Studie TIME:

Treatment in the Morning versus Evening

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OSTRAVSKÁ UNIVERZITA LÉKAŘSKÁ FAKULTA

FNO FAKULTNÍ NEMOCNICE OSTRAVA

University of Dundee

TIME STUDY
Antihypertensive Study

British Heart Foundation

Results of the Treatment In the Morning versus Evening (TIME) Study

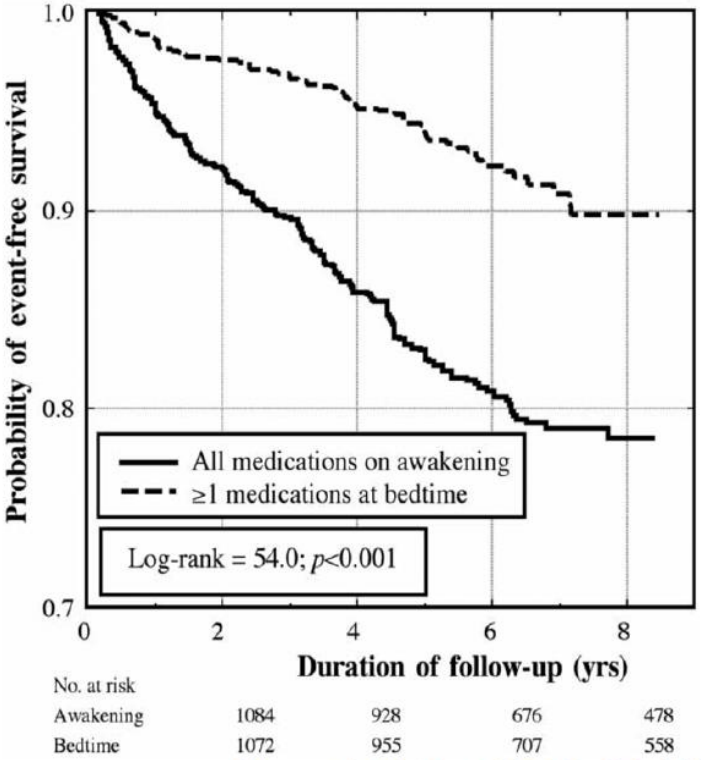
Tom MacDonald

on behalf of the TIME study investigators

ESC Hot Line 26th August

CV Events: MAPEC Study

n=1186, 255 events, 12,073pye = 2.1%/y

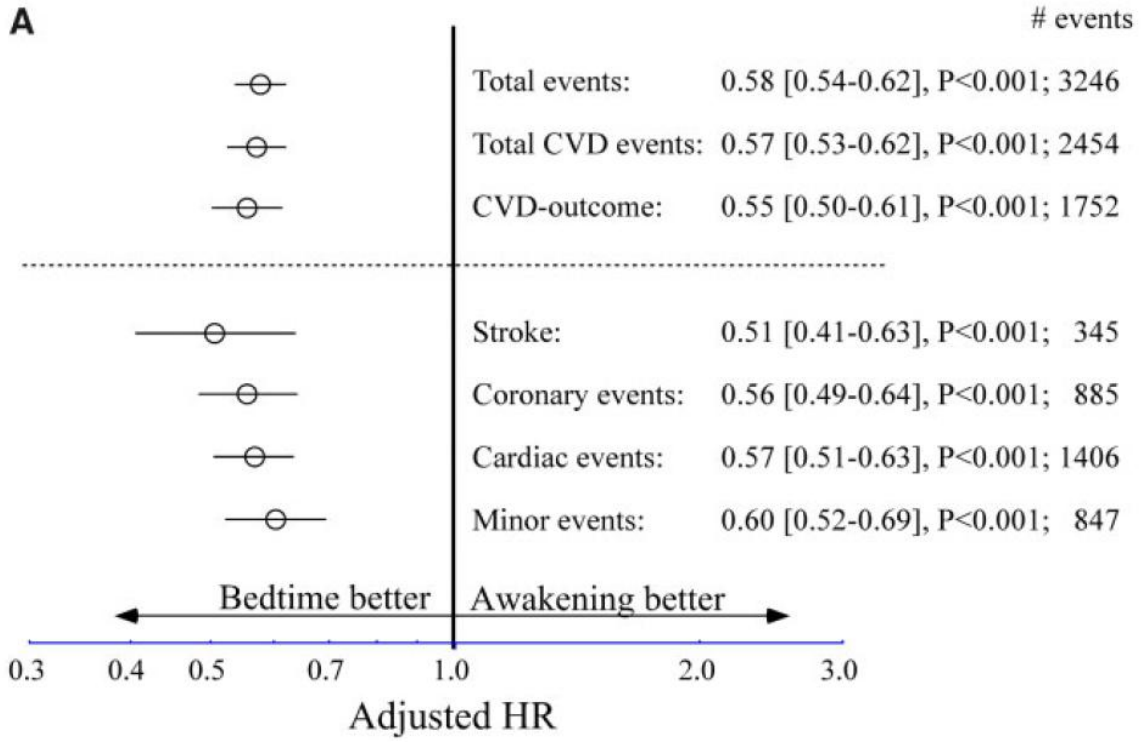


2156 pacientů

Adjusted relative risk 0·33 [95% CI 0·19–0·55]

Chronobiol Int 2010;27:1629-51 (Sept 2010)

Studie Hygia Chronotherapy



19084 pacientů

Adjusted hazard ratio 0·55 [95% CI 0·50–0·61]

European Heart Journal (2020) 41, 4565–4576

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FAKULTNÍ NEMOCNICE OSTRAVA

TIME Study

- Is evening dosing of antihypertensives prescribed in usual care superior to morning dosing with respect to cardiovascular outcomes?
- Primary endpoint: time to first occurrence of hospitalised MI, hospitalised stroke or cardiovascular death
- Prospective Randomised open label Blinded Endpoint (PROBE) design decentralised trial

A Decentralised Trial

Received: 12 July 2021 | Revised: 15 December 2021 | Accepted: 17 December 2021

DOI: 10.1111/bcp.15205

ORIGINAL ARTICLE

BJCP BRITISH PHARMACOLOGICAL SOCIETY

A systematic review of methods used to conduct decentralised clinical trials

Amy Rogers[1] | Giorgia De Paoli[1] | Selvarani Subbarayan[1] | Rachel Copland[1] | Kate Harwood[1] | Joanne Coyle[1] | Lyn Mitchell[1] | Thomas M. MacDonald[1] | Isla S. Mackenzie[1] | Trials@Home Consortium[2]

Br J Clin Pharmacol. 2022 Jun;88:2843-2862

Procedures

- All screening, consent, randomisation, and follow-up were performed through an online study portal and by email.
- Consenting participants were randomised (1:1) to take their usual prescribed antihypertensive therapy in the morning (6am-10am) or the evening (8pm-midnight)

Study Portal

TIME STUDY
Antihypertensive Study

call us free on:
0800 917 3509

memo hrc

For more Information about the Medicines Monitoring Unit or any of our other studies - Click here.

Time Study Trial (Pilot Phase)

The Medicines Monitoring Unit at the University of Dundee is running a large study, monitoring and comparing evening dosing of antihypertensive therapy with conventional morning dosing. If you take antihypertensive medication you could help us with this study.

We would like to change the time that some patients take their hypertensive medication, from morning to evening and vice versa. We would like to follow up both sets of patients as a comparison group.

To take part, first view the information sheet about the study. If you have any questions you can call us free on **0800 917 3509**. Please register for the Time Study trial using the registration form on the right of the screen.

If you'd like to know more about the Medicines Monitoring Unit, or other trials that we are running please visit us at: www.dundee.ac.uk/memo/

Register Today!

Enter your email

Choose a password

Confirm password

Register

Already Registered?

Login Here

Email

Password

Forgot password

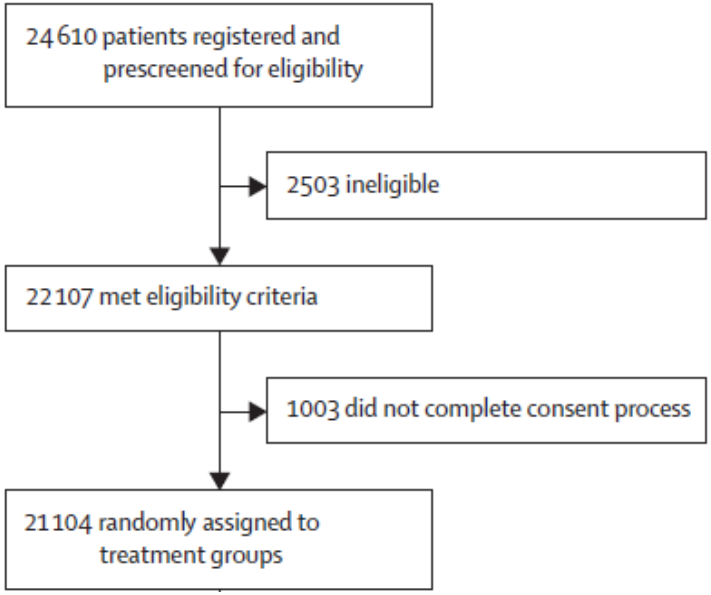
Submit

University of Dundee

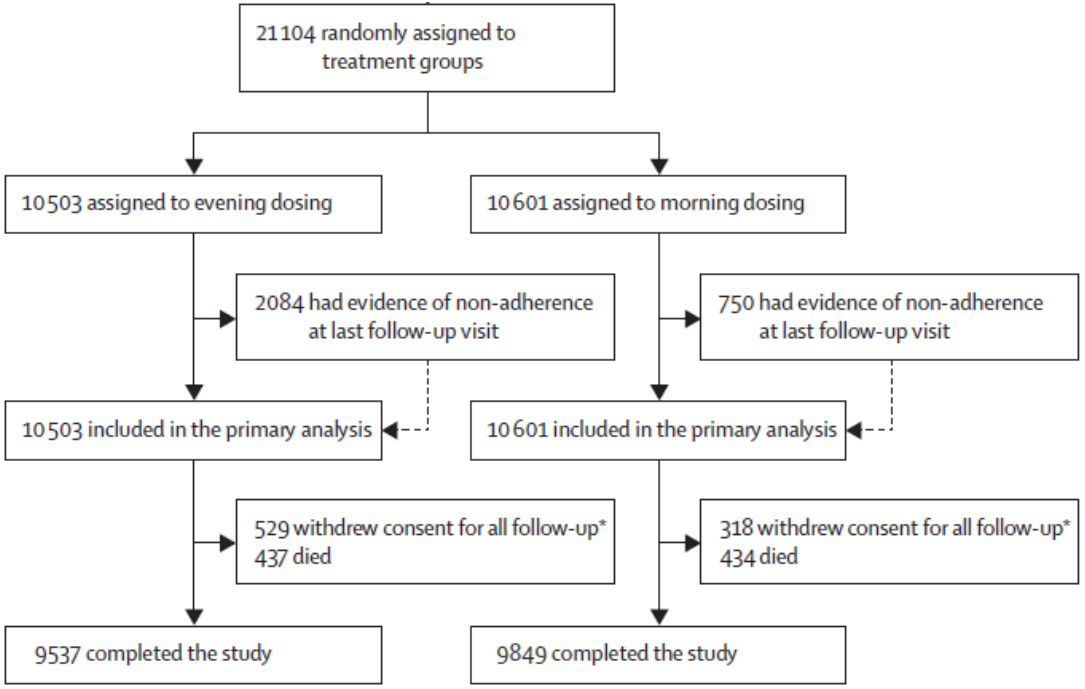
Medicines Monitoring Unit, Ninewells Hospital & Medical School
Telephone: **01382 632575** or Freephone: **0800 917 3509** or Email: **info@timestudy.co.uk**

BHS

Zařazení pacienti

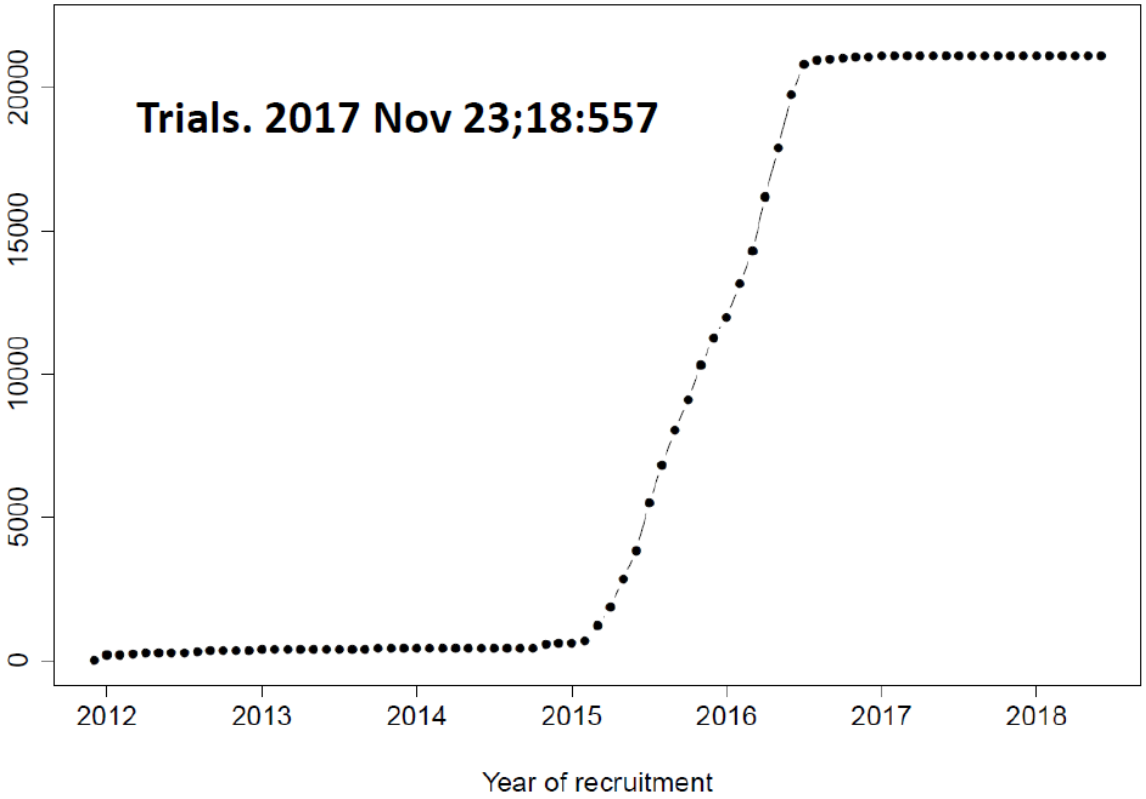


Randomizováni k rannímu nebo večernímu užívání své stávající antihypertenzní terapie



Lancet 2022; 400: 1417–25.

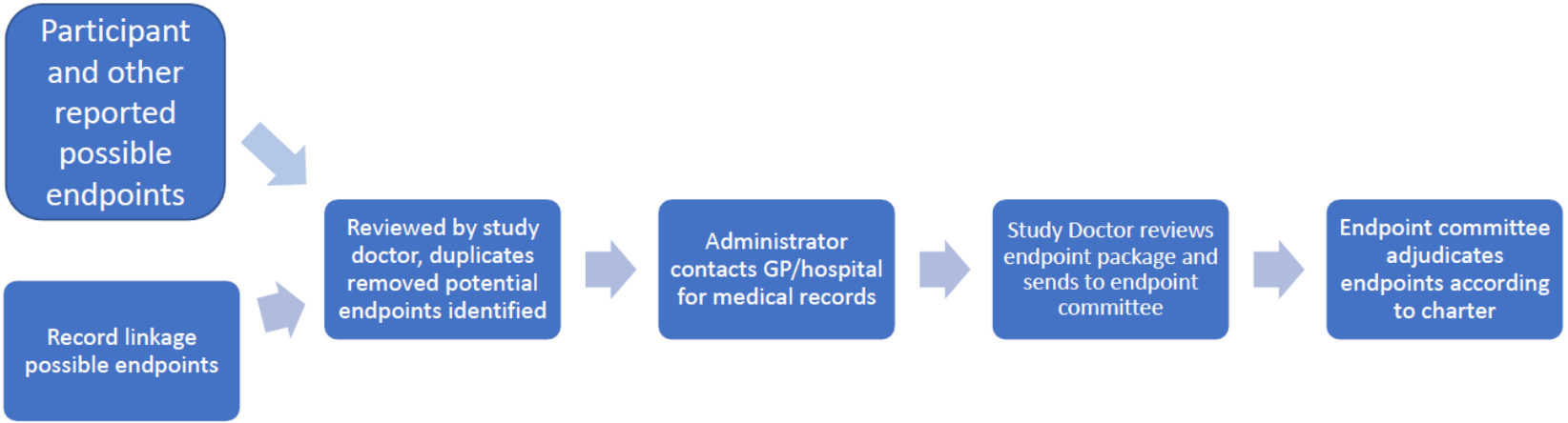
Cumulative Recruitment



Statistics

- 631 subjects with a first primary endpoint to detect 20% superiority of evening compared to morning dosing with 80% power

Endpoint capture and adjudication

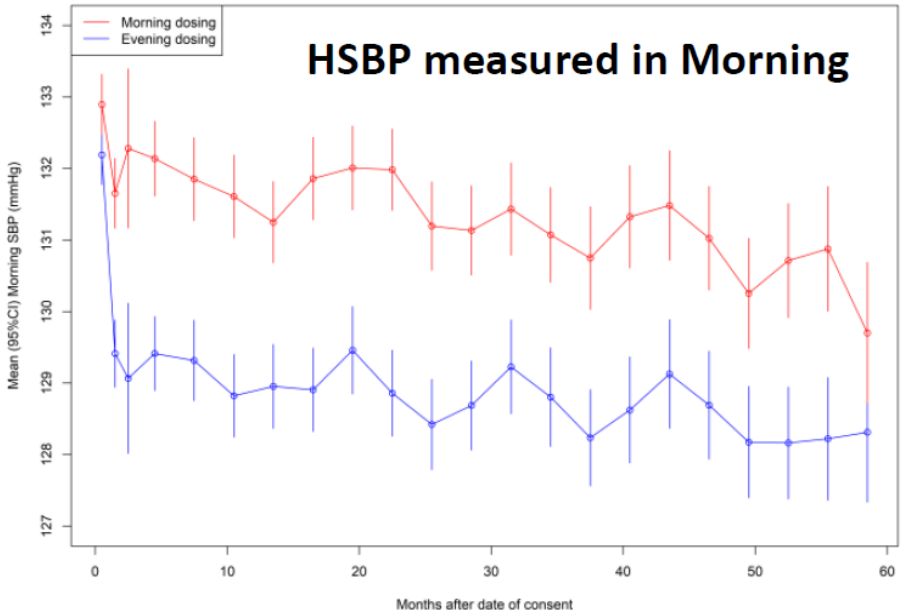


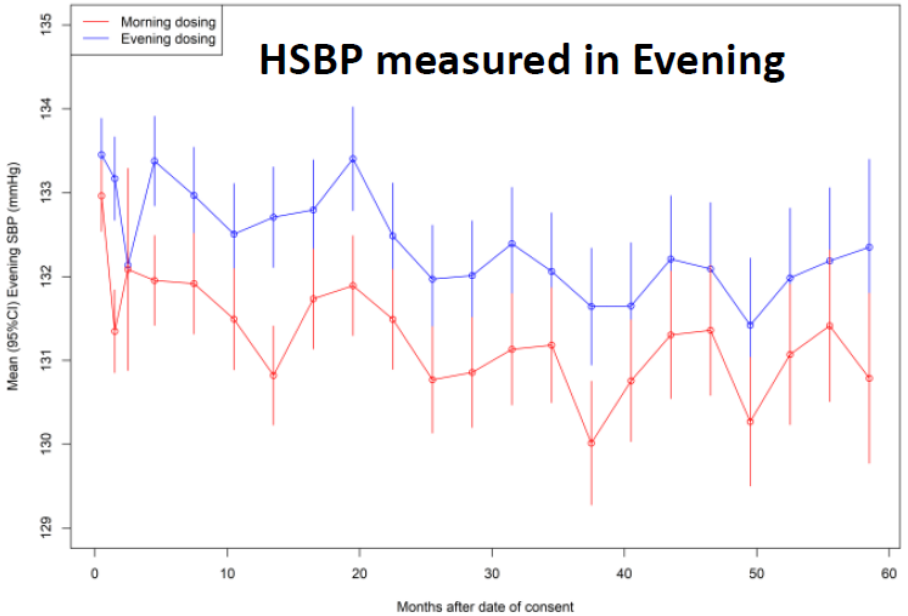
5,301 **3,386**

Baseline Demographics

Variable	Statistic	All = 21104	Morning = 10601	Evening = 10503
Age	Mean Range	65.1 (19.5-95.3)	65.2 (19.5-95.3)	65.0 (19.9-94.4)
Male	%	57.5	57.5	57.5
BMI	Mean	28.4	28.4	28.4
Current smoking	Mean %	4.2	4.3	4.1
Diabetes	Mean %	13.8	13.9	13.5
Impaired Renal	Mean %	3.4	3.5	3.3
Prior CVD	Mean%	13.0	12.9	13.0
BP	Mean	135/79	135/79	135/79

Home SBP


Morning dosing
Evening dosing
HSBP measured in Morning
Mean (95%CI) Morning SBP (mmHg)
Months after date of consent


Morning dosing
Evening dosing
HSBP measured in Evening
Mean (95%CI) Evening SBP (mmHg)
Months after date of consent

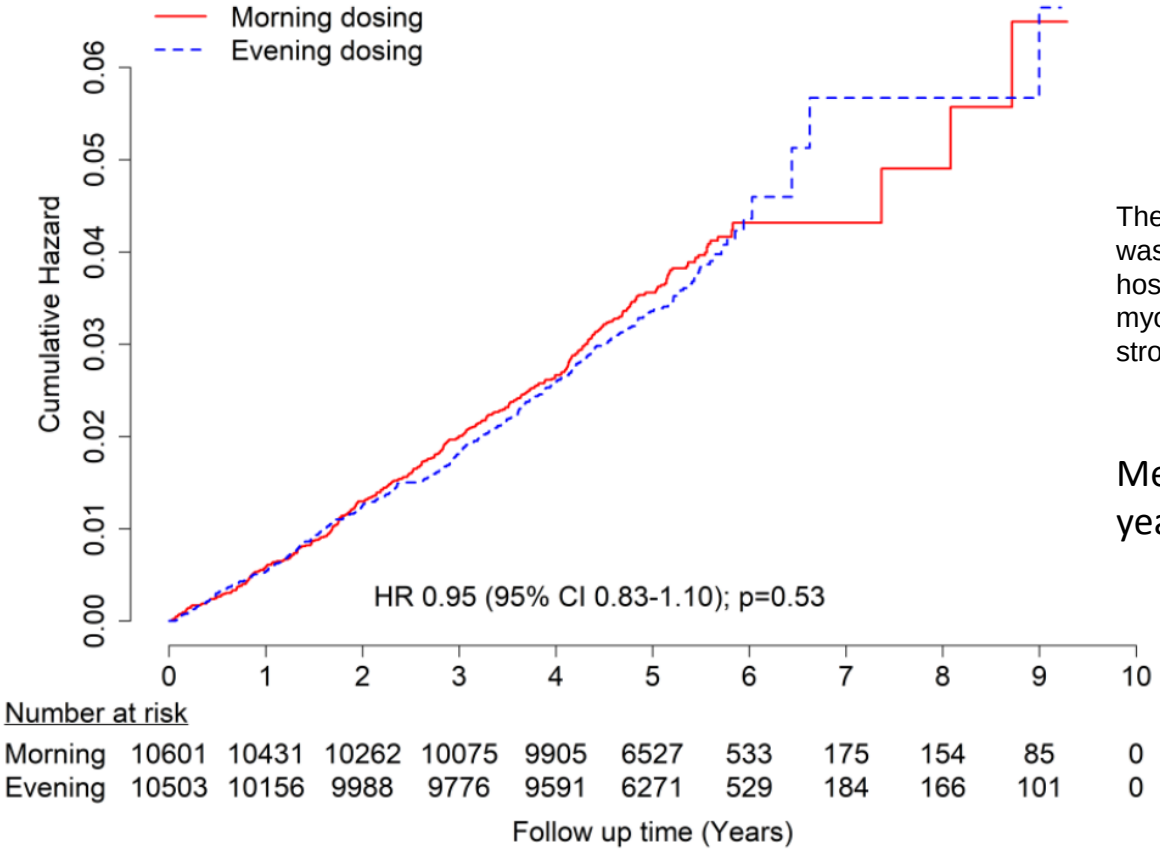
Withdrawals/Adherence to dose time

- Withdrawal of consent:
  - 318 (3.0%) morning v 529 (5.0%) evening.
- Reported non-adherence at any time:
  - morning 2384 (22·5%), v evening 4091 (39·0%), Chi sq P<0.0001).
- Last known non-adherence:
  - Morning 750 (7·5%) v evening 2084 (21·8%)

Adjudicated Endpoints

- 752 subjects with an adjudicated first primary endpoint

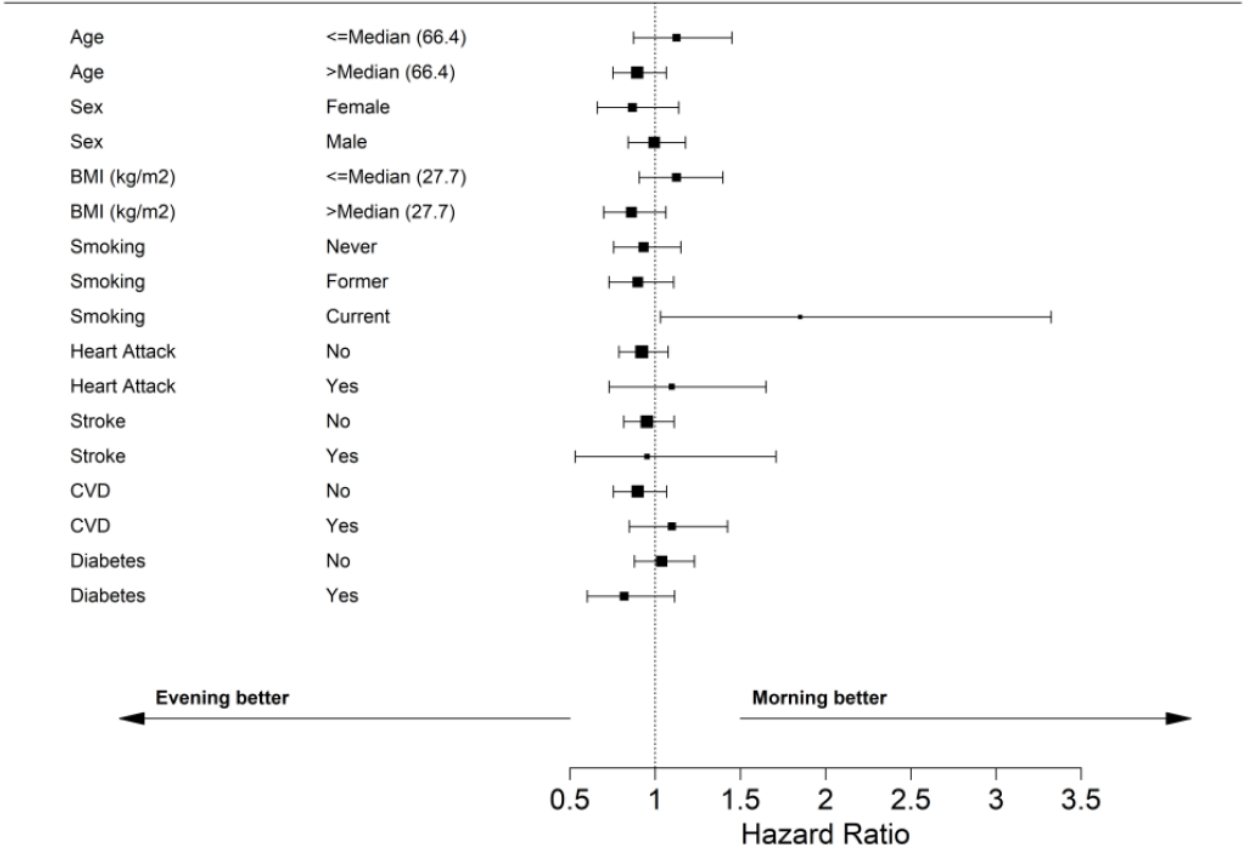
Primary Endpoint



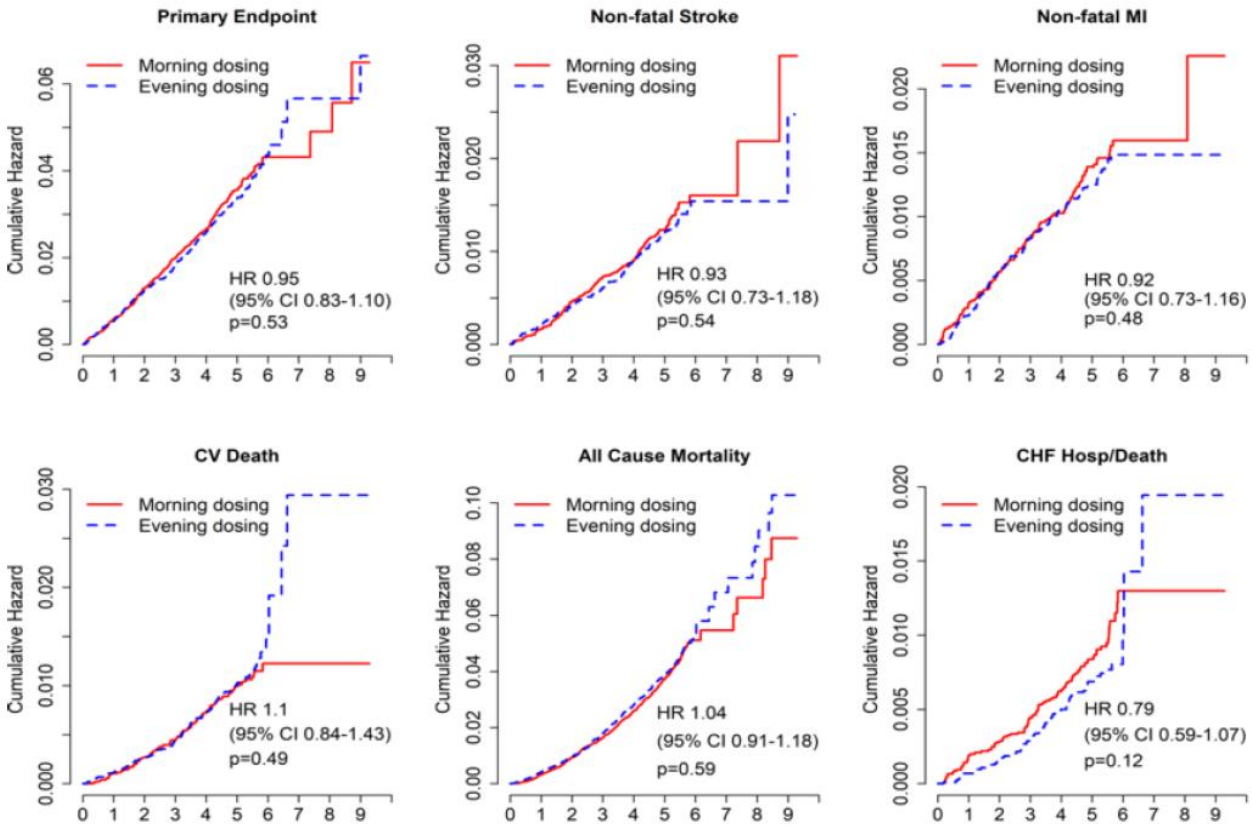
The primary composite endpoint was vascular death or hospitalisation for non-fatal myocardial infarction or non-fatal stroke

Median follow-up was 5·2 years (IQR 4·9–5·7)

Forest Plot: Primary EP by Baseline Factors



Secondary EPs



Nežádoucí účinky

	Evening dosing group (n=9574)*	Morning dosing group (n=10 054)*	Between-group difference (95% CI)†
Dizziness or light-headedness	3511 (36·7%)	4007 (39·9%)	−3·2% (−4·6 to −1·8)
Excessive visits to the toilet during the day or night	3825 (40·0%)	3660 (36·4%)	3·6% (2·2 to 4·9)
Sleep problems	4017 (42·0%)	4125 (41·0%)	0·9% (−0·5 to 2·3)
Upset stomach or indigestion	2639 (27·6%)	3050 (30·3%)	−2·8% (−4·1 to −1·5)
Diarrhoea	1803 (18·8%)	2170 (21·6%)	−2·8% (−3·9 to −1·6)
Feeling generally less well	3079 (32·2%)	3311 (32·9%)	−0·8% (−2·1 to 0·6)
Muscle aches	3724 (38·9%)	4352 (43·3%)	−4·4% (−5·8 to −3·0)
Other (not specified)	2970 (31·0%)	2686 (26·7%)	4·3% (3·0 to 5·6)

Numbers reported are the number of participants who indicated that they had experienced each prespecified symptom. *Number of participants who submitted at least one completed study follow-up form. †Difference in percentage: evening dosing group minus morning dosing group.

Table 3: **Prespecified adverse events (symptoms) in safety analysis population (n=19 628)**

Lancet 2022; 400: 1417–25.

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Závěry

Ve studii TIME se nelišil výskyt kardiovaskulárních příhod ani nežádoucích příhod u pacientů, užívajících antihypertenziva ráno nebo večer

Pacienti mohou antihypertenziva podávaná jednou denně užívat tehdy, kdy jim to více vyhovuje a kdy vnímají méně nežádoucích účinků léčby

Lancet 2022; 400: 1417–25.

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