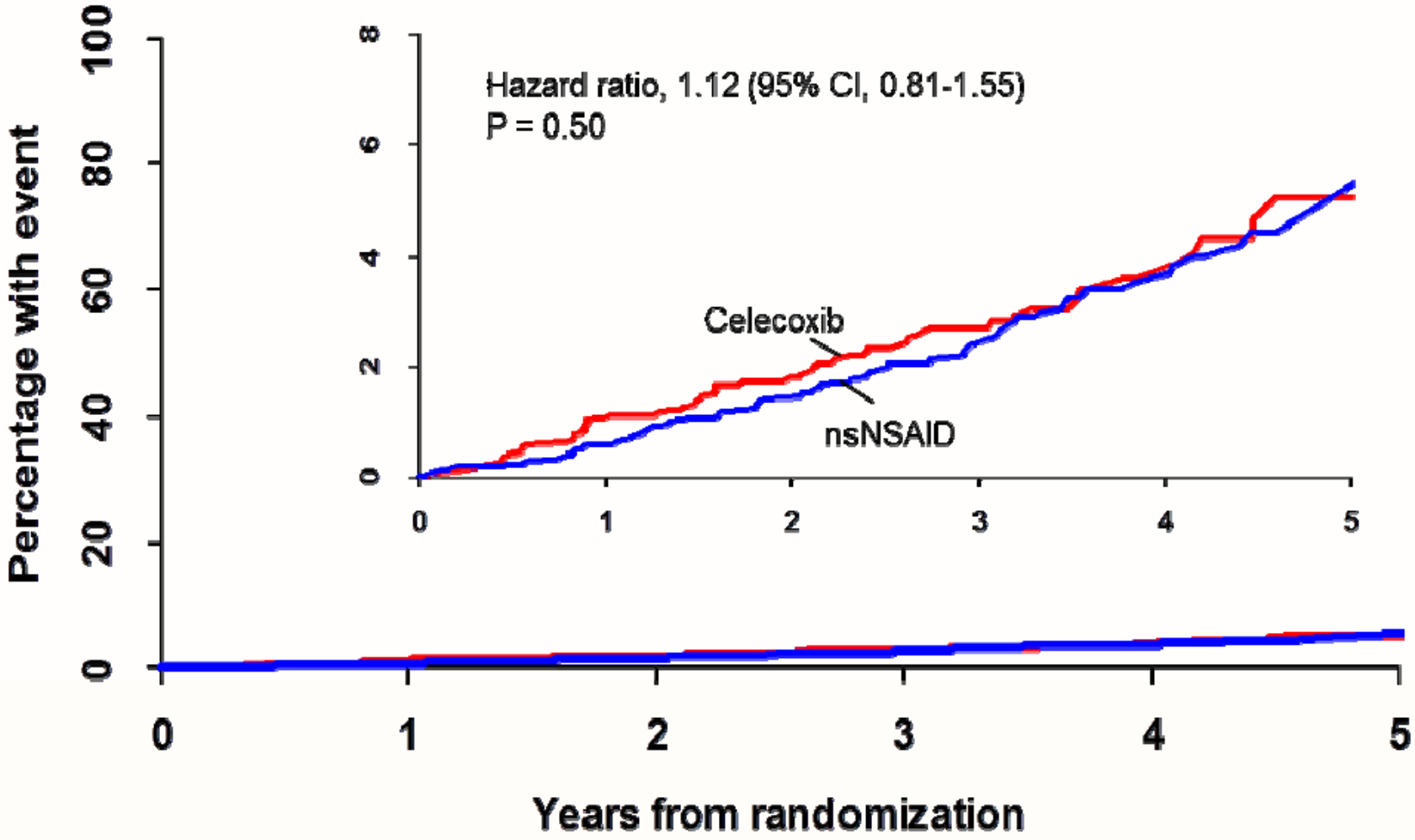
# Baseline Characteristics

| | Celecoxib | nsNSAIDs |
|---|---|---|
| Age | 68.8y | 68.2y |
| % Male | 41.9% | 39.2% |
| BMI | 29.2% | 29.8% |
| Current smoker | 15.0% | 16.0% |
| Diabetes | 8.3% | 7.8% |
| High BP | 44.8% | 44.0% |
| High Cholesterol | 34.8% | 33.2% |
| Statin Rx | 21.1% | 20.5% |
| Aspirin Rx | 11.5% | 11.9% |
| Ulcer Healing Rx | 38.4% | 37.2% |
| Peptic Ulcer History | 7.0% | 6.5% |
| Diclofenac | 38.7% | 38.7% |
| Ibuprofen | 31.5% | 31.6% |

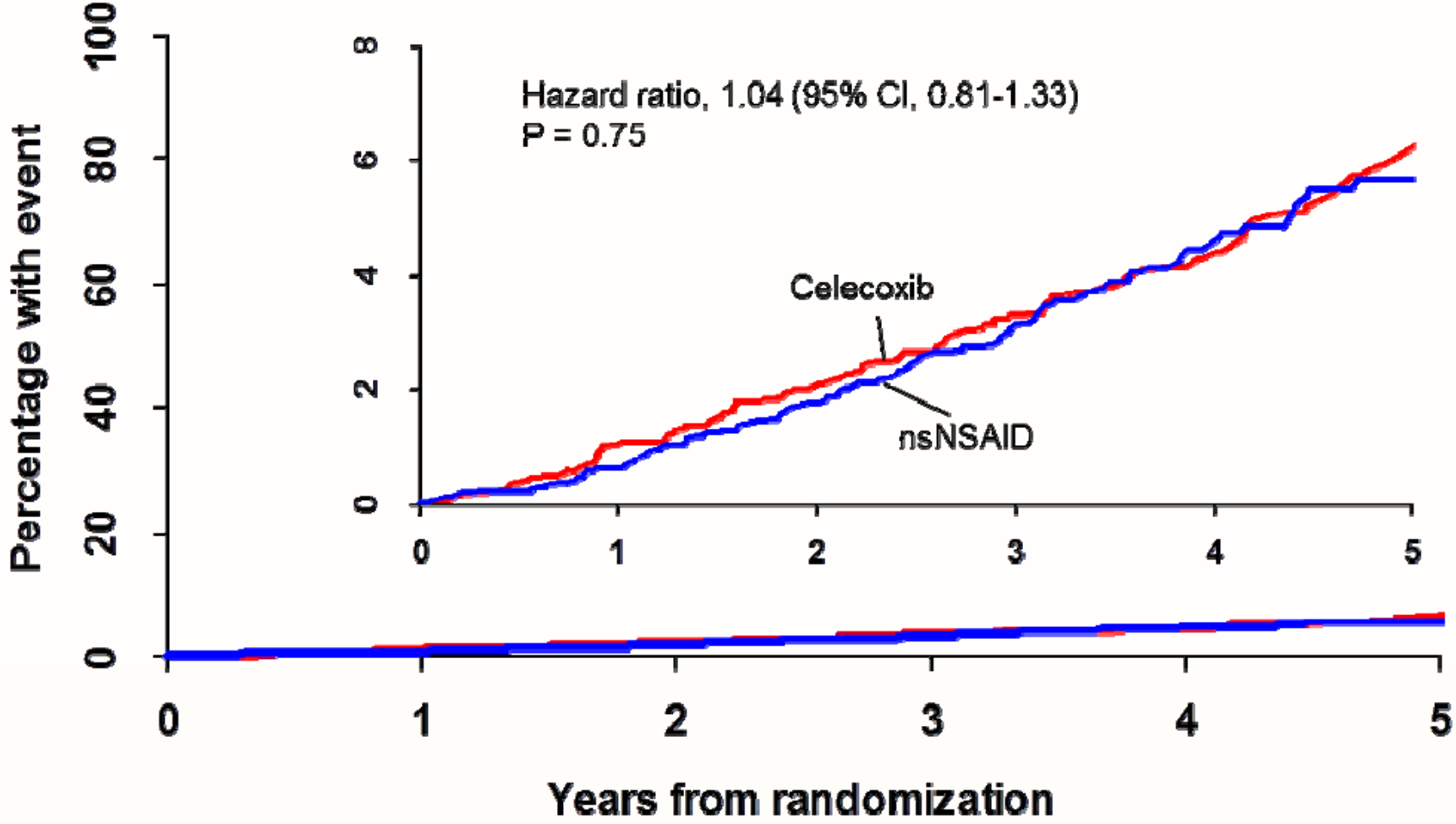
# Adjudicated event Rates

- On treatment primary event rate:
  - 0.9 per 100 patient years
- Intention to Treat primary event rate:
  - 1.1 per 100 patient years
- On treatment Ulcer-related UGI Complications
  - 12 events
- ITT Ulcer-related UGI Complications
  - 15 events

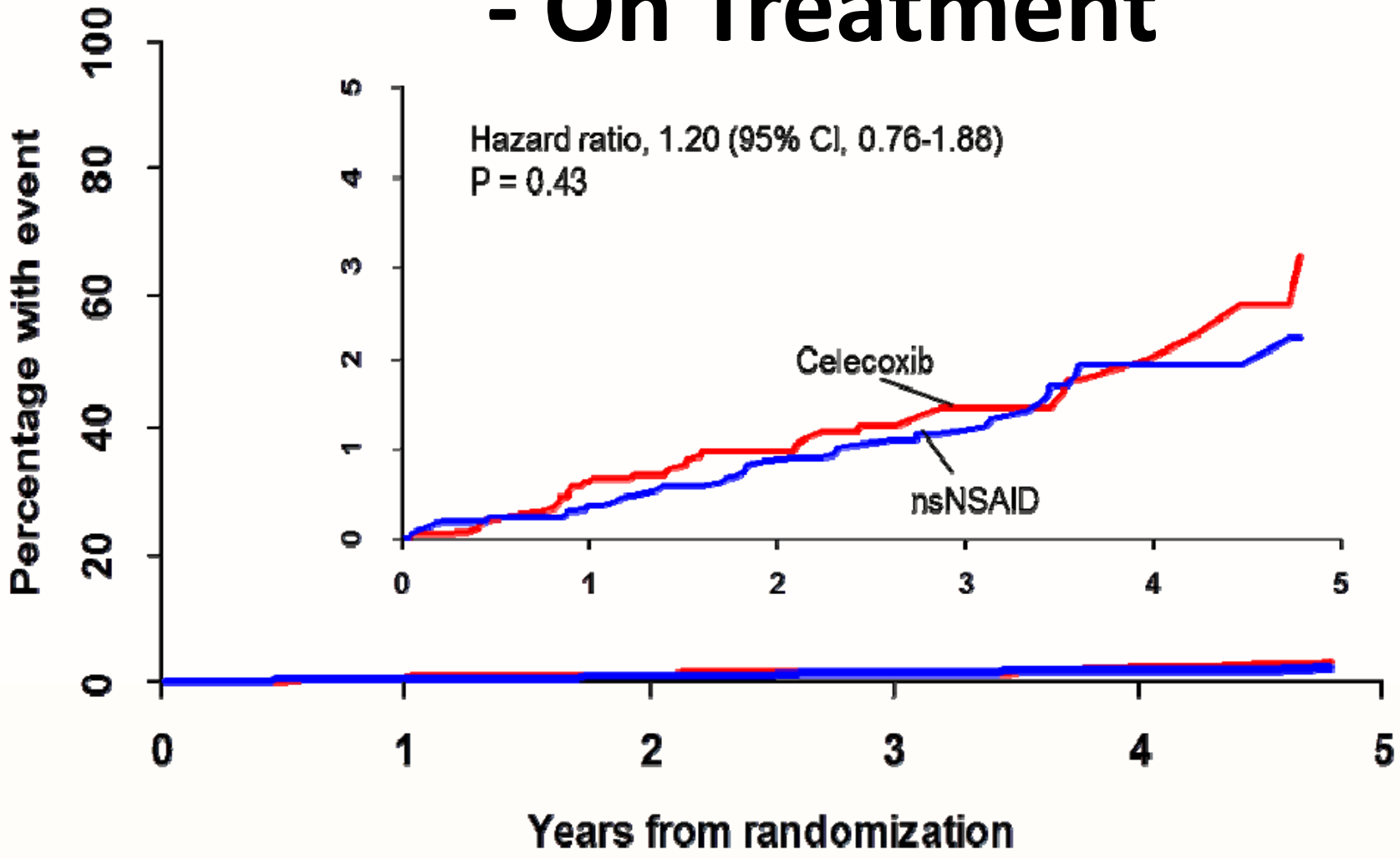
# Primary Composite End Point - On Treatment



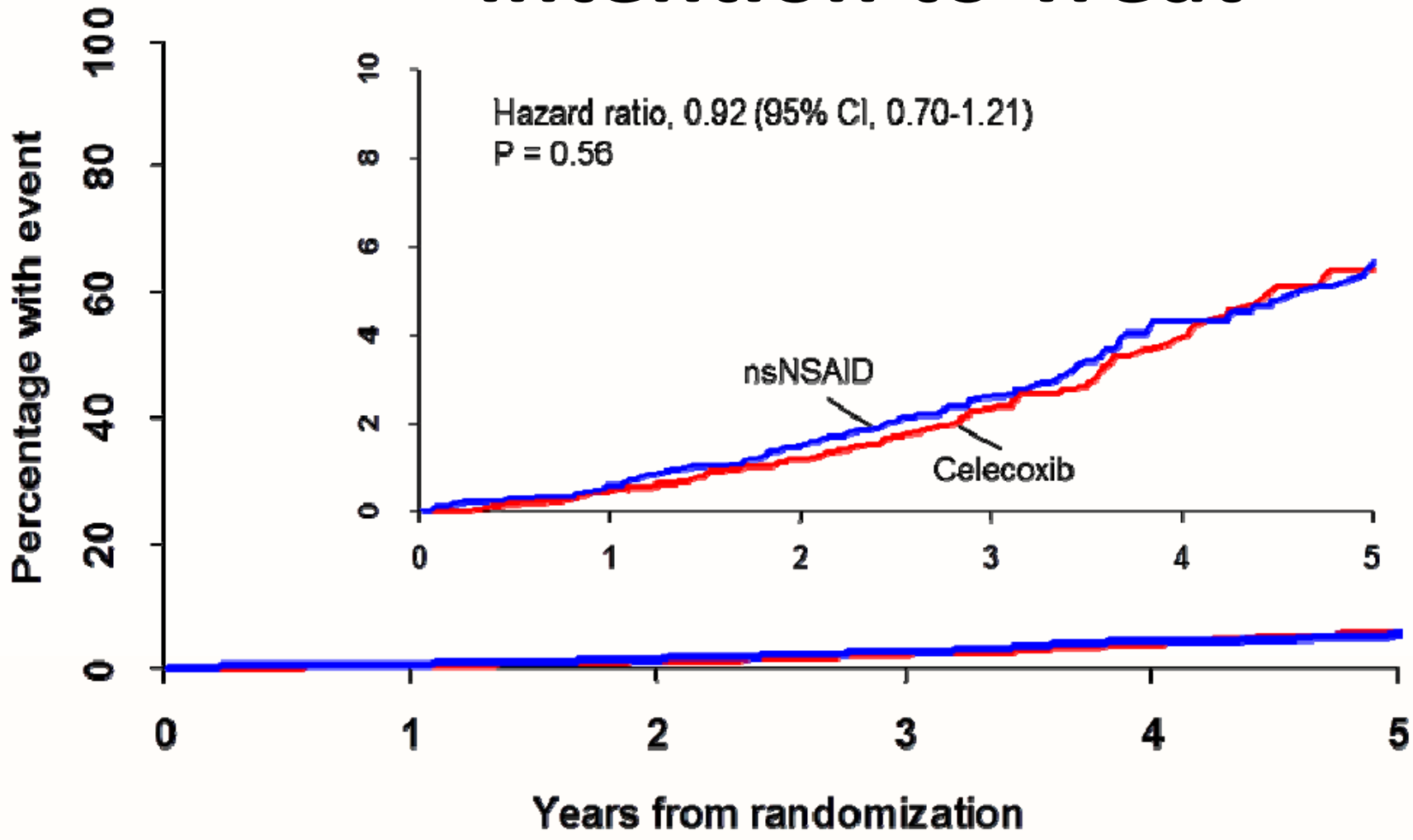
# Primary Composite Endpoint - Intention to Treat



# All-Cause Mortality - On Treatment

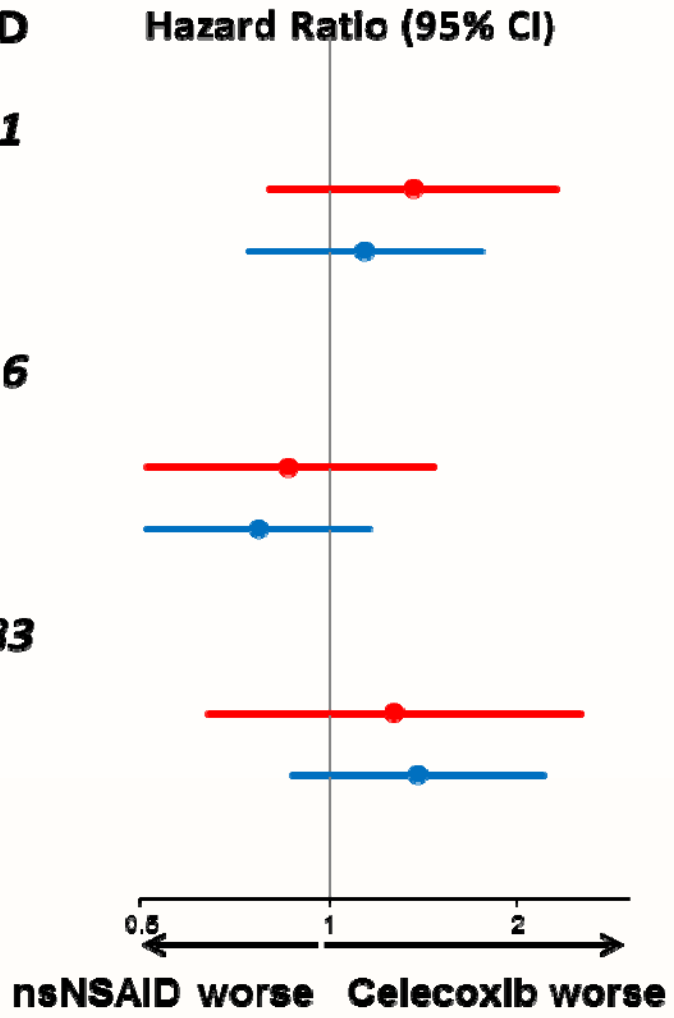


# All-Cause Mortality - Intention to Treat



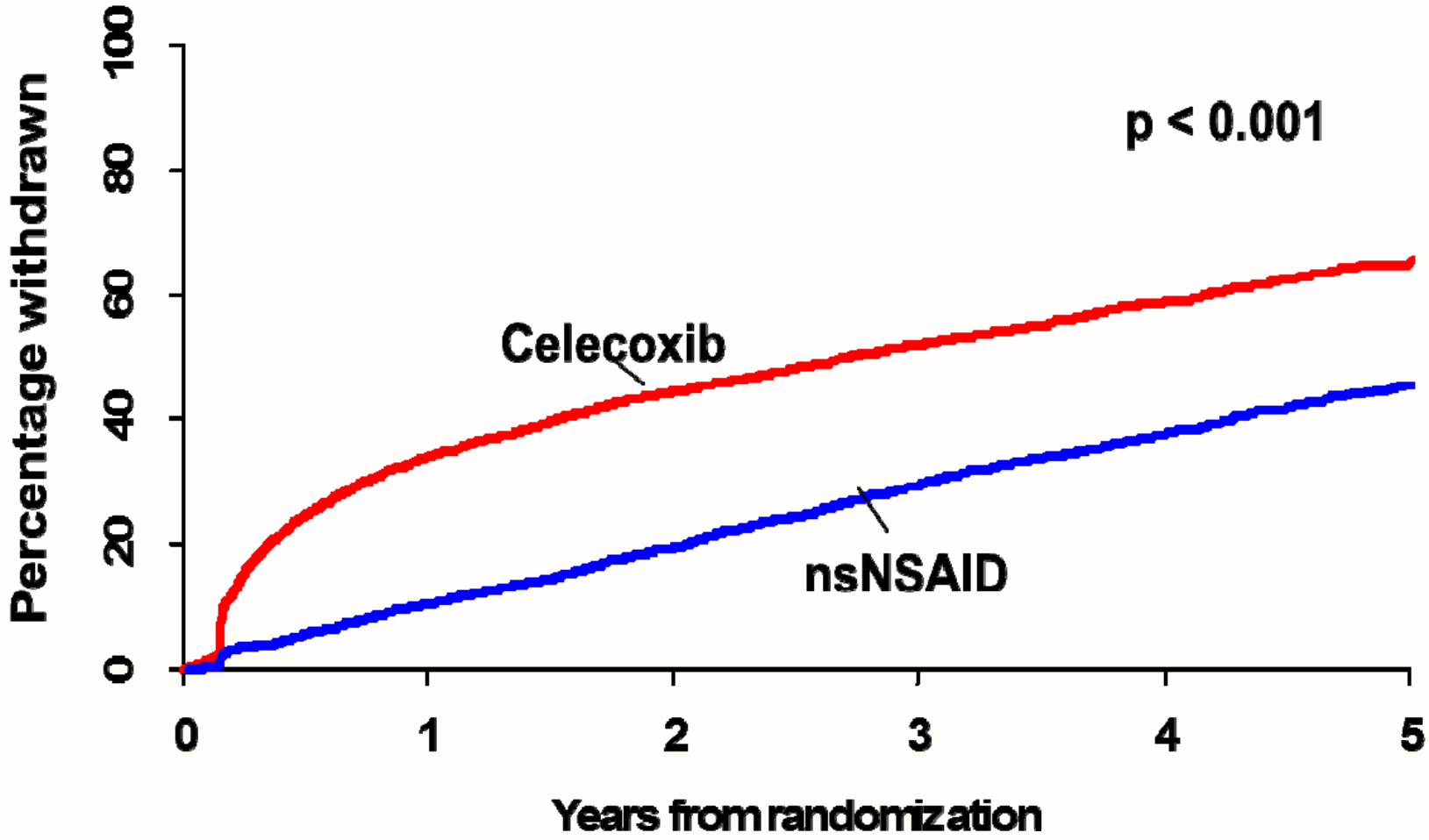
# Primary Endpoint by Baseline NSAID Subgroups

| Baseline NSAID | Celecoxib | nsNSAID |
|---|---|---|
| *Ibuprofen* | *1149* | *1151* |
| On-Treatment | | |
| Intention-to-treat | | |
| *Diclofenac* | *1410* | *1416* |
| On-Treatment | | |
| Intention-to-treat | | |
| *Other nsNSAID* | *1088* | *1083* |
| On-Treatment | | |
| Intention-to-treat | | |



# Withdrawal from randomized treatment group

**50.9% withdrew from celecoxib vs 30.2% from any nsNSAID**



# % Reasons recorded in those withdrawn from randomised Rx

| Reason recorded | Celecoxib | nsNSAID |
|---|---|---|
| Lack of efficacy | 11.2% | 3.0% |
| Switch or stopped | 6.6% | 8.1% |
| Adverse Event | 8.3% | 4.4% |
| Doctor recommended (non-AE) | 4.7% | 6.0% |
| Patient requested | 6.0% | 2.3% |
| Not tolerated | 3.9% | 1.2% |
| Serious Adverse Event | 2.6% | 1.9% |
| Protocol Violation | <0.1% | <0.1% |
| Other | 4.6% | 4.4% |

# Safety Outcomes

- **Serious Adverse Events:**
  - **1155 (31.7%) celecoxib**
  - **1183 (32.4%) nsNSAID**
- **Serious Adverse Reactions:**
  - **190 (5.2%) celecoxib**
  - **213 (5.8%) nsNSAID**
- **Serious gastrointestinal Adverse Reactions**
  - **38 celecoxib**
  - **66 gastrointestinal nsNSAIDs P<0.007**

# Safety Outcomes

- **Adverse Reactions:**
  - **804 (22%) celecoxib**
  - **586 (16.1%) nsNSAIDs (p<0.001)**

# Summary

**In patients with arthritis, without known cardiovascular disease, CV event rates were low and serious ulcer-related complication rates very low, and neither outcome differed significantly between nsNSAIDs and celecoxib**

# Implications for patient care

- In the study population, nsNSAIDs and celecoxib both appeared acceptably safe.
- In patients who get significant symptomatic relief from these medicines the benefit / risk balance appears positive.