# WRAP UP IN FRENCH

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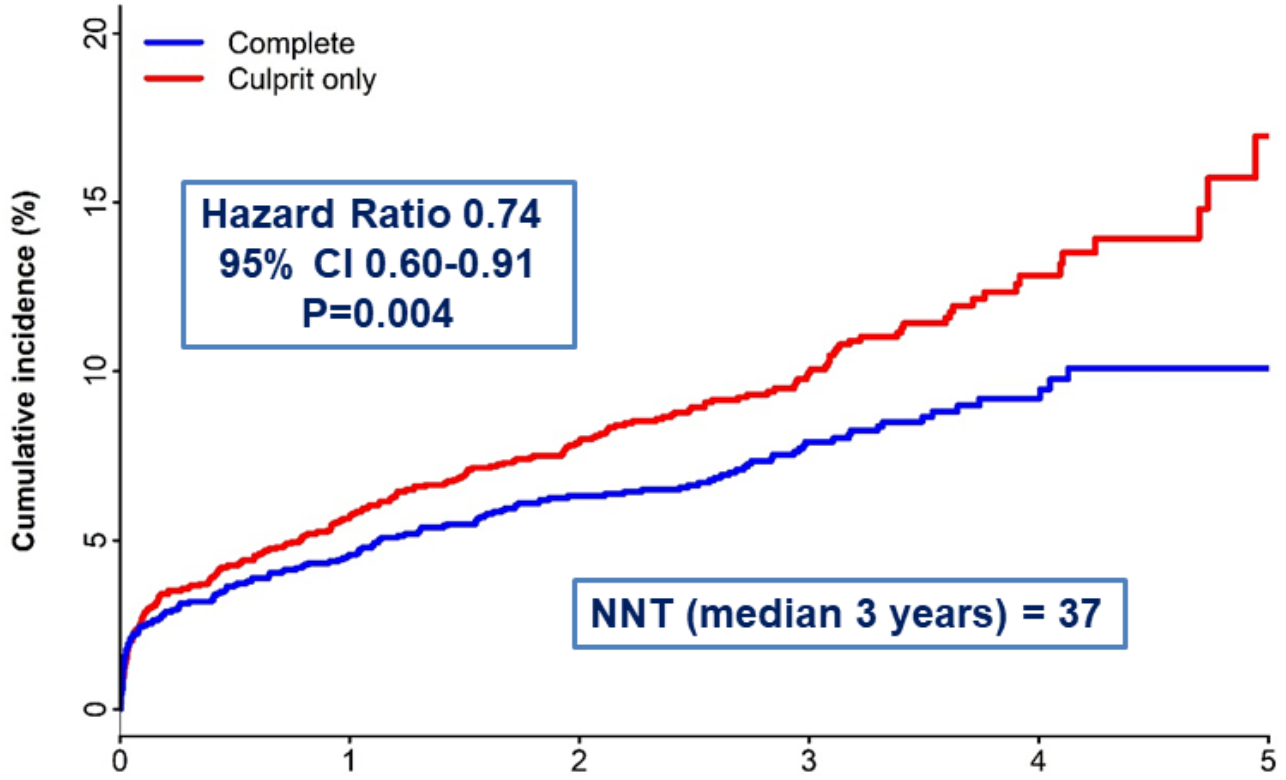
COMPLETE TRIAL

# First Co-Primary Outcome: CV Death or New MI




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Complete | 2016 | 1904 | 1677 | 938 | 337 | 70 |
| Culprit only | 2025 | 1897 | 1666 | 933 | 310 | 59 |

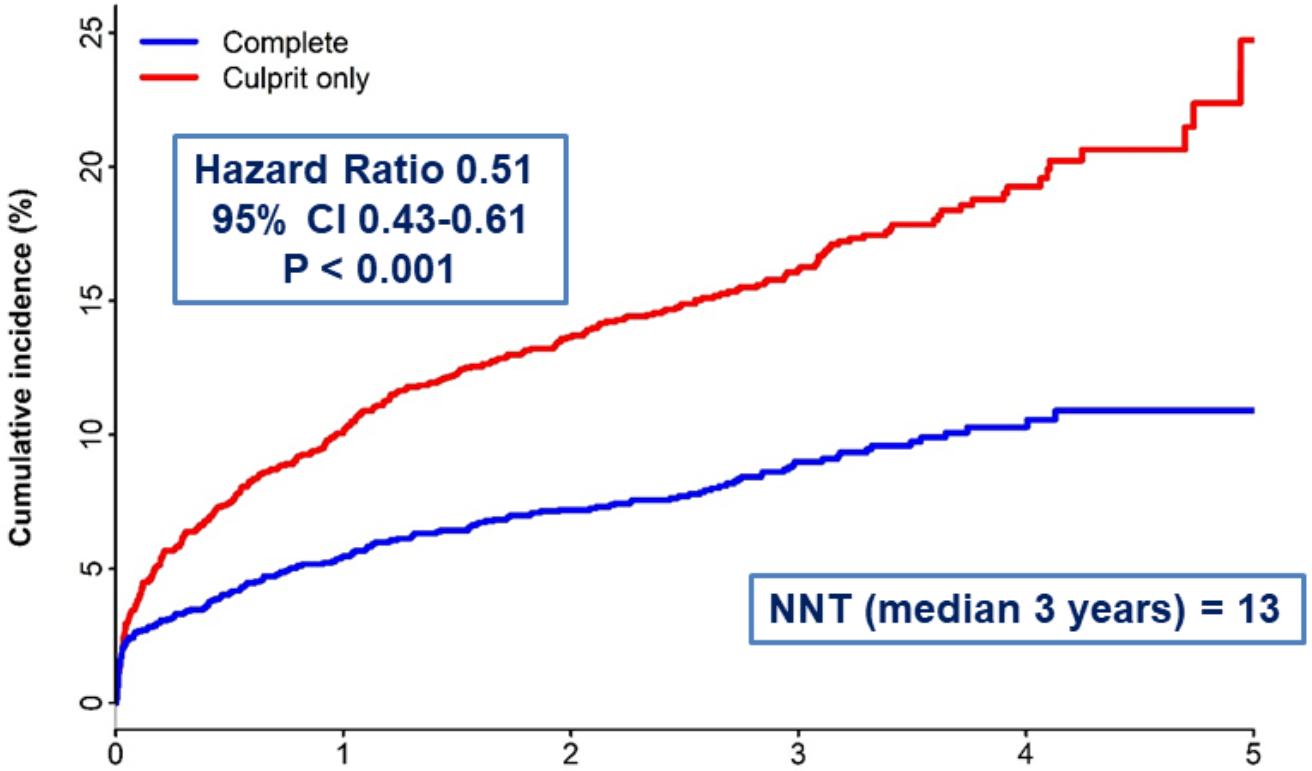
Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Hamilton Health Sciences

McMaster University HEALTH SCIENCES

COMPLETE TRIAL

# 2nd Co-Primary Outcome: CV Death, New MI, or IDR




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Complete | 2016 | 1886 | 1659 | 925 | 329 | 66 |
| Culprit only | 2025 | 1808 | 1559 | 865 | 294 | 57 |

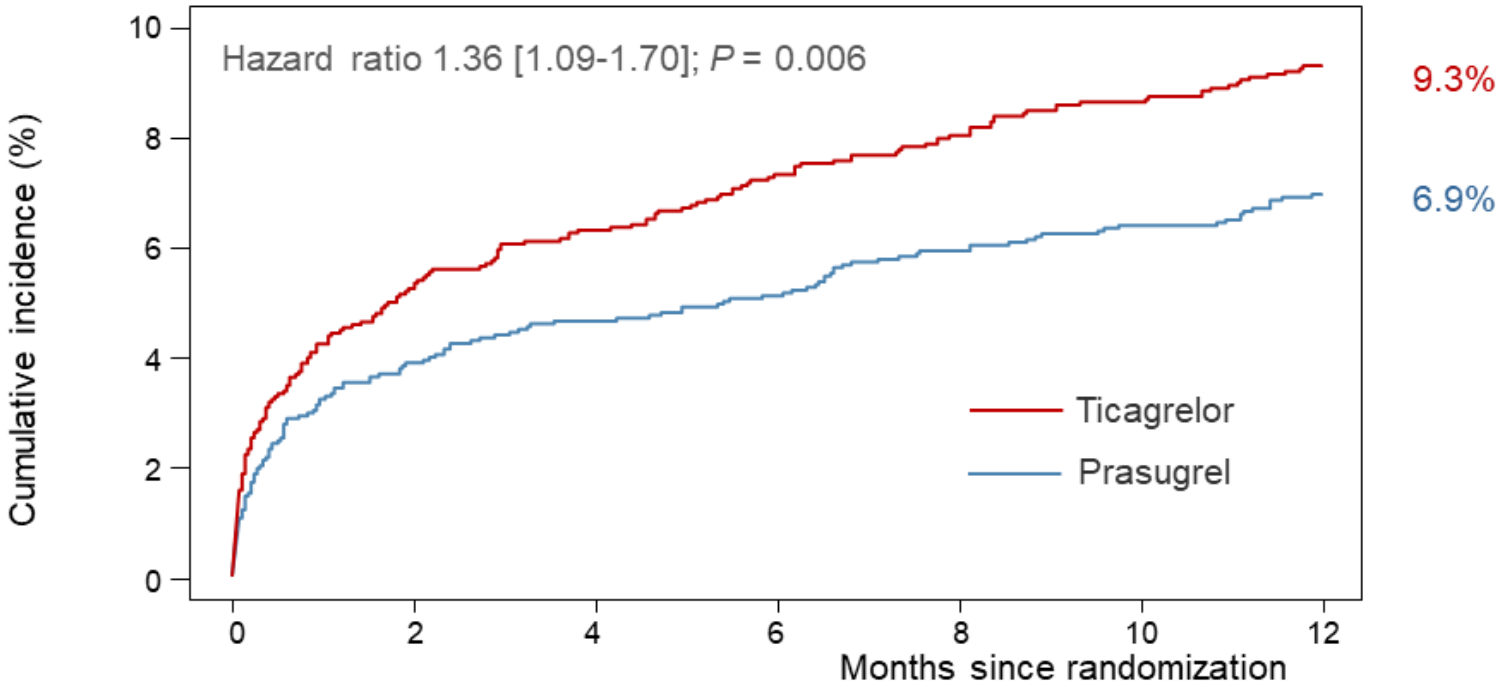
Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Hamilton Health Sciences

McMaster University HEALTH SCIENCES

# Primary End point

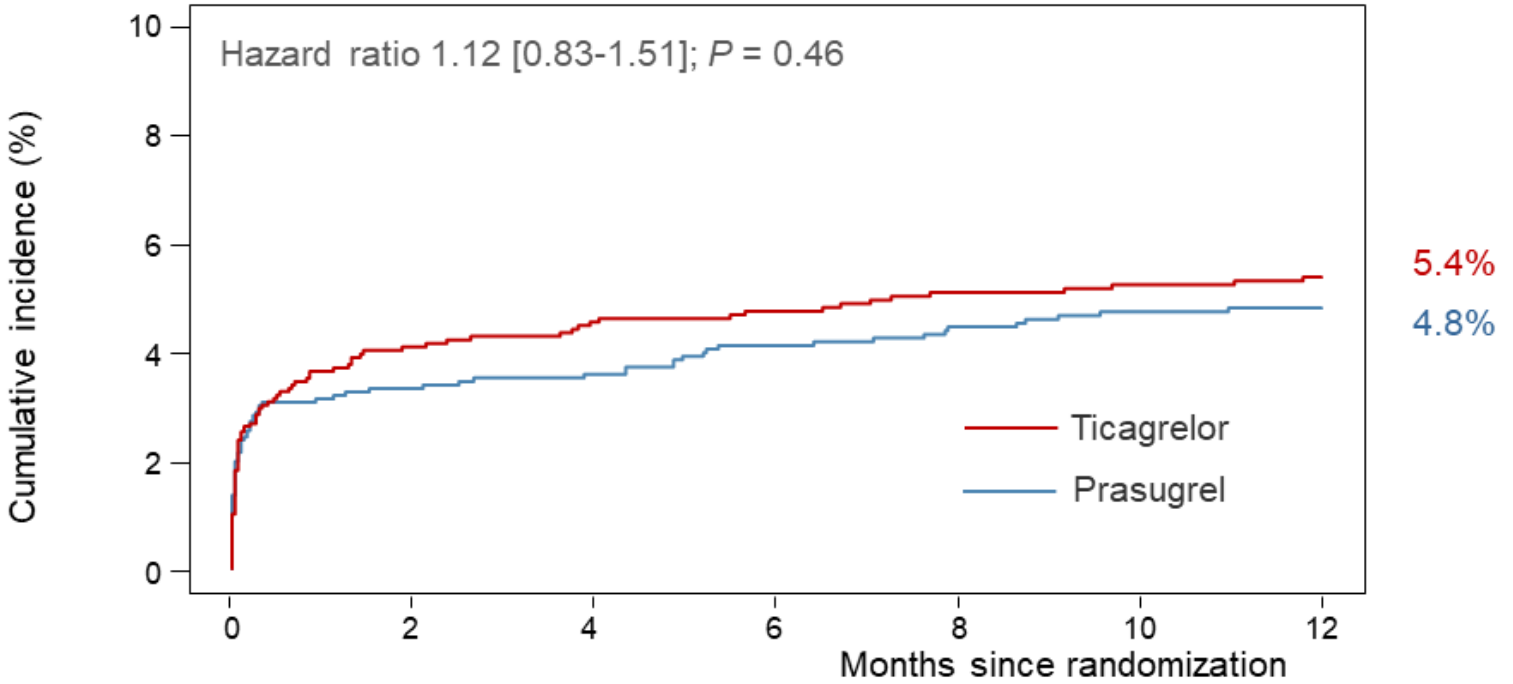
## (Composite of Death, MI, or Stroke)




| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ticagrelor | 2012 | 1877 | 1857 | 1835 | 1815 | 1801 | 1772 |
| Prasugrel | 2006 | 1892 | 1877 | 1862 | 1839 | 1829 | 1803 |

# BARC Type 3-5 Bleeding

(Safety End point)




**No. at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ticagrelor | 1989 | 1441 | 1399 | 1356 | 1319 | 1296 | 1266 |
| Prasugrel | 1773 | 1465 | 1427 | 1397 | 1357 | 1333 | 1307 |

# Summary And Conclusion

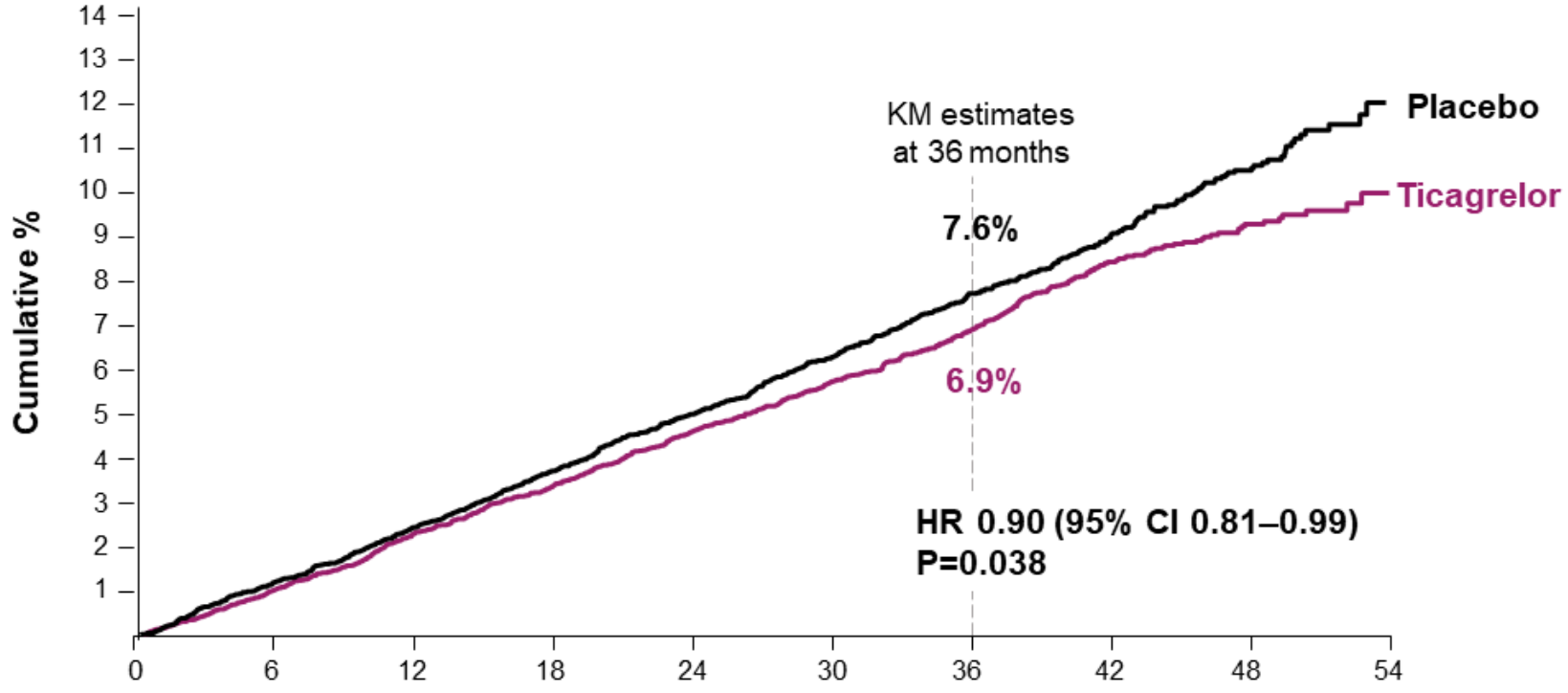
DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.

Technische Universität München

**In ACS patients with or without ST-segment elevation, treatment with Prasugrel as compared with Ticagrelor significantly reduced the composite rate of death, myocardial infarction, or stroke without an increase in major bleeding.**

# THEMIS - Primary Composite Endpoint

## Cardiovascular death/MI/stroke




| N at Risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Ticagrelor | 9619 | 9416 | 9237 | 9074 | 8909 | 8692 | 5974 | 3664 | 1684 | 170 |
| Placebo | 9601 | 9414 | 9246 | 9076 | 8909 | 8692 | 5934 | 3682 | 1685 | 174 |

CI=confidence interval; HR=hazard ratio; KM=Kaplan-Meier; MI=myocardial infarction; N=number of patients

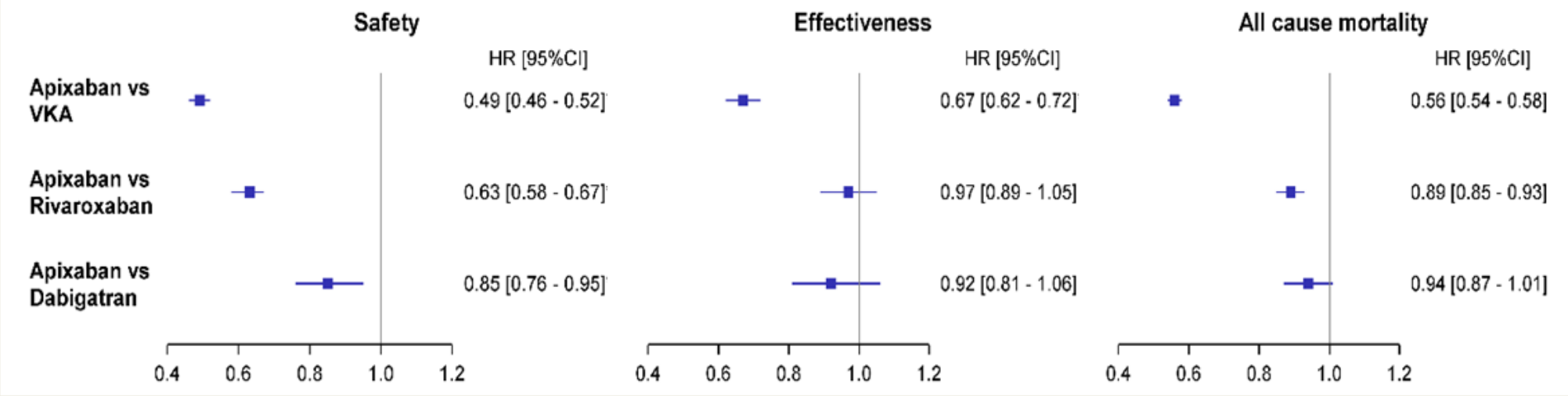
# THEMIS

- In patients with stable coronary artery disease and diabetes, but without a prior history of myocardial infarction or stroke, compared with aspirin alone, the combination of ticagrelor plus aspirin reduced the primary endpoint of CV death, MI, or stroke.
- This benefit was achieved at the expense of increased major bleeding.
- This strategy of long-term DAPT may be beneficial in selected patients at low risk of bleeding but with a high risk of ischemic events.

CV = cardiovascular; DAPT= dual antiplatelet therapy; MI=myocardial infarction

NAXOS
Apixaban in patients with atrial fibrillation in Real Life French Study

# Comparative safety and effectiveness (propensity score adjusted comparison)




major bleeding events leading to hospitalisation

Stroke and systemic thromboembolism

NAXOS

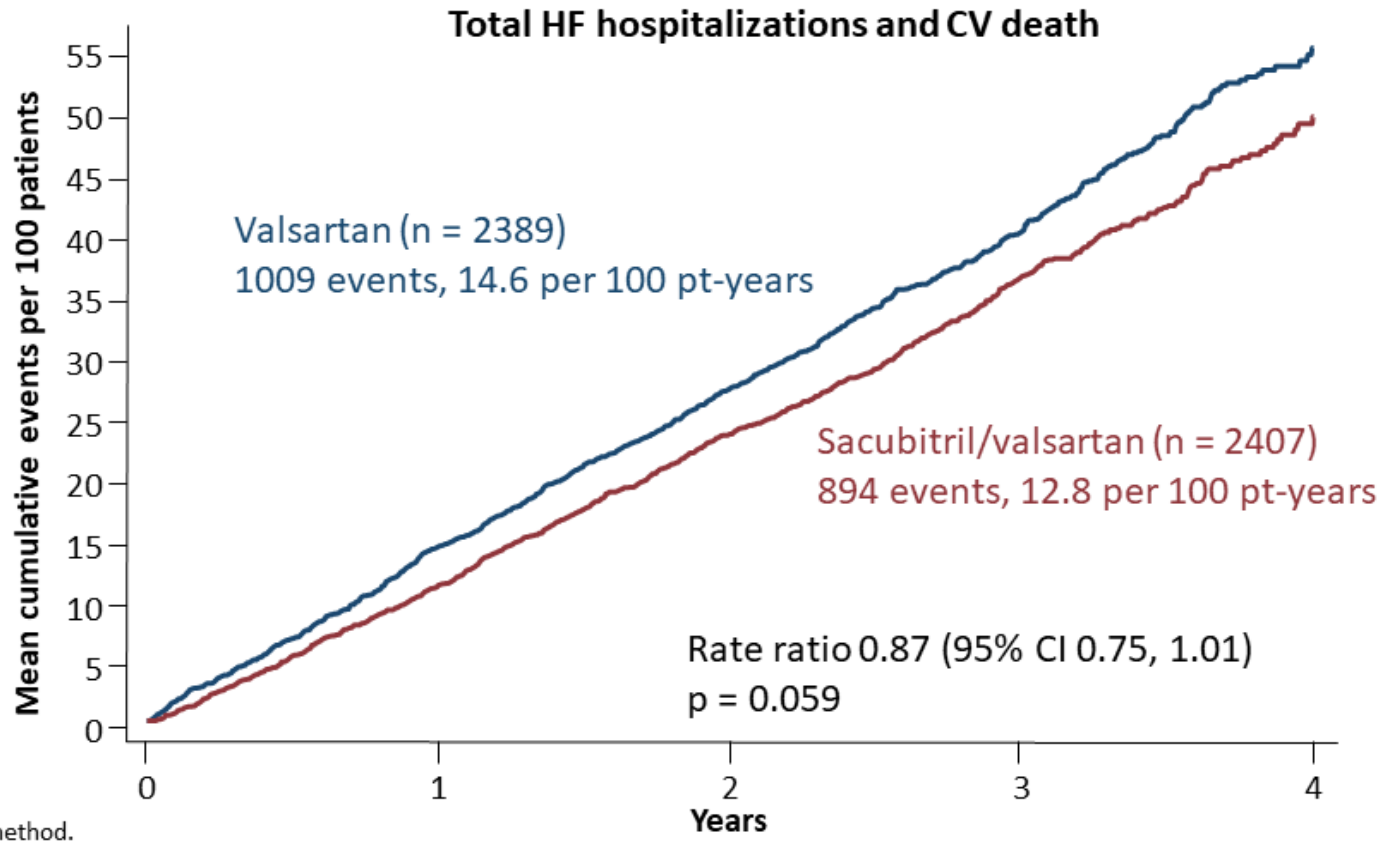
Apixaban in patients with atrial fibrillation in Real Life French Study

# Conclusions

- In this large observational population-based comparison of OACs initiation in patients with NVAF, apixaban use was associated with superior safety, superior effectiveness and lower mortality than VKAs, consistent with the results from ARISTOTLE.
- Apixaban use was associated with lower bleeding and similar effectiveness as rivaroxaban or dabigatran.
- However, given the observational nature of these analyses, they should be viewed as hypothesis-generating.
- Given the lack of randomised comparisons between DOACs, these observations are of interest to patients, clinicians, regulators and payers.
- The magnitude of some differences between DOACs suggest that head-to-head RCTs appear warranted.

# PARAGON-HF primary results

## Recurrent event analysis of total HF hospitalizations and CV death*

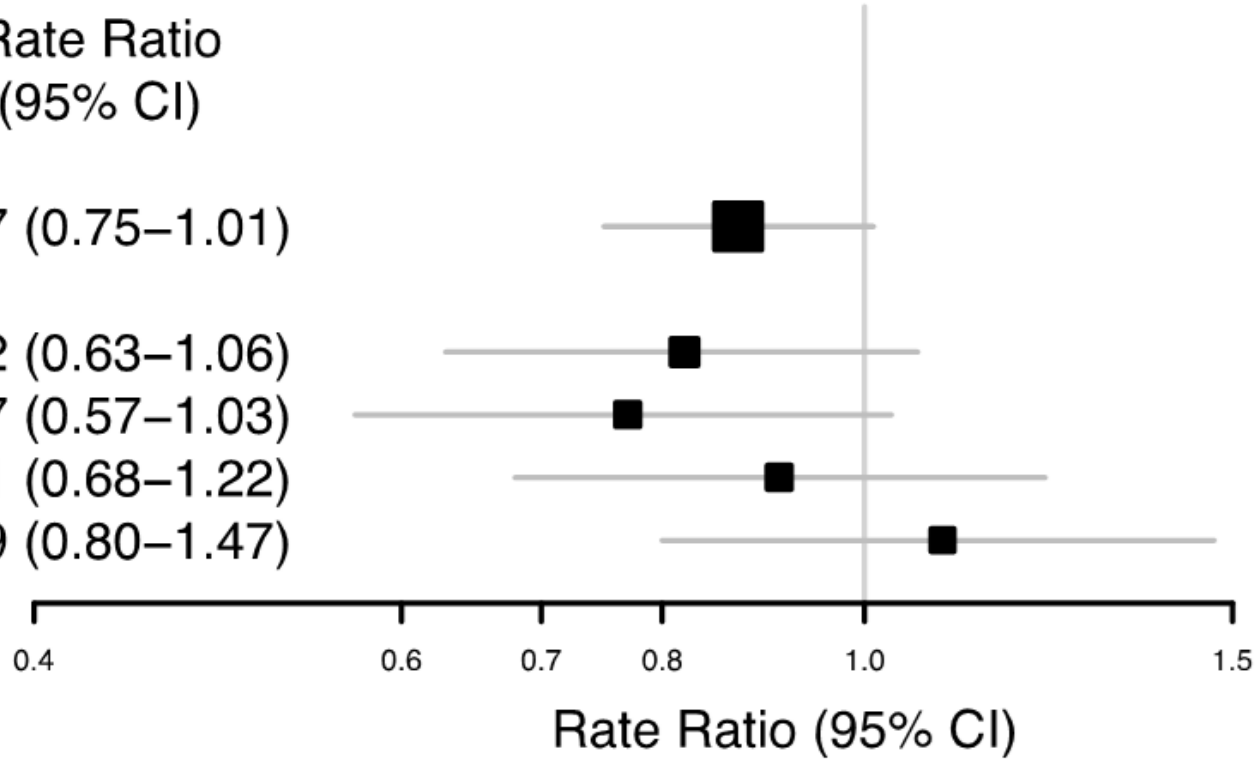



*Semiparametric LWYY method.

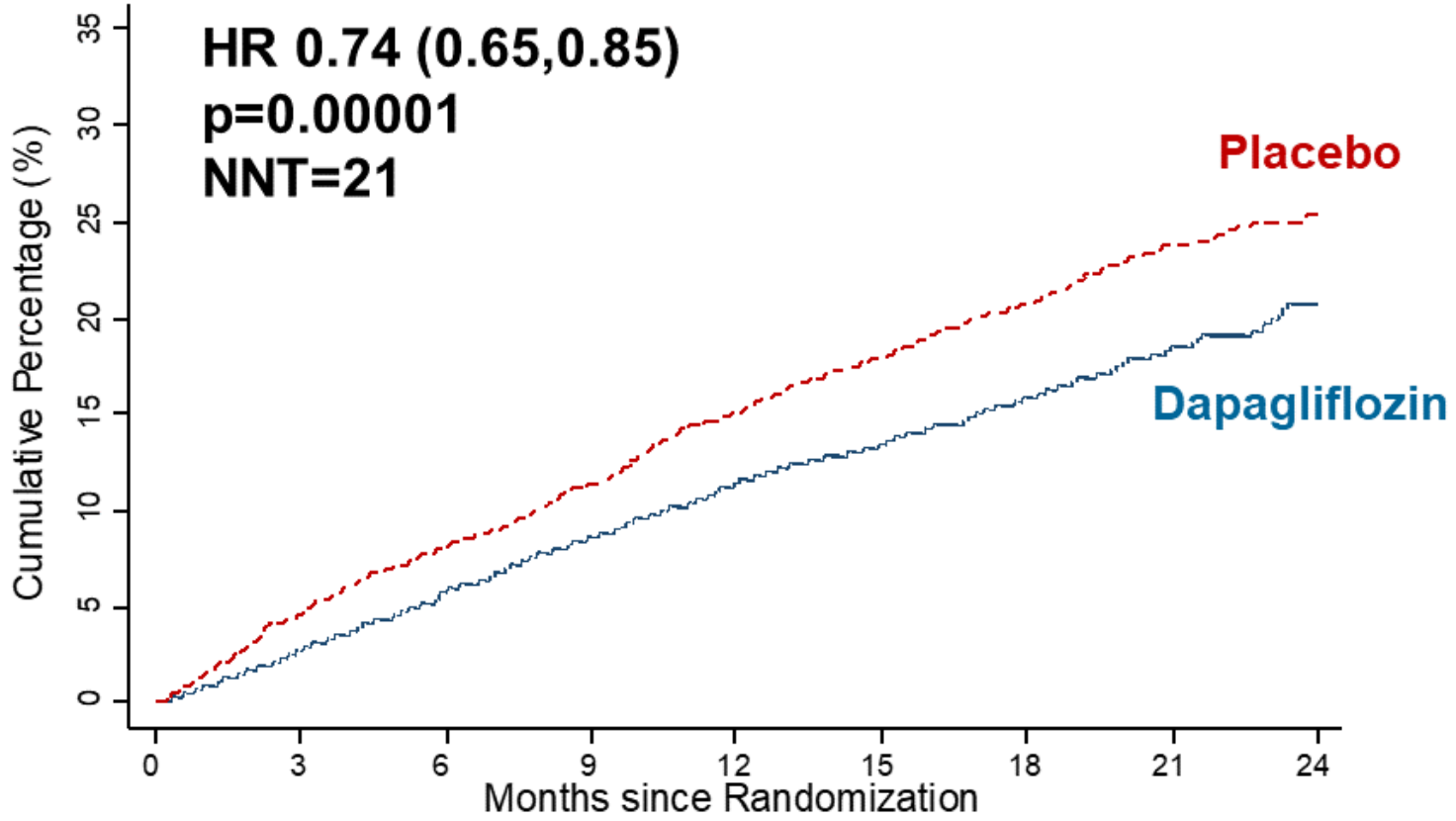
# Treatment effect by ejection fraction quartiles

## Primary composite total HF hospitalizations and CV death

| Subgroup | No. of Events/Patients | Rate Ratio (95% CI) |
|---|---|---|
| Overall | 1903/4796 | 0.87 (0.75–1.01) |
| EF | | |
| <=50 | 512/1208 | 0.82 (0.63–1.06) |
| >50–57 | 536/1287 | 0.77 (0.57–1.03) |
| >57–63 | 467/1202 | 0.91 (0.68–1.22) |
| >63 | 388/1099 | 1.09 (0.80–1.47) |



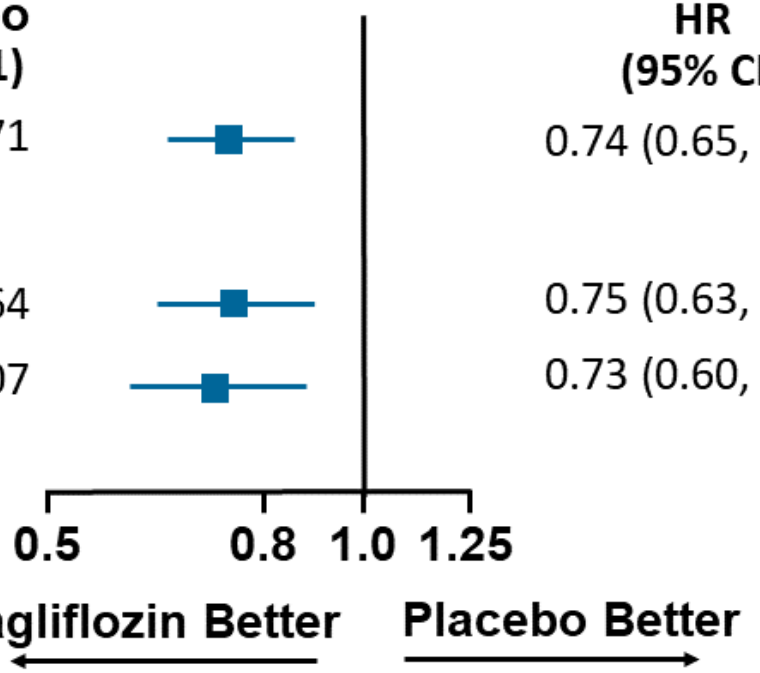
# DAPA-HF
# Primary composite outcome
## CV Death/HF hospitalization/Urgent HF visit




| Number at Risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Dapagliflozin | 2373 | 2305 | 2221 | 2147 | 2002 | 1560 | 1146 | 612 | 210 |
| Placebo | 2371 | 2258 | 2163 | 2075 | 1917 | 1478 | 1096 | 593 | 210 |

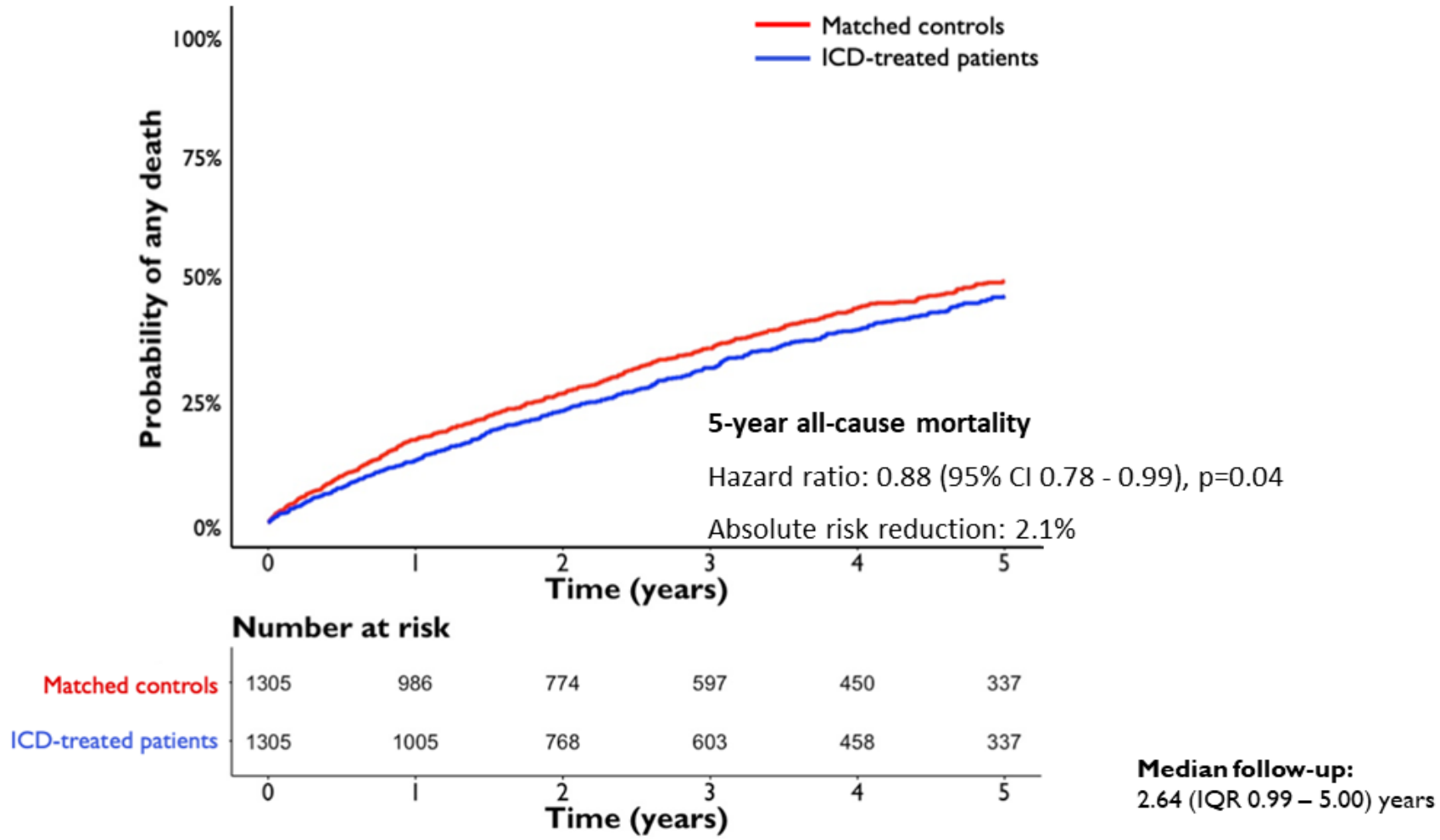
# DAPA-HF
# No diabetes/diabetes subgroup: Primary endpoint

| | Dapagliflozin (n=2373) | Placebo (n=2371) | HR (95% CI) |
|---|---|---|---|
| **All patients** | 386/2373 | 502/2371 | 0.74 (0.65, 0.85) |
| **Type 2 diabetes at baseline*** | | | |
| Yes | 215/1075 | 271/1064 | 0.75 (0.63, 0.90) |
| No | 171/1298 | 231/1307 | 0.73 (0.60, 0.88) |



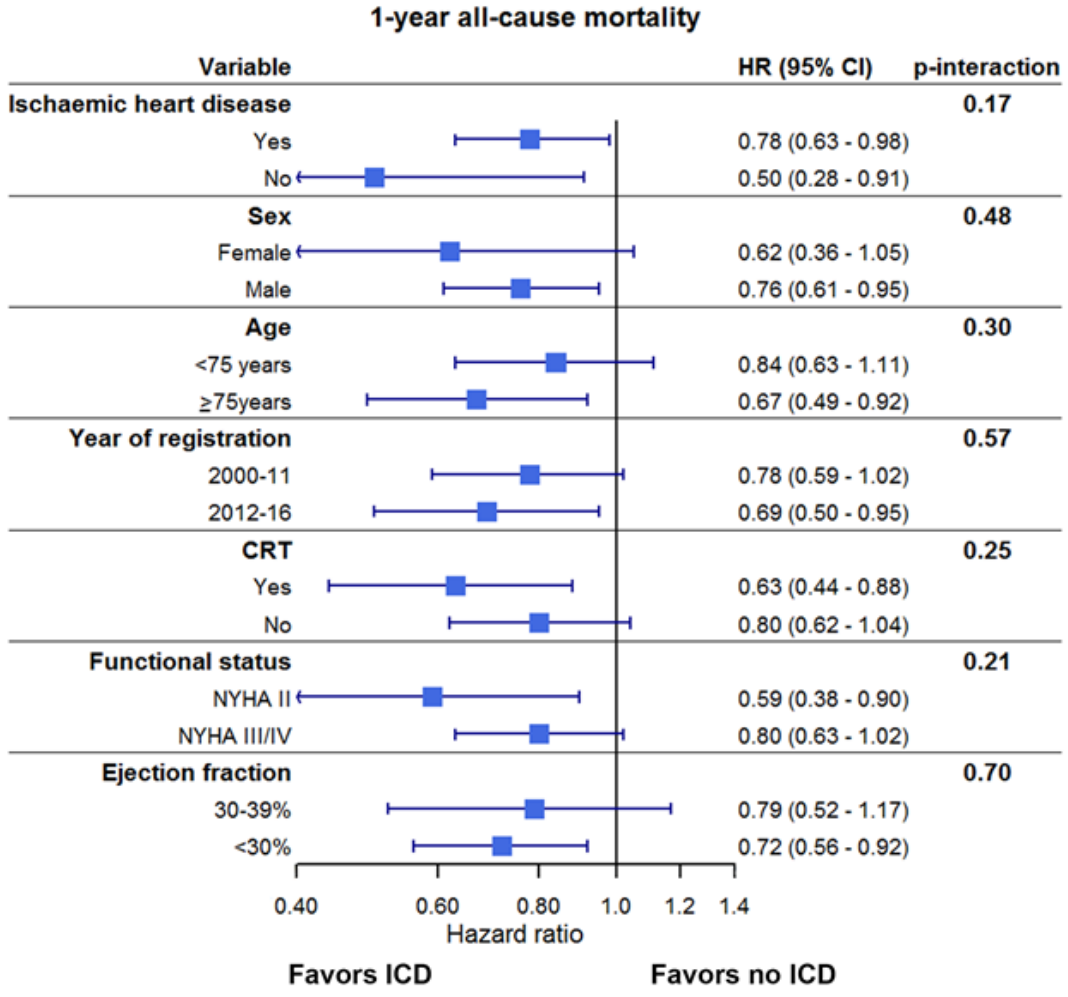

*Defined as history of type 2 diabetes or HbA1c ≥6.5% at both enrollment and randomization visits.

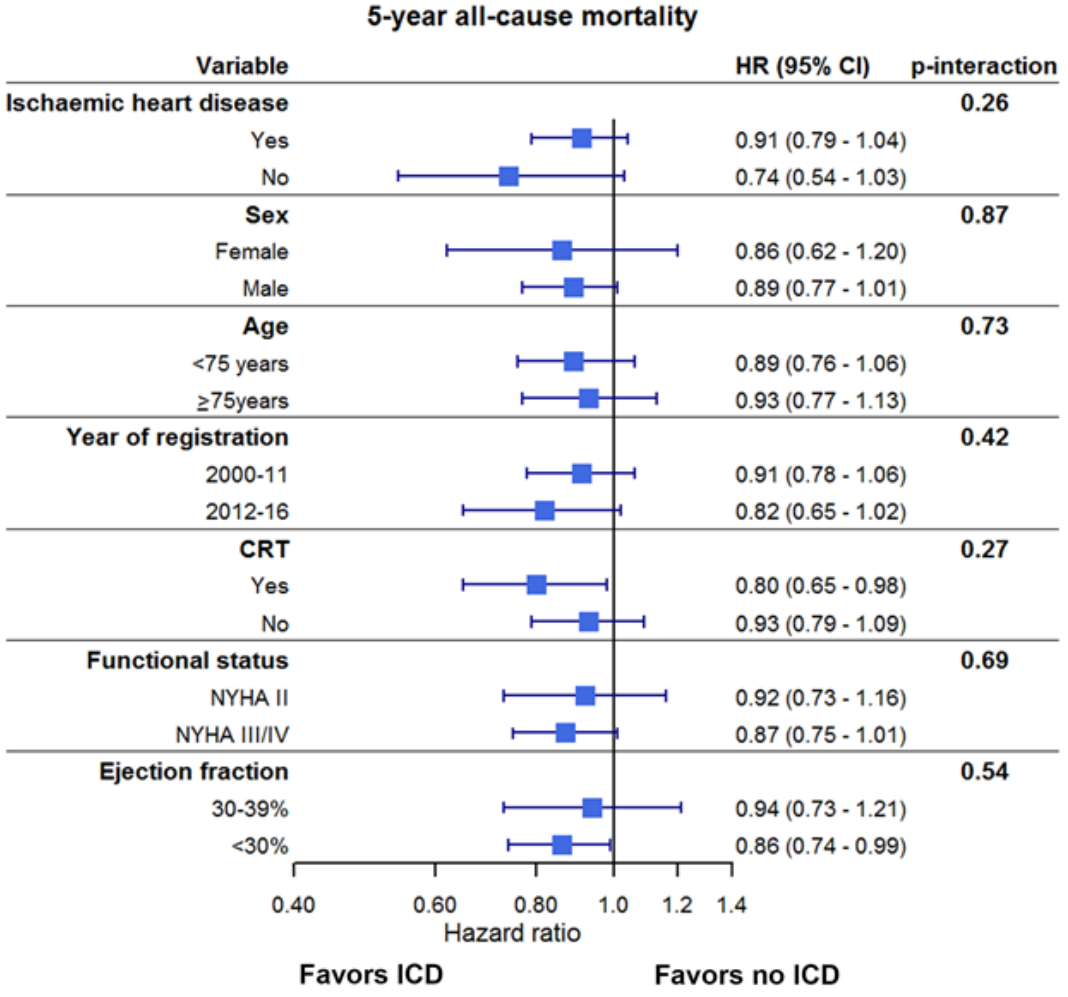
# Five-year all-cause mortality

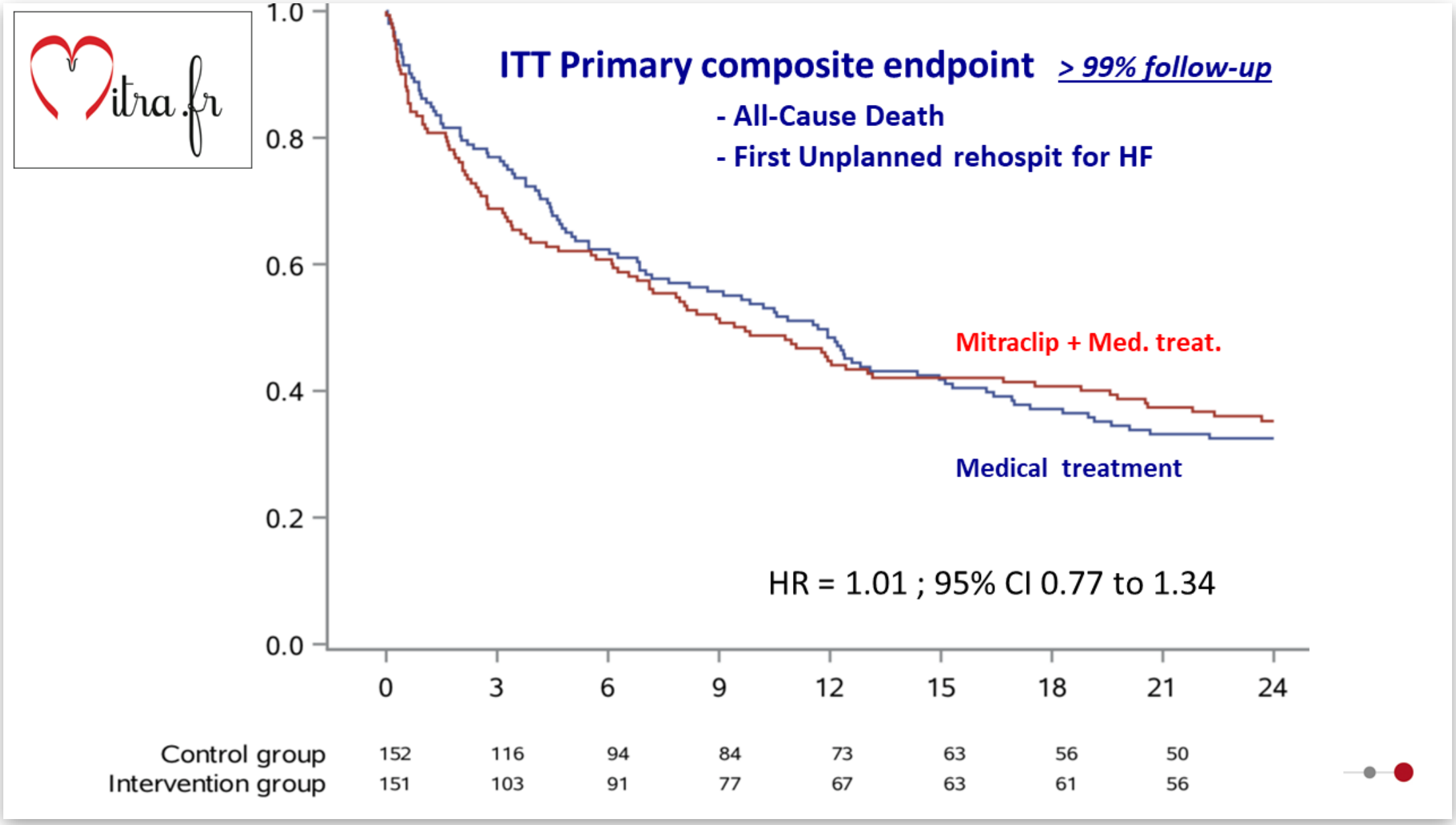


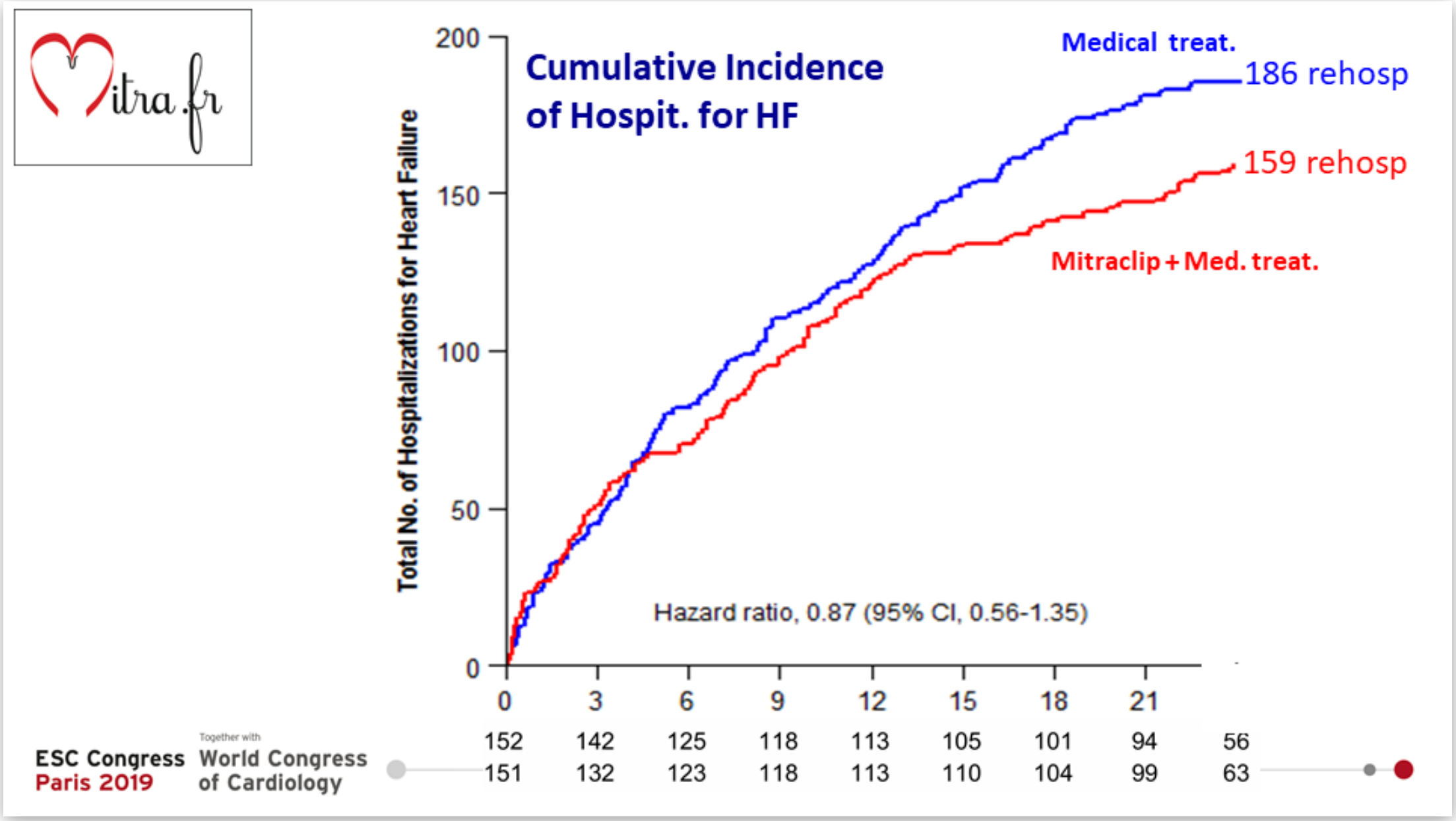

**Median follow-up:**
2.64 (IQR 0.99 – 5.00) years

# Sub-group analyses




ITT Primary composite endpoint > 99% follow-up
- All-Cause Death
- First Unplanned rehospit for HF
Mitraclip + Med. treat.
Medical treatment
HR = 1.01 ; 95% CI 0.77 to 1.34
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 9 12 15 18 21 24
Control group 152 116 94 84 73 63 56 50
Intervention group 151 103 91 77 67 63 61 56


Mitra.fr
Cumulative Incidence of Hospit. for HF
Medical treat.
186 rehosp
159 rehosp
Mitraclip + Med. treat.
Total No. of Hospitalizations for Heart Failure
200
150
100
50
0
Hazard ratio, 0.87 (95% CI, 0.56-1.35)
0 3 6 9 12 15 18 21
152 142 125 118 113 105 101 94 56
151 132 123 118 113 110 104 99 63
ESC Congress Paris 2019
Together with
World Congress of Cardiology

# Salt substitution and community-wide reductions in blood pressure and hypertension incidence - Conclusions

- Our project established an effective pragmatic population-wide salt substitute strategy
  - Reductions in the whole population's blood pressure
  - Higher reductions in high-risk groups
    - Individuals with hypertension, ≥60 years old
  - 55% reduction in hypertension incidence (HR 0.45)

# Salt substitution and community-wide reductions in blood pressure and hypertension incidence - Key messages

- Hypertension rates and non-adherence to medication are global concerns, and non-pharmacological interventions at the population level to improve blood pressure control are required
- Our social marketing intervention demonstrated population-wide benefits
  - Public health gains through shifting the population distribution
  - Clinical and health systems impacts by halving hypertension incidence
- Switching to low-sodium high-potassium salts is feasible and it is effective in reducing blood pressure

**Combined effect of lower LDL-C and lower SBP on the lifetime risk of cardiovascular disease**

# Clinical implications

- The results of this study confirm that most cardiovascular events are preventable, and *suggest* that most cardiovascular events *potentially can be prevented* with prolonged exposure to the combination of both lower LDL-C and lower SBP
- Because the benefit appears to accumulate over time, long-term exposure to even small differences in LDL-C and SBP can potentially substantially reduce the lifetime risk of cardiovascular disease, *if they are sustained over time*
  - *The results of this study thus strongly support the 2019 ESC/EAS Guidelines for the management of dyslipidaemias focus on a lifetime approach to CV risk reduction & and therapeutic lifestyle interventions to achieve lower LDL-C goals at all risk levels*
- The results of this study can be used to design of new algorithms to estimate lifetime risk of cardiovascular disease based on a person's cumulative exposure to LDL-C and SBP; and inform the next generation of cardiovascular prevention guidelines