ADVORtising clinical research to change clinical practice – *Case of the ADVOR trial*

Pieter Martens, MD, PhD

Cardiologist, Advanced heart failue specialist, clinical trialist

ADVOR

Ziekenhuis Oost-Limburg

The ADVOR trial – pure Belgian trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

W. Mullens, J. Dauw, P. Martens, F.H. Verbrugge, P. Nijst, E. Meekers, K. Tartaglia, F. Chenot, S. Moubayed, R. Dierckx, P. Blouard, P. Troisfontaines, D. Derthoo, W. Smolders, L. Bruckers, W. Droogne, J.M. Ter Maaten, K. Damman, J. Lassus, A. Mebazaa, G. Filippatos, F. Ruschitzka, and M. Dupont, for the ADVOR Study Group*

Advor tested the effect of acetazolamide on top of loop diuretics in patients with acute heart failure

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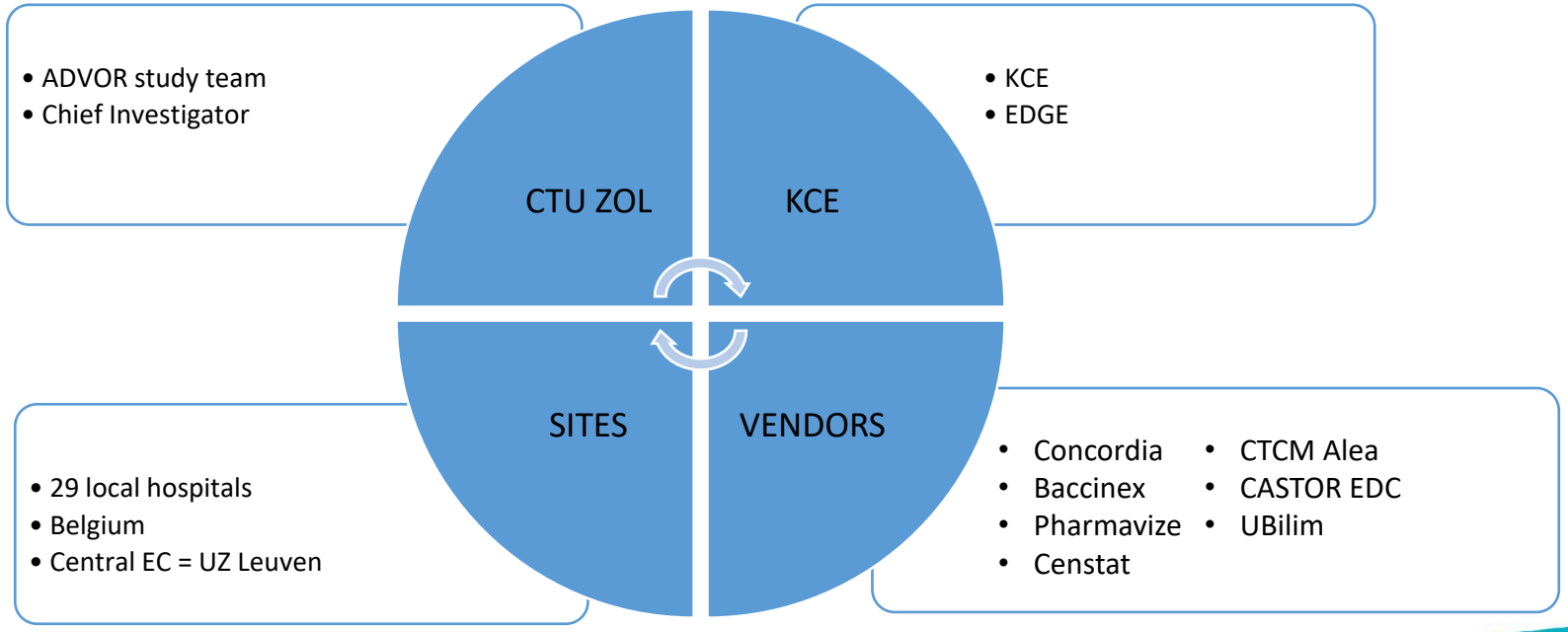
Introduction ADVOR study

- Non-commercial developed within BWGHF - HFA
- Multi-center
- Study sponsor = Ziekenhuis Oost Limburg (ZOL) AV
- Funder = Federaal Kenniscentrum voor de Gezondheidszorg (KCE)



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29 Sites across Belgium

Hospital	Principal Investigator
AZ Groeninge, Kortrijk	D. Derthoo
AZ Delta Roeselare-Menen	M. Deceunick
Jan Yperman	E. Viaene
AZ Maria Middelares Gent	D. Vervloet
OLV Ziekenhuis Aalst-Asse-Ninove	R. Dierckx
AZ Turnhout	P.J. Hofkens
UZ Antwerpen	E. Van Craenenbroeck
AZ klina, Antwerpen	W. Smolders
Imeldaziekenhuis, Bonheiden	B. Ector
GZA, sint-Vincentius, Wilrijk	D. Raes
ZNA Middelheim	E. Prihadi
UZ Brussel	S. Lochy
Hôpital Erasme, Brussel	J.L. Vachiery
UZ Saint-Luc, Brussel	A.C. Pouleur
UZ Leuven	W. Droogne
Grand Hôpital de Charleroi	F. Chenot
Clinique Saint-Luc Bouge	P. Blouard
CHU UCL Namur	L. Gabriel
Ziekenhuis Maas en Kempen	M. Hulselmans
Jessa Ziekenhuis, Hasselt	P. Timmermans
Ziekenhuis Oost Limburg AV	W. Mullens
CHR de la Citadelle, Luik	P. Troisfontaines
UZ Gent	M. Depauw
AZ Glorieux	F. Van Durme

Hospital	Principal Investigator
AZ Sint-Maarten (Mechelen)	G. Vervoort
AZ Sint-Lucas (Gent)	H. Vandekerckhove
AZ Nikolaas (St Niklaas)	K. Goossens
H. Hartziekenhuis Mol	H. Striekwold
CHU Charleroi	S. Moubayed

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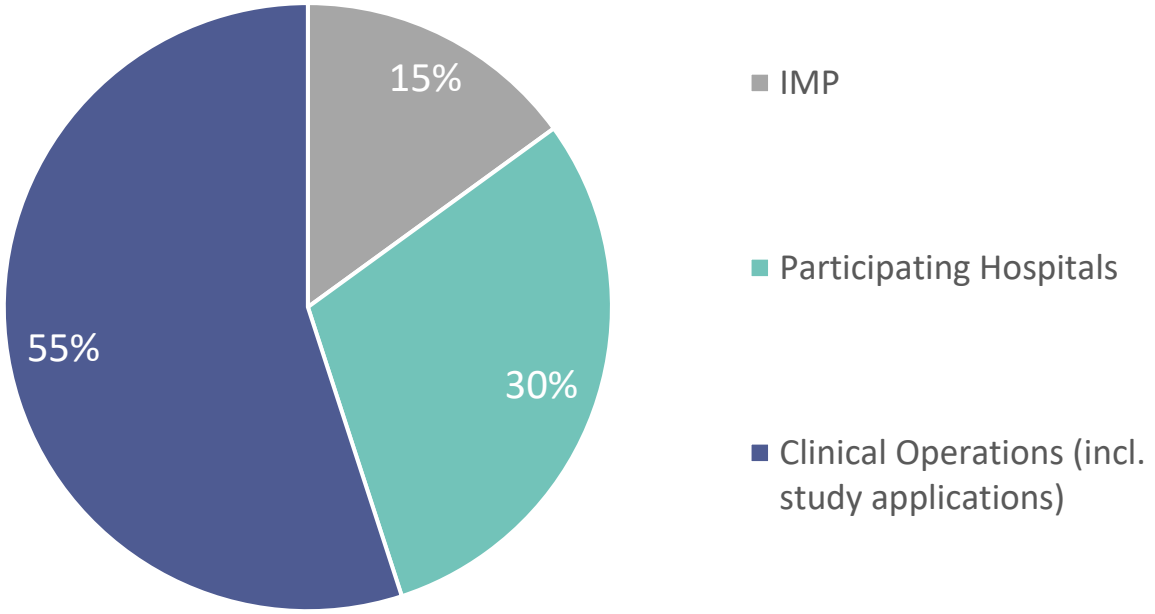
Budget/funding of the ADVOR trial

During the **start-up phase**:

- Funding (2.6 M euro)

KCE TRIALS
Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

https://kce.fgov.be/en/kce-trials



Study was only possible thanks to the funding as acetazolamide is a drug that has been commercially available since 1952

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PRIMARY ENDPOINT

Treatment success (decongestion achieved) on the morning of day 4 without the need for escalating diuretic strategy (doubling loop diuretic dose, addition of chlorthalidone, or ultrafiltration)

SECONDARY ENDPOINTS

1) Combined end-point of all-cause mortality and heart failure readmission during 3 months of follow-up

2) Length of index hospital admission

3) Longitudinal changes in EuroQoL five dimensions questionnaire (baseline, day 4, any HF readmission, and 3 months)

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Table of trial procedures

	Screening phase	Treatment phase				Follow up phase		
		Study Day 1	Morning of Study Day 2	Morning of Study Day 3	Morning of Study Day 4	Discharge	Re-admission	3 Months after study start dose
Informed consent	X							
In- and exclusion criteria	X							
Randomization	X							
Demographics[1]	X							
Medical history	X							
Vitals[2]	X		X	X	X			X
Weight[12]	X		X	X	X	X		X
EQ5D	X				X		X[11]	X
Volume assessment	X		X	X	X	X		X
Study treatment		X[3]	X[4]	X[4]				
Urinary collection[5]		X	X					
Local lab	X[6]		X[7]	X[7]	X[7]			X[7]
Laboratory sub-study[13] blood	X				X[14]			X
Laboratory sub-study[13] Urine		X	X					
Plasma BNP or NT-proBNP[8]	X				X			X
Urine pregnancy testing[9]	X							
Dose of neurohumoral blockers	X				X	X		X
Dose of diuretics	X					X		X
Concomitant medication	X	X	X	X	X			
Adverse Events[10]	X	X	X	X	X	X	X	X

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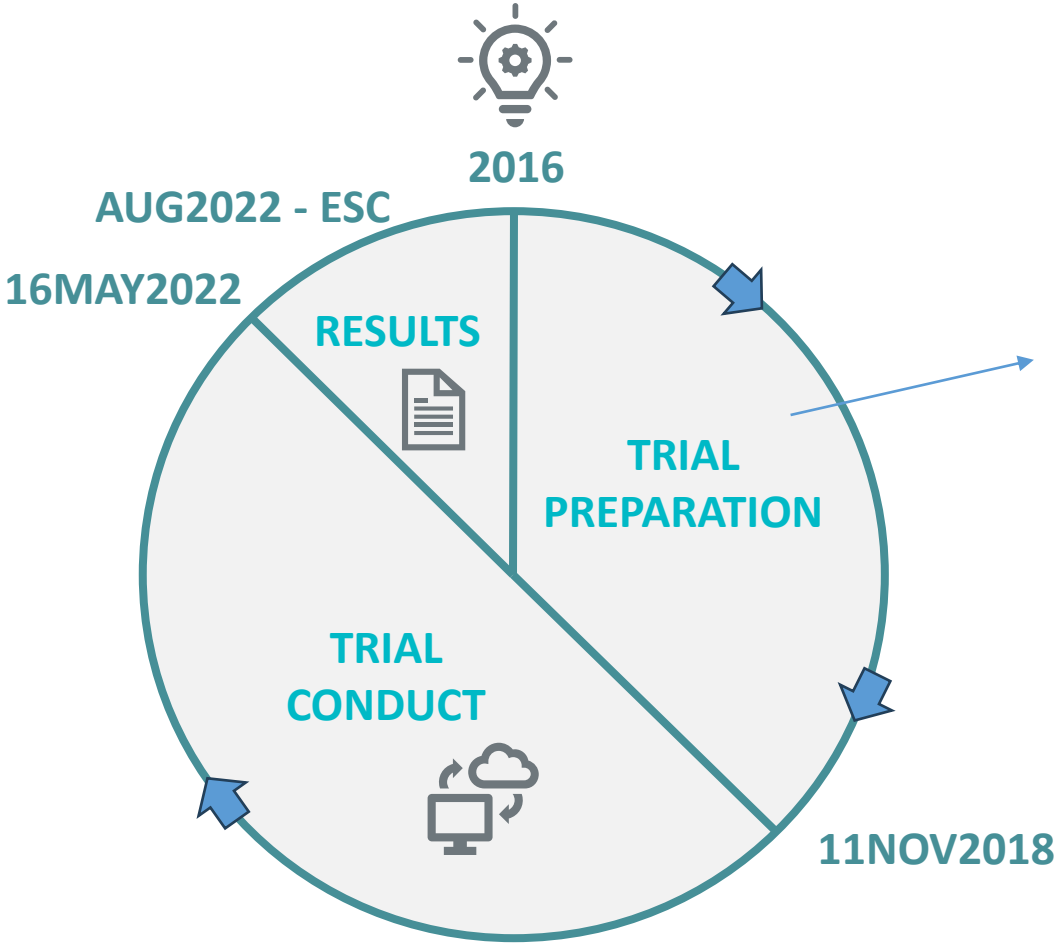
Lifecycle of ADVOR



Small pilot trial

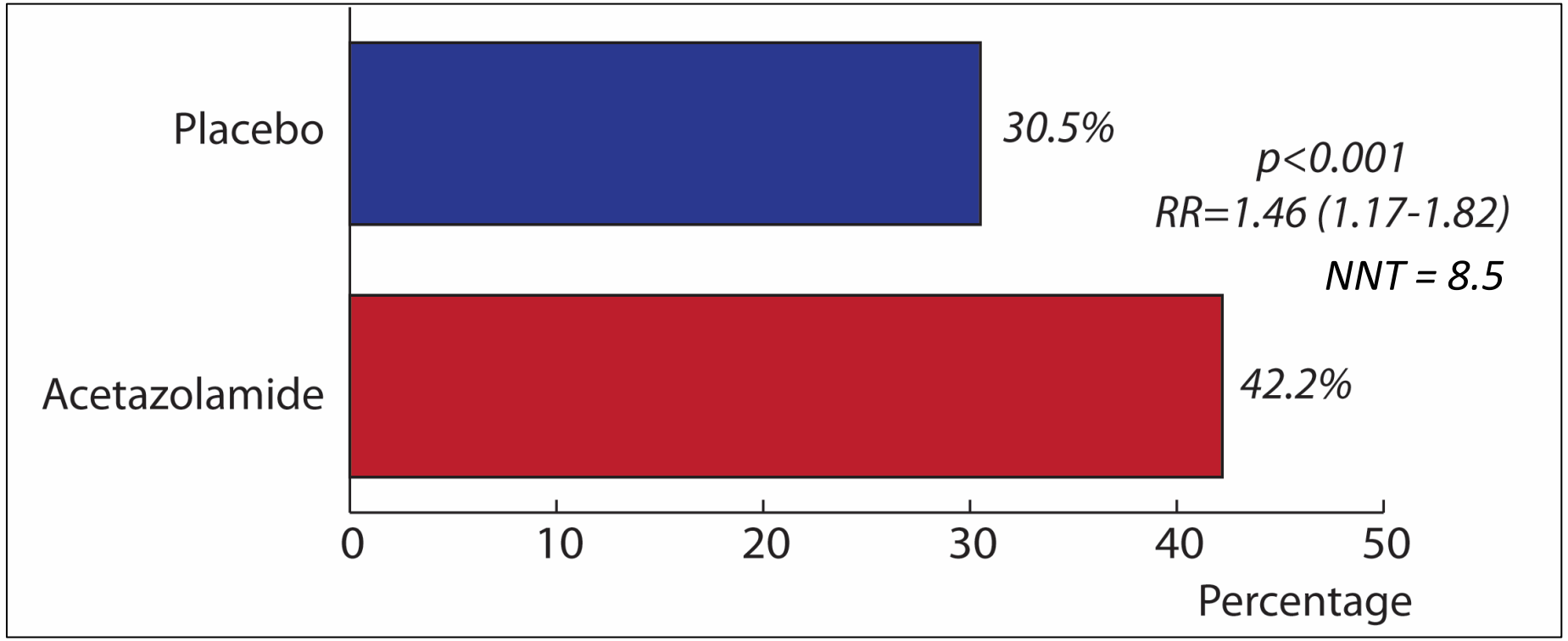
ESC European Society of Cardiology
European Journal of Heart Failure (2019)
doi:10.1002/ejhf.1478
RESEARCH ARTICLE

Acetazolamide to increase natriuresis in congestive heart failure at high risk for diuretic resistance

Frederik H. Verbrugge[1]*, Pieter Martens[1], Koen Ameloot[1], Veerle Haemels[2],

Ziekenhuis Oost-Limburg

Trial results



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Publication

New England Journal of medicine: 1
Circulation: 1
European Heart Journal: 3
Journal of the American College of Cardiology: 1
European Journal of Heart Failure: 3

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RESEARCH & INNOVATION
TRANSFORMING EUROPEAN HEALTHCARE

ADVORtising clinical research to change clinical practice: from Belgium to Slovenia and Europe

Professor Mitja Lainscak, FESC, FHFA

Faculty of Medicine, University of Ljubljana & General Hospital Murska Sobota

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The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

New Decongestion Strategies in an Evolving Heart Failure Landscape

G. Michael Felker, M.D.

ESC European Society of Cardiology
European Heart Journal (2023) 00, 1–13
https://doi.org/10.1093/eurheartj/ehad195

ESC GUIDELINES

2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Theresa A. McDonagh *†, (Chairperson) (United Kingdom), Marco Metra *†, (Chairperson) (Italy), Marianna Adamo ‡, (Task Force Co-ordinator) (Italy), Roy S. Gardner ‡, (Task Force Co-ordinator) (United Kingdom), Andreas Baumbach (United Kingdom), Michael Böhm (Germany), Haran Burri (Switzerland), Javed Butler (United States of America), Jelena Čelutkienė (Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom), Maria Generosa Crespo-Leiro (Spain), Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans (Netherlands), Arno W. Hoes (Netherlands), Tiny Jaarsma (Sweden), Ewa A. Jankowska (Poland), Mitja Lainscak (Slovenia), Carolyn S.P. Lam (Singapore), Alexander R. Lyon (United Kingdom), John J.V. McMurray (United Kingdom), Alexandre Mebazaa (France), Richard Mindham (United Kingdom), Claudio Muneretto (Italy), Massimo Francesco Piepoli (Italy), Susanna Price (United Kingdom), Giuseppe M. C. Rosano (United Kingdom), Frank Ruschitzka (Switzerland), Anne Kathrine Skibelund (Denmark), and ESC Scientific Document Group

4. Acute heart failure

Treatment of acute HF was outlined in the recent 2021 ESC HF Guidelines and a Heart Failure Association scientific statement on HF.[1,25] Since these publications, trials have been conducted with diuretics, as well as on management strategies for patients with acute HF. The results are summarized here.

4.1. Medical therapy

4.1.1. Diuretics

ADVOR was a multicentre, randomized, parallel-group, double-blind, placebo-controlled trial that enrolled 519 patients with acute decompensated HF, clinical signs of volume overload (i.e. oedema, pleural effusion, or ascites), and an NT-proBNP level of >1000 pg/mL or a B-type natriuretic peptide level of >250 pg/mL. They were randomized to receive intravenous (i.v.) acetazolamide (500 mg once daily) or placebo added to standardized i.v. loop diuretic treatment.[2] The primary endpoint of successful decongestion, defined as the absence of signs of volume overload, within 3 days after randomization and without an indication for escalation of decongestive therapy, was achieved in 108 of 256 patients (42.2%) in the acetazolamide group and in 79 of 259 patients (30.5%) in the placebo group (risk ratio [RR] 1.46, 95% CI 1.17–1.82; $P < .001$). Rehospitalization for HF or all-cause death occurred in 76 patients (29.7%) in the acetazolamide group and in 72 patients (27.8%) in the placebo group (HR 1.07, 95% CI 0.78–1.48). Length of hospital stay was 1 day shorter with acetazolamide compared with placebo (8.8 [95% CI 8.0–9.5] vs. 9.9 [95% CI 9.1–10.8] days). No difference between the acetazolamide and placebo groups was found for other outcomes and adverse events.[2] Although these results may support the addition of acetazolamide to a standard diuretic regimen to aid decongestion, further data on outcomes and safety are needed.

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- Increasing the inspired oxygen concentration may provide relief of dyspnoea.
- Diuretic management can be used to relieve severe congestion or optimize symptom control (congestion and thirst).
- Reduce HF drugs that reduce blood pressure to maintain sufficient oxygenation and reduce the risk of falls.

Ideally these therapies should be delivered in the patient's home. In the majority of cases the whole family should receive social support.[652]

A management plan should be developed through discussion with the patient and family. It should include

- A discussion about stopping medication that does not have an immediate effect on symptom management or health-related quality of life, such as agents to lower cholesterol or treat osteoporosis
- Documentation of the patient's decision regarding resuscitation attempts
- Deactivation of an ICD at end-of-life (according to local legal regulations)
- Preferred place for care and death
- Emotional support to the patient and family/caregiver with appropriate referral for psychological or spiritual support

Clearly, symptoms and quality of life change over time and regular reassessment is recommended. Palliative scores provide an objective assessment of the patient's symptoms and needs and may help establish the effectiveness of therapy.

Palliative outcome scores include the Palliative Care Outcome Scale,[657] Karnofsky Performance Status[658] and Functional Assessment of Chronic Illness Therapy – Palliative Care (FACIT-Pal).[659]

15. Gaps in evidence

Clinicians responsible for managing patients with HF must frequently make treatment decisions without adequate evidence or a consensus of expert opinion. The following is a short list of selected, common issues that deserve to be addressed in future clinical research.

1. Definition, diagnosis, epidemiology

- For HFmrEF/HFpEF, research into the underlying characteristics, pathophysiology and diagnosis (with new modalities)
- Updated epidemiology on HF incidence and prevalence including patients from all continents
- For imaging and biomarkers, studies on effects of specific imaging modalities and biomarkers to improve clinical outcome (e.g. biomarker-guided therapies, detection of CAD/myocardial ischaemia, late-gadolinium enhancement CMR, echocardiographic strain measurements, stress echocardiography, etc.)
- Increasing awareness of HF in the medical community, lay public and among policy makers.

2. Strategies aimed at prevention and screening of HF

- Evaluate the comparative clinical effectiveness and cost-effectiveness of different strategies to screen for HF.

3. Pharmacological therapy

- Identification of non-responders to current guideline-advised medical treatment
- Targeted therapies for specific aetiologies of HFrEF (e.g. myocarditis, peripartum cardiomyopathy)
- Therapies directly improving cardiomyocyte function (e.g. acto-myosin cross-bridge activation, sarco/endoplasmic reticulum Ca^{2+}-ATPase activation, ryanodine receptor stabilization, energetic modulation) or targeting non-myocytic compartment (e.g. anti-fibrosis/matrix remodelling)
- Therapies for HFmrEF/HFpEF (ARNIs, beta-blockers, soluble guanyl cyclase inhibitors, i.v. iron)

4. Devices and interventions

- Indications for ICDs in specific subgroups (e.g. ARVC and HFmrEF/HFpEF) and optimal selection of ICD candidates
- QRS morphology or duration as a predictor of response to CRT
- CRT in patients with AF
- Efficacy of PV ablation as a rhythm-control strategy in patients with AF
- Interventional approach to recurrent, life-threatening ventricular tachyarrhythmias
- The role of remote monitoring strategies in HF
- Non-surgical (percutaneous) correction of functional mitral and tricuspid regurgitations
- Identification of indications for coronary angiography/revascularization in patients with HF and chronic stable CAD
- Effects of novel LVADs as destination therapy and bridge to transplantation

5. Co-morbidities

- A better understanding of pathophysiology and potential treatments in specific HF populations, including the
  - very elderly,
  - young patients,
  - eGFR <30 mL/min,
  - diabetic patients,
  - cardiotoxic chemotherapy-induced HF,
  - muscular dystrophies,
  - cachexia and depression.
- Therapies for HF-related sleep-disordered breathing in HFrEF/HFpEF/HFmrEF.

6. Acute heart failure

- Prospective evaluation of the 'time-to-treatment' concept in AHF
- Evaluation of whether inadequate phenotyping is responsible for the failure of treatments to improve outcome in AHF
- Better definition and treatment of diuretic resistance
- Role of nitrates in the management of AHF
- Treatments improving mortality and morbidity
- Strategies and therapies to prevent early rehospitalization after discharge for a hospital admission for AHF.

7. Other/remaining aspects

- Treatment algorithms for patients with HF excluded by pivotal clinical trials
- Palliative and end-of-life care management and assessment of outcome
- Optimal integration of multidisciplinary care, self-management of patients and their adherence.

ESC HF guidelines 2016 to 2021

16 Gaps in evidence

Major advances in the diagnosis and treatment of patients with HF have occurred over recent years. Strong evidence for new treatment options have been given by recent RCTs and HF management may undergo major changes in the next years. New discoveries, however, pose new challenges and many areas with lack of evidence still remain. The following is a short list of selected, common issues that deserve to be addressed in future clinical research.

(1) **Definition and epidemiology**
- i. Further research into the underlying characteristics, pathophysiology, and diagnosis of HFmrEF and HFpEF
- ii. Consensus about normal values/ranges of EF
- iii. Better phenotyping of HFpEF
- iv. More information on the incidence and prevalence of 'recovered LV' systolic function

(2) **Diagnosis**
- i. Definitive studies on the role of biomarkers, focusing on their additive value in the diagnosis of HF
- ii. More randomized studies on screening for HF in asymptomatic subjects that may translate into improved outcomes
- iii. Studies on biomarkers showing the impact on outcome of their measurements for the identification of subjects at risk of developing HF as well as to guide treatment in patients with HF
- iv. Validated diagnostic protocols for the diagnosis of HFmrEF and HFpEF

(3) **Pharmacotherapy of CHF**
- i. Pragmatic studies on the order of adding disease-modifying drugs for HFrEF
- ii. Specific therapies for HFmrEF and HFpEF and, likely, their different phenotypes
- iii. More data and prospective clinical trials of HFrEF therapies in patients with eGFR <30 mL/min/1.73 m^2
- iv. Further evidence from prospective RCTs for the treatment of specific HF phenotypes: myocarditis, cardiotoxicity, inherited CMPs, PPCM, amyloidosis
- v. Management strategies and therapies for 'recovered LV' systolic function
- vi. More evidence on the effects of fluid restriction, dietary salt restriction, and nutrition

(4) **Devices and interventions**
- i. Indications for ICDs in specific subgroups of HFmrEF/HFpEF and optimal selection of ICD candidates in HFrEF, including patients with ischaemic and non-ischaemic cardiomyopathy
- ii. More research on CRT efficacy in AF
- iii. Further prospective randomized studies showing the impact on outcomes of AF ablation strategies compared to OMT in HF patients
- iv. Further research on the percutaneous treatment of valve heart disease and its impact on patients' outcomes and QOL
- v. Larger RCTs on CCM and baroreceptor stimulation in HFrEF

(5) **Disease management**
- i. The role of remote monitoring strategies in HF in the post COVID-19 era
- ii. Studies on optimal models for follow-up of stable HF patients
- iii. Studies to determine specific options for palliative care

(6) **Advanced HF**
- i. Better definition of risk profiles according to INTERMACS and other classifications
- ii. RCTs to establish the effects on outcomes of long-term MCS in hospitalized patients as well as in ambulatory outpatients (for instance INTERMACS 4–6 profiles)
- iii. Advances in long-term MCS, including strategies to reduce the risk of bleeding, thromboembolic events, and infection
- iv. Advances in medical treatment for the many patients who cannot undergo MCS or heart transplantation including development of treatment strategies, novel inotropes or myotropes for patients with advanced HF

(7) **AHF**
- i. Better definition and classification of patient phenotypes to facilitate improved treatment
- ii. Evidence-based use of imaging techniques and biomarkers that have an impact on patients' clinical course
- iii. Development of better strategies for congestion relief, including monitoring of diuretic administration, and/or to improve organ perfusion
- iv. Identification of treatments with an impact on post-discharge outcomes
- v. New devices for short-term MCS
- vi. Definition of evidence-based treatment options and therapeutic algorithms for patients with cardiogenic shock

(8) **CV comorbidities**
- i. RCTs showing best strategies for the treatment of ventricular arrhythmias
- ii. RCTs to establish the role of coronary revascularization procedures in different patient subsets
- iii. RCTs to establish the impact on patients' outcomes and/or QOL of percutaneous treatment of mitral or tricuspid valve disease in patients with HF

(9) **Non-CV comorbidities**
- i. RCTs addressing cachexia and/or sarcopenia and/or frailty and showing the impact of treatment on QOL and/or outcome
- ii. RCTs of medical therapies or devices in patients with severe CKD and HF
- iii. RCTs showing the effects on outcomes of medical treatment of electrolyte abnormalities
- iv. RCTs showing the effects on outcomes of treatment of CSA
- v. Prospective studies showing the impact on outcomes and/or QOL of early diagnosis, better prevention and treatment of cardiotoxicity of cancer therapies
- vi. Better treatment of infections and prevention of cardiac injury with infection

(10) **Special conditions**
- i. RCTs of treatment for PPCM
- ii. Better phenotyping of CMPs through genetic testing, biomarkers and imaging modalities, and tailoring of therapy
- iii. RCTs of treatment of different types of myocarditis, including immunosuppressive therapies
- iv. RCTs of new treatments of different forms of cardiac amyloid
- v. Better definition and treatment of LA myopathy.

ESC European Society of Cardiology
European Journal of Heart Failure (2022) 24, 132–142
doi:10.1002/ejhf.2371

RESEARCH ARTICLE

European Society of Cardiology quality indicators for the care and outcomes of adults with heart failure. Developed by the Working Group for Heart Failure Quality Indicators in collaboration with the Heart Failure Association of the European Society of Cardiology

Suleman Aktaa[1,2,3]*, Marija Polovina[4], Giuseppe Rosano[5], Amr Abdin[6], Manuel Anguita[7], Mitja Lainscak[8,9], Lars H. Lund[10], Theresa McDonagh[11,12], Marco Metra[13], Richard Mindham[14], Massimo Piepoli[15], Stefan Störk[16], Mariya P. Tokmakova[17], Petar Seferović[4], Chris P. Gale[1,2,3†], and Andrew J.S. Coats[18†]

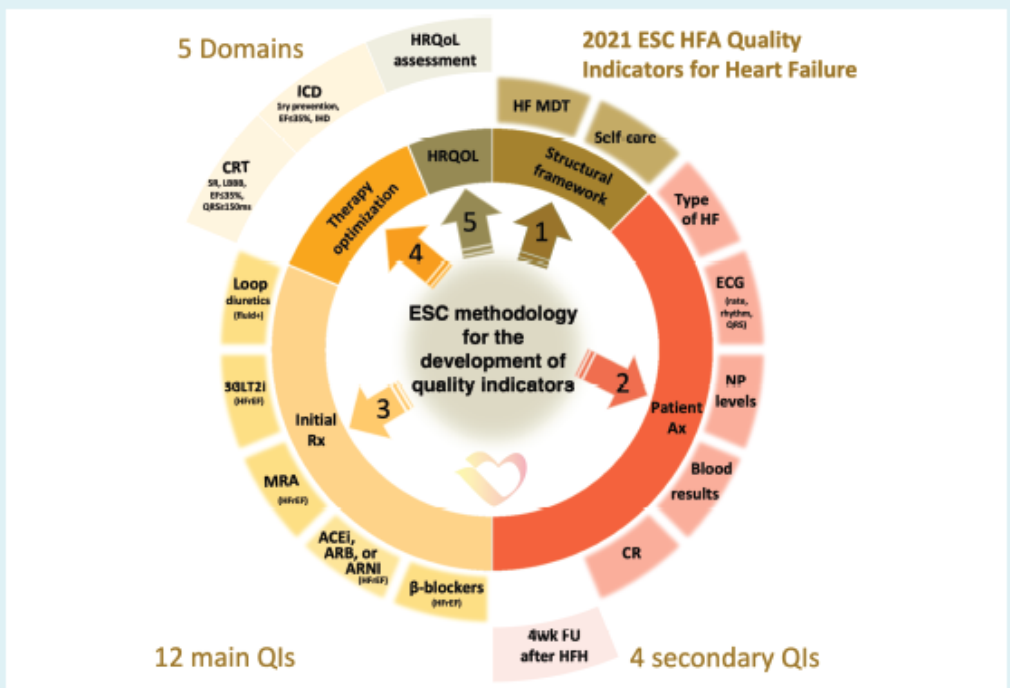

Figure 2 ESC HFA quality indicators for the management of patients with heart failure. Blood results include: urea, creatinine, electrolytes, full blood count, glucose, glycated haemoglobin, thyroid-stimulating hormone, liver function test, lipids and iron profile. Beta-blockers are bisoprolol, carvedilol, sustained-release metoprolol succinate, or nebivolol. Ax, assessment; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; CR, cardiac rehabilitation; CRT, cardiac resynchronization therapy; ECG, electrocardiogram; EF, ejection fraction; ESC, European Society of Cardiology; FU, follow-up; HF, heart failure; HFA, Heart Failure Association; HFH, hospitalization for heart failure; HFrEF, heart failure with reduced ejection fraction; HRQoL, health-related quality of life; ICD, implantable cardioverter defibrillator; IHD, ischaemic heart disease; LBBB, left bundle branch block; MDT, multidisciplinary team; MRA, mineralocorticoid receptor antagonist; NP, natriuretic peptide; QI, quality indicator; Rx, treatment; SGLT2i, sodium–glucose co-transporter 2 inhibitor; SR, sinus rhythm.

Table 2 Composite quality indicators

Composite main: Opportunity-based

Calculated on 6 individual QIs in patients with LVEF >40%:

1. Proportion of patients with HF who have a documentation of their HF clinical type (HFrEF, HFmrEF, HFpEF).
2. Proportion of patients with HF who have a documentation of their ECG findings.
3. Proportion of patients with HF who have their NPs measured (within a 3-month period from the time of HF diagnosis).
4. Proportion of patients with HF who have their blood tests checked.
5. Proportion of patients hospitalized with HF who have been referred for a cardiac rehabilitation programme.
6. Proportion of patients hospitalized with HF who have a follow-up review by a healthcare professional within 4 weeks of their hospital discharge.

Calculated on 12 individual QIs in patients with LVEF ≤40%:

1. Proportion of patients with HF who have a documentation of their HF clinical type (HFrEF, HFmrEF, HFpEF).
2. Proportion of patients with HF who have a documentation of their ECG findings.
3. Proportion of patients with HF who have their NPs measured (within a 3-month period from the time of HF diagnosis).
4. Proportion of patients with HF who have their blood tests checked.
5. Proportion of patients hospitalized with HF who have been referred for a cardiac rehabilitation programme.
6. Proportion of patients hospitalized with HF who have a follow-up review by a healthcare professional within 4 weeks of their hospital discharge.
7. Proportion of patients with HFrEF who are prescribed the beta-blocker bisoprolol, carvedilol, sustained-release metoprolol succinate, or nebivolol in the absence of any contraindications.
8. Proportion of patients with HFrEF who are prescribed an ACE inhibitor, ARB or ARNI in the absence of any contraindications.
9. Proportion of patients with HFrEF who are prescribed an MRA in the absence of any contraindications.
10. Proportion of patients with HFrEF who are prescribed a SGLT2 inhibitor in the absence of any contraindications.
11. Proportion of symptomatic patients with HFrEF in sinus rhythm with a QRS duration ≥150 ms and LBBB QRS morphology and with LVEF ≤35% despite OMT who are offered CRT.
12. Proportion of symptomatic patients with HF, LVEF ≤35% despite ≥3 months of OMT, and IHD who are offered primary prevention ICD.

Numerator: Number of times each of the above individual QIs were accomplished correctly.[a]

Denominator: Number of chances existed to deliver individual QIs based on the inclusion criteria of each QI (*Table 1*).

Composite secondary: All-or-none

1. Proportion of patients with HFrEF who are prescribed the beta-blocker bisoprolol, carvedilol, sustained-release metoprolol succinate, or nebivolol in the absence of any contraindications.
2. Proportion of patients with HFrEF who are prescribed an ACE inhibitor, ARB or ARNI in the absence of any contraindications.
3. Proportion of patients with HFrEF who are prescribed an MRA in the absence of any contraindications.
4. Proportion of patients with HFrEF who are prescribed a SGLT2 inhibitor in the absence of any contraindications.

Numerator: Number of patients who are eligible for and have accomplished all the above individual QIs.

Denominator: Number of patients who are eligible for all the above individual QIs based on the inclusion criteria of each QI (*Table 1*).

- 2 MIO inhabitants
- 14 hospitals with acute admissions
- Existing sources (all 100% coverage)
  - National hospitalization database
  - Central population registry
  - Registry of issues prescriptions
- Finances
  - Max 400kE/year

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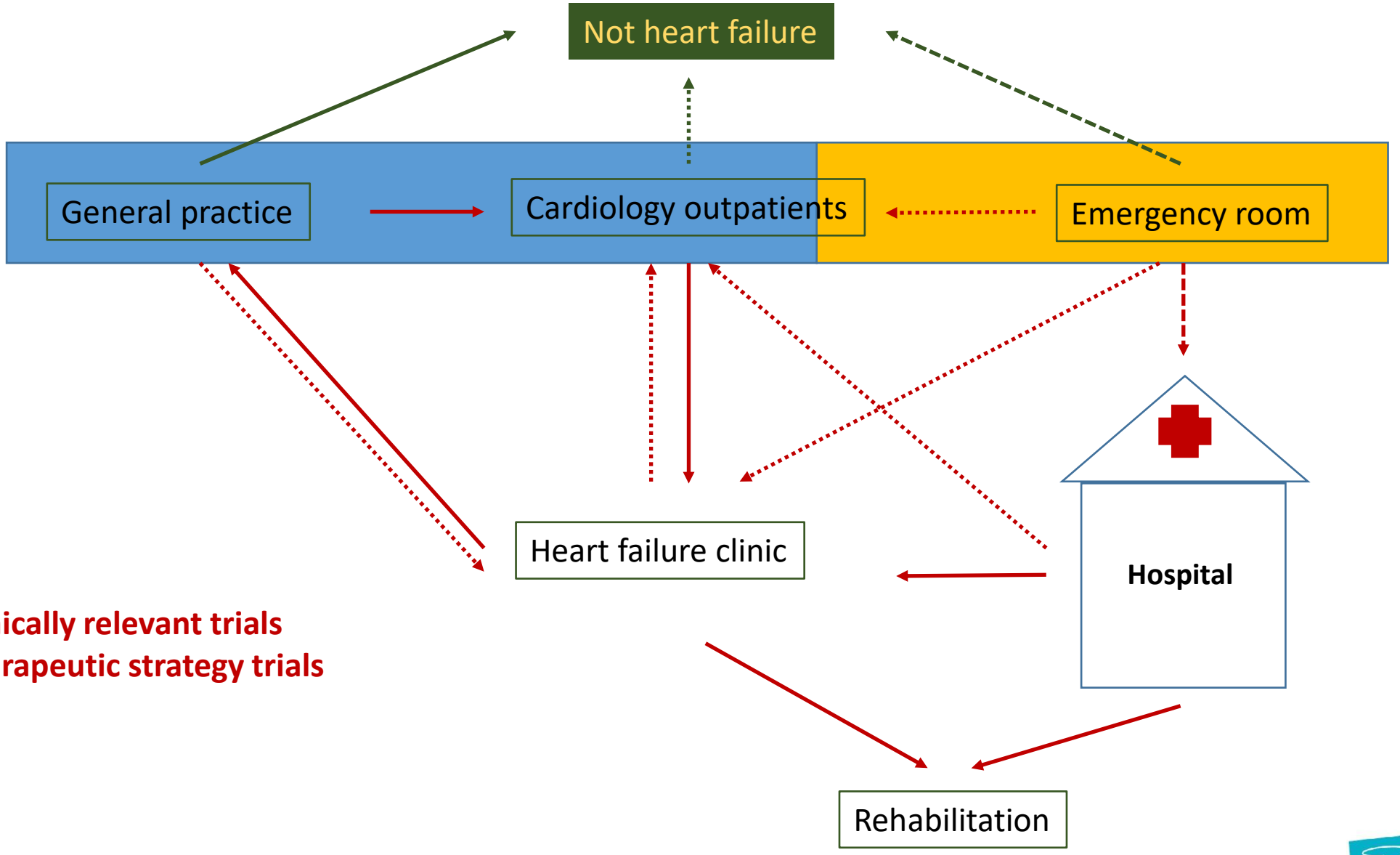

Clinically relevant trials
Therapeutic strategy trials

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European Journal of Heart Failure (2016) 18, 1321–1328
doi:10.1002/ejhf.617

RESEARCH ARTICLE

National trends in heart failure hospitalization rates in Slovenia 2004–2012

Daniel Omersa[1], Jerneja Farkas[1], Ivan Erzen[1], and Mitja Lainscak[2,3]*

[1]National Institute of Public Health, Ljubljana, Slovenia; [2]Department of Cardiology, Department of Research and Education, General Hospital Celje, Celje, Slovenia; and [3]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski, Karen Sliwa, Adriaan A Voors, Christopher Edwards, Maria Novosadova, Koji Takagi, Albertino Damasceno, Hadiza Saidu, Etienne Gayat, Peter S Pang, Jelena Celutkiene, Gad Cotter

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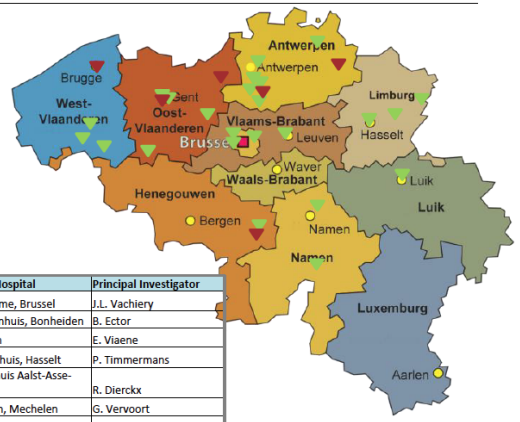

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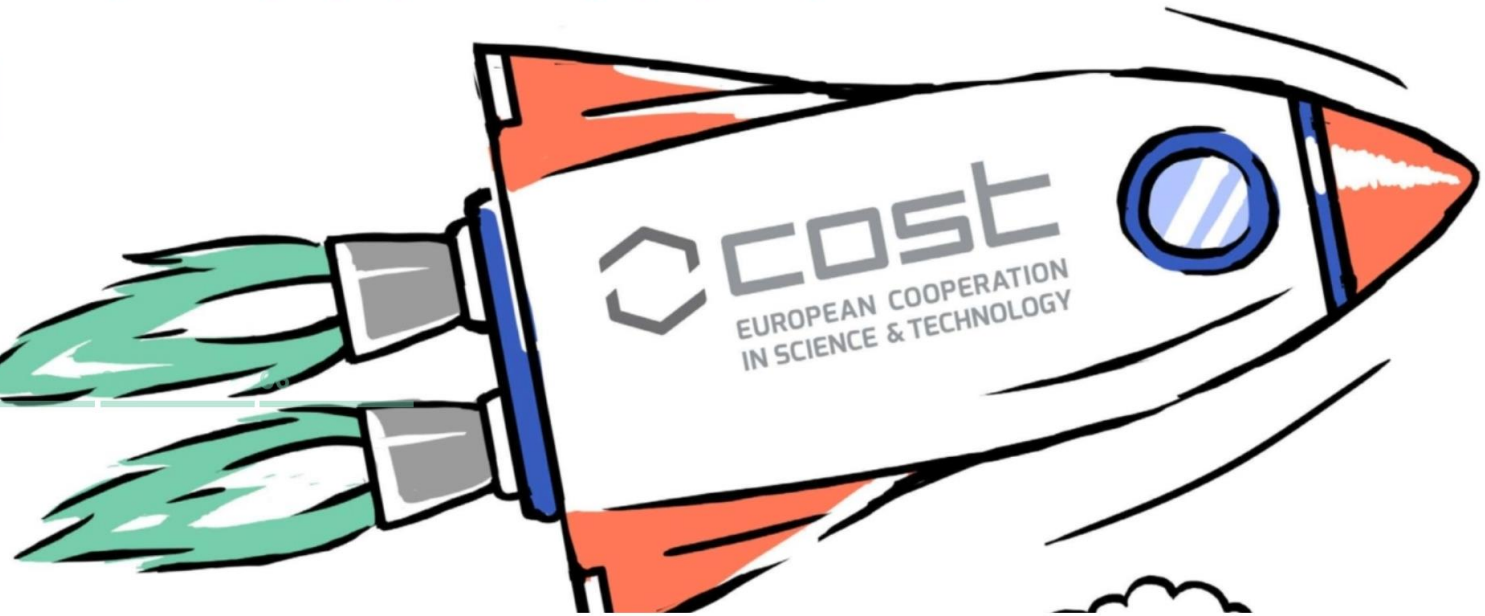

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