REACH-HFpEF Trial

Facilitator Training

22nd & 23rd June and 6th & 7th July 2021

SUPPORTED BY
NIHR | National Institute for Health Research

HF Burden

- HF, described as an epidemic, affects 1-2% of the adult population in developed countries
- Most common reason for hospitalisation in people aged over 65, and up to 20-30% of patients die within a year of diagnosis
- Direct annual healthcare costs are almost £2-3 billion in England alone
- **Approximately half of patients** with HF have a normal, or preserved, left ventricular ejection fraction (HFpEF)

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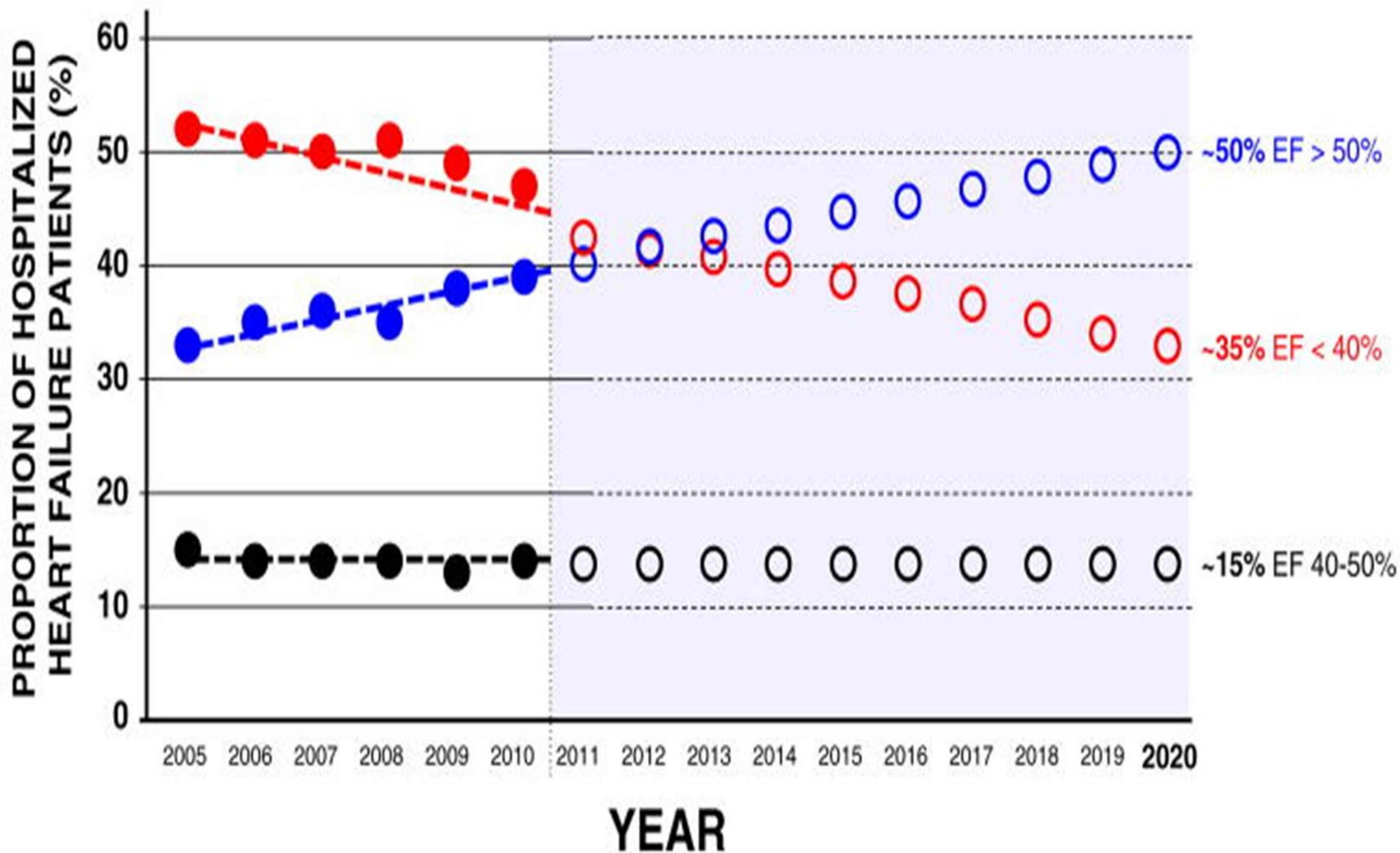
HFpEF: Increasing prevalence (in contrast to HFrEF)



HFpEF: Lacking in evidenced drug treatment options (ESC Guidelines)

Recommendations	Class [a]	Level [b]	Ref [c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

HFpEF: Manage the co-morbidities

COR	LOE	Recommendations	Comment/Rationale
I	B	Systolic and diastolic blood pressure should be controlled in patients with HF*p*EF in accordance with published clinical practice guidelines to prevent morbidity.[164,165]	2013 recommendation remains current.
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HF*p*EF.	2013 recommendation remains current.
IIa	C	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HF*p*EF despite GDMT.	2013 recommendation remains current.
IIa	C	Management of AF according to published clinical practice guidelines in patients with HF*p*EF is reasonable to improve symptomatic HF.	2013 recommendation remains current (Section 9.1 in the 2013 HF guideline).
IIa	C	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HF*p*EF.	2013 recommendation remains current.
IIb	B-R	In appropriately selected patients with HF*p*EF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations.[83,166,167]	**NEW:** Current recommendation reflects new RCT data.
See Online Data Supplement C.			

‘HFpEF represents the single largest unmet need in cardiovascular medicine’.

Circulation

WHITE PAPER

Research Priorities for Heart Failure With Preserved Ejection Fraction

National Heart, Lung, and Blood Institute Working Group Summary

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HFpEF: Different Clinical Phenotypes?

Circulation
Volume 134, Issue 1, 5 July 2016, Pages 73-90
https://doi.org/10.1161/CIRCULATIONAHA.116.021884

STATE OF THE ART - IN DEPTHIN DEPTH

Phenotype-Specific Treatment of Heart Failure With Preserved Ejection Fraction

A Multiorgan Roadmap

Sanjiv J. Shah, MD, Dalane W. Kitzman, MD, Barry A. Borlaug, MD, Loek van Heerebeek, MD, PhD, Michael R. Zile, MD, David A. Kass, MD, and Walter J. Paulus, MD, PhD

ABSTRACT: Heart failure (HF) with preserved ejection fraction (EF; HFpEF) accounts for

HFpEF Phenotypes: Potential role for Exercise

HFpEF Predisposition Phenotypes	HFpEF Clinical Presentation Phenotypes				
	Lung Congestion	+Chronotropic Incompetence	+Pulmonary Hypertension (CpcPH)	+Skeletal muscle weakness	+Atrial Fibrillation
Overweight/obesity/ metabolic syndrome/ type 2 DM	• **Diuretics (loop diuretic in DM)** • **Caloric restriction** • Statins • Inorganic nitrite/nitrate • Sacubitril • Spironolactone	+Rate adaptive atrial pacing	+Pulmonary vasodilators (e.g. PDE5I)	**+Exercise training program**	+Cardioversion +Rate Control **+Anticoagulation**
+Arterial hypertension	+ACEI/ARB	+ACEI/ARB +Rate adaptive atrial pacing	+ACEI/ARB +Pulmonary vasodilators (e.g. PDE5I)	+ACEI/ARB **+Exercise training program**	+ACEI/ARB +Cardioversion +Rate Control **+Anticoagulation**
+Renal dysfunction	+Ultrafiltration if needed	+Ultrafiltration if needed +Rate adaptive atrial pacing	+Ultrafiltration if needed +Pulmonary vasodilators (e.g. PDE5I)	+Ultrafiltration if needed **+Exercise training program**	+Ultrafiltration if needed +Cardioversion +Rate Control **+Anticoagulation**
+CAD	+ACEI +Revascularization	+ACEI +Revascularization +Rate adaptive atrial pacing	+ACEI +Revascularization +Pulmonary vasodilators (e.g. PDE5I)	+ACEI +Revascularization **+Exercise training program**	+ACEI +Revascularization +Cardioversion +Rate Control **+Anticoagulation**

REACH-HF evidence base

Full research paper

European Journal of Preventive Cardiology | ESC European Society of Cardiology

European Journal of Preventive Cardiology
0(00) 1–11
DOI: 10.1177/2047487318806358
journals.sagepub.com/home/ejpc
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The effects and costs of home-based rehabilitation for heart failure with reduced ejection fraction: The REACH-HF multicentre randomized controlled trial

Hasnain M Dalal[1,2], Rod S Taylor[1], Kate Jolly[3], Russell C Davis[4],

MLWHF	Mean Diff (95% CI) at 12mth	P-value
Total	-5.7 (-10.6 to -0.7)	0.025
Physical	-3.2 (-5.7 to -0.6)	0.02
Emotional	-0.8 (-2.2 to 0.6)	0.27

Julia Frost, Jennifer Wingham,[2]
Charles Abraham,[5,6] Fiona C Warr
Jackie Miles,[10] Sally J Singh,[11] Ke

Full research paper

European Journal of Preventive Cardiology | ESC European Society of Cardiology

European Journal of Preventive Cardiology
0(00) 1–10
DOI: 10.1177/2047487319833507
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The cost effectiveness of REACH-HF and home-based cardiac rehabilitation compared with the usual medical care for heart failure with reduced ejection fraction: A decision model-based analysis

REACH-HF costs	£15,452
Usual care costs	£15,051
Difference	+£400
CR QALYs	4.47
Usual care QALYs	4.24
Difference in QALYs	+0.23
Cost per QALY	£1720/QALY

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Open Access Research

BMJ Open

A randomised controlled trial of a facilitated home-based rehabilitation intervention in patients with heart failure with preserved ejection fraction and t
Pilot

	Baseli						
	REACH (n=25)						
MLHFQ score Mean (SD							
Overall	38.2 (27.6)						
Physical	21.6 (13.4)	19.8 (12.4)	19.4 (13.5)	20.7 (12.8)	16.2 (12.3)*	20.3 (13.6)	**–4.7 (–10.1 to 0.8)**
Emotional	7.8 (9.1)	7.8 (8.4)	8.0 (8.5)	9.1 (8.6)	6.8 (8.1)*	9.0 (8.5)	**–2.7 (–6.0 to 0.6)**

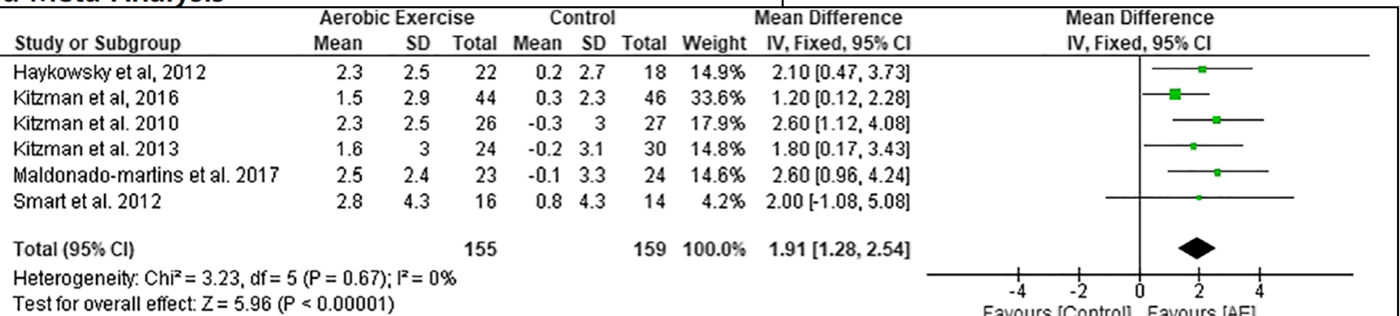
"Our findings support the feasibility and rationale for delivering the REACH-HF facilitated home-based rehabilitation intervention for patients with HFpEF and their caregivers and progression to a full multicentre randomised clinical trial to test its clinical effectiveness and cost-effectiveness."

Current Atherosclerosis Reports (2019) 21: 45
https://doi.org/10.1007/s11883-019-0806-6

EVIDENCE-BASED MEDICINE, CLINICAL TRIALS AND THEIR INTERPRETATIONS (L. ROEVER, SECTION EDITOR)

Effect of Aerobic Exercise on Peak Oxygen Consumption, VE/VCO$_2$ Slope, and Health-Related Quality of Life in Patients with Heart Failure with Preserved Left Ventricular Ejection Fraction: a Systematic Review and Meta-Analysis

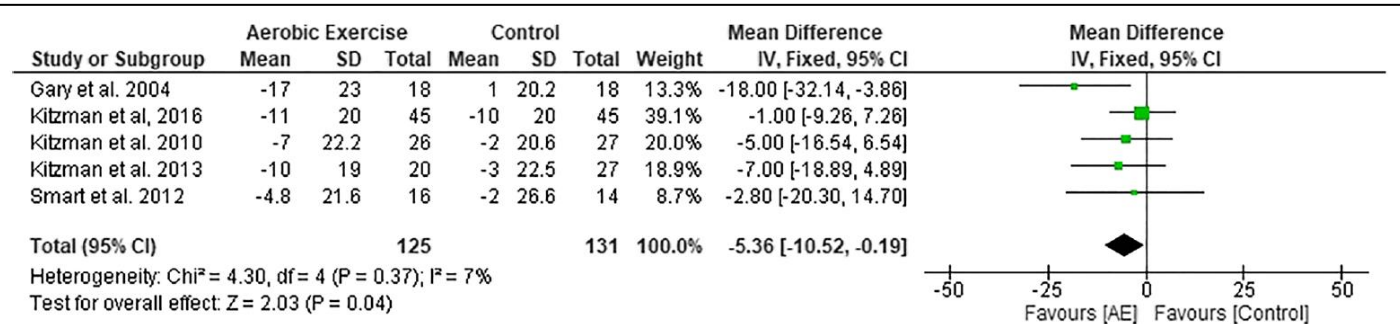
Mansueto Gomes-Neto[1,2,3,4,5] · Ar
Tong Liu[7] · Gary Tse[8] · Giuseppe
Øyvind Ellingsen[11,12] · Vitor Olive



Study or Subgroup	Aerobic Exercise Mean	Aerobic Exercise SD	Aerobic Exercise Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Haykowsky et al, 2012	2.3	2.5	22	0.2	2.7	18	14.9%	2.10 [0.47, 3.73]
Kitzman et al, 2016	1.5	2.9	44	0.3	2.3	46	33.6%	1.20 [0.12, 2.28]
Kitzman et al. 2010	2.3	2.5	26	-0.3	3	27	17.9%	2.60 [1.12, 4.08]
Kitzman et al. 2013	1.6	3	24	-0.2	3.1	30	14.8%	1.80 [0.17, 3.43]
Maldonado-martins et al. 2017	2.5	2.4	23	-0.1	3.3	24	14.6%	2.60 [0.96, 4.24]
Smart et al. 2012	2.8	4.3	16	0.8	4.3	14	4.2%	2.00 [-1.08, 5.08]
Total (95% CI)			**155**			**159**	**100.0%**	**1.91 [1.28, 2.54]**

Heterogeneity: Chi² = 3.23, df = 5 (P = 0.67); I² = 0%
Test for overall effect: Z = 5.96 (P < 0.00001)

Fig. 2 Aerobic exercise versus control: Outcome: Peak VO$_2$. Review Manager (RevMan), Version 5.3; The Cochrane Collaboration, 2013



Study or Subgroup	Aerobic Exercise Mean	Aerobic Exercise SD	Aerobic Exercise Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Gary et al. 2004	-17	23	18	1	20.2	18	13.3%	-18.00 [-32.14, -3.86]
Kitzman et al, 2016	-11	20	45	-10	20	45	39.1%	-1.00 [-9.26, 7.26]
Kitzman et al. 2010	-7	22.2	26	-2	20.6	27	20.0%	-5.00 [-16.54, 6.54]
Kitzman et al. 2013	-10	19	20	-3	22.5	27	18.9%	-7.00 [-18.89, 4.89]
Smart et al. 2012	-4.8	21.6	16	-2	26.6	14	8.7%	-2.80 [-20.30, 14.70]
Total (95% CI)			**125**			**131**	**100.0%**	**-5.36 [-10.52, -0.19]**

Heterogeneity: Chi² = 4.30, df = 4 (P = 0.37); I² = 7%
Test for overall effect: Z = 2.03 (P = 0.04)

Fig. 4 Aerobic exercise versus control: Outcome: HRQoL. Review Manager (RevMan), Version 5.3; The Cochrane Collaboration, 2013

REACH-HFpEF
In a nutsell

- **Design**
  - Multicentre parallel 2 group RCT with individual 1:1 level randomisation (parallel economic & process evaluation) – 20 UK sites
- **Population**
  - 520 people with HFpEF (see detailed project description for i/e criteria) & their caregiver
- **Intervention**
  - REACH-HF + usual care
- **Control**
  - Usual care alone
- **Outcomes**
  - Primary: MLwHF & multiple secondaries @baseline (pre-randomisation) & 4 and 12 months post-rando

REACH-HFpEF
Inclusion criteria

1. Currently symptomatic HF (NYHA Class II-IV)
2. Prescribed loop diuretics & need for intermittent loop diuretics for the management of symptoms or signs of congestion
3. LVEF (by echocardiography) ≥45% within 12 months prior to randomisation
4. At least one of the following risk factors:
   - Hospital admission in last 12 months for which HF was a major contributor
   - N-terminal proBNP >300 pg/ml for patients with sinus rhythm
   - N-terminal proBNP >900 pg/ml for patients in atrial fibrillation

REACH-HF

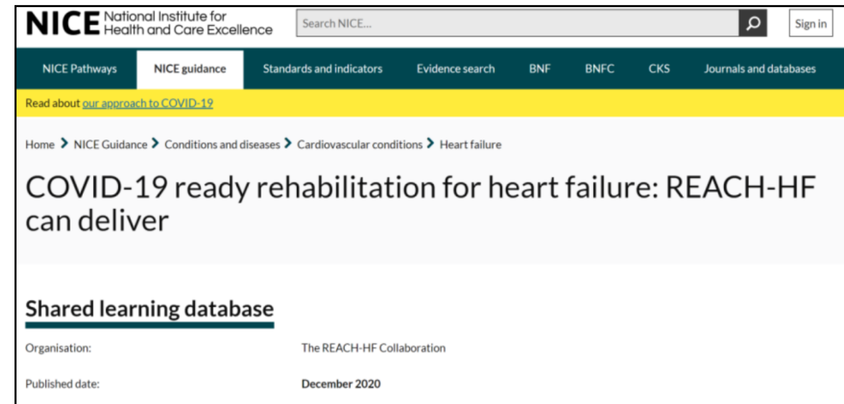
Patient/Caregiver data collection

Patients	Baseline (pre-randomisation)	Follow up 4 months post-randomisation	Follow up 12 months post-randomisation
Primary outcome			
1. Minnesota Living with Heart Failure questionnaire (MLWHFQ)	X	X	X
Secondary outcomes			
2. Mortality (HF-relatedness determined by an independent adjudication panel)	X	X	X
3. Hospitalisation (HF-relatedness determined by an independent adjudication panel)	X	X	X
4. Blood sample for NT-proBNP levels	X	X	X
5. Physical activity (over a 9-day period by accelerometry - GeneActive)	X	X	X
6. Short-Form 12 questionnaire (SF-12)	X	X	X
7. EQ-5D-5L questionnaire	X	X	X
8. Self-Care in Heart Failure Index (SCHFI)	X	X	X
9. Hospital Anxiety and Depression Scale (HADS)	X	X	X
10. Clinical Frailty Scale (CF			
11. Incremental shuttle walk			
12. Self-efficacy for key beh			
13. Healthcare utilization qu			
14. Adverse events			

Caregivers	Baseline (pre-randomisation)	Follow up 4 months post-randomisation	Follow up 12 months post-randomisation
Secondary outcomes			
1. Family Caregiver Quality of Life Scale questionnaire (FamQol)	X	X	X
2. Caregiver Burden Questionnaire HF (CBQ-HF)	X	X	X
3. Caregiver Contribution to Self-care of HF Index questionnaire (CC-SCHFI)	X	X	X
4. Hospital Anxiety and Depression Scale (HADS)	X	X	X
5. EQ-5D-5L questionnaire	X	X	X

REACH-HFpEF

- **Intervention delivery**
  - With COVID-19, summer 2020 we ‘repurposed’ REACH-HF so can be entirely remotely delivered
  - However, with reducing social restrictions, many trusts/health boards & CR/HF teams able to now make home visits (1st & last contact of 12 weeks of REACH-HF)….**<u>if possible, that would be our preference!</u>**



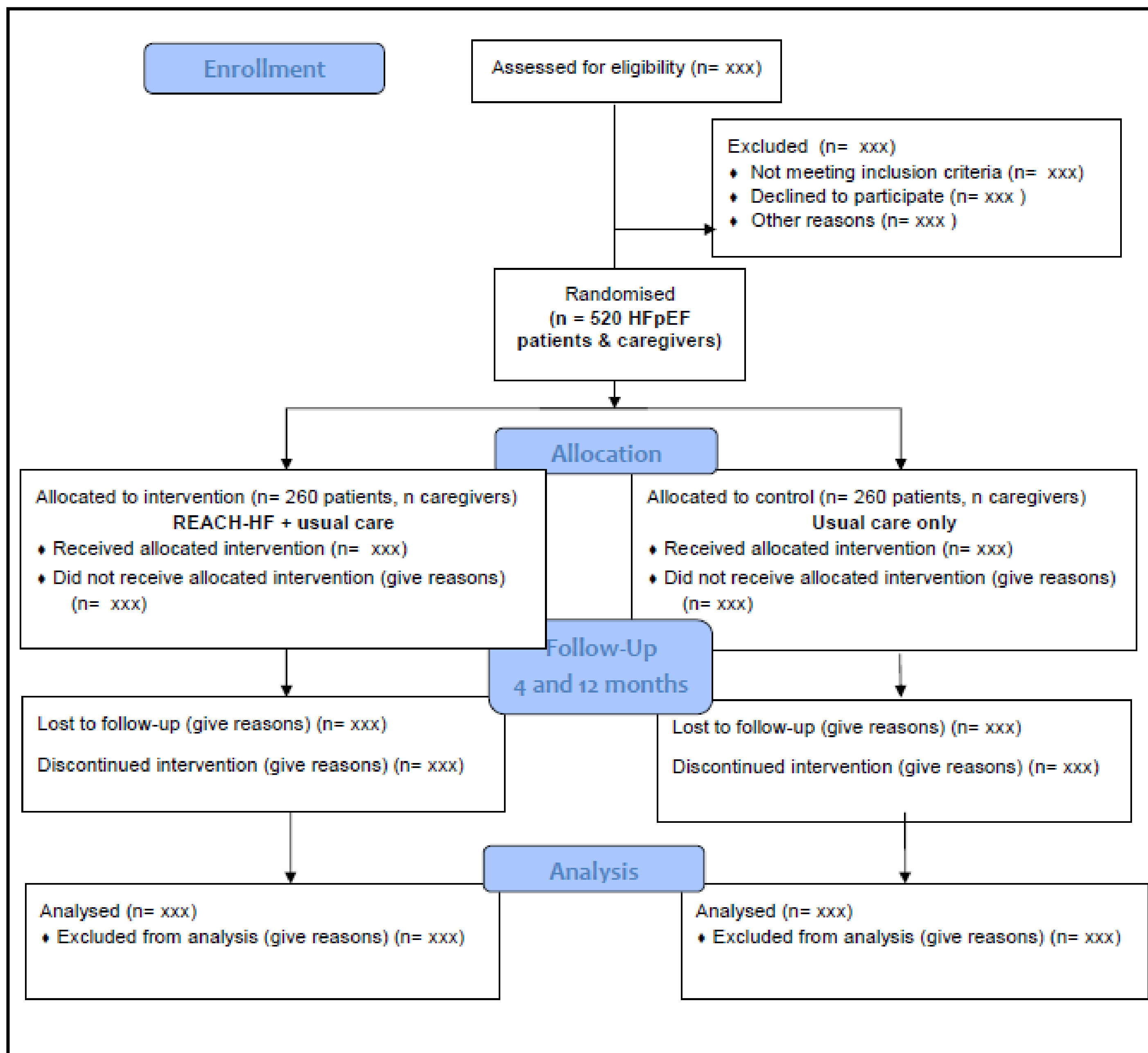
REACH-HF

What data collection from me?

- **Facilitator log**
  - For each patient in your case load we will be asking you to complete ***simple log record*** of each of your patient contacts over 12 wks: (1) nature (home F2F/phone/web video); (2) duration; (3) caregiver present; (4) any notes (log sheets provided by Glasgow team)
- **Intervention fidelity**
  - We will approach a sample of you to ***audio record your patient/caregiver contacts*** (Exeter research team follow up directly on this)
- **Understanding implementation**
  - We will approach a sample of you for a ***phone structured interview*** (near end of study) to seek your perceptions of REACH-HF delivery [also interviewing patients/caregivers] (Exeter research team follow up directly on this)

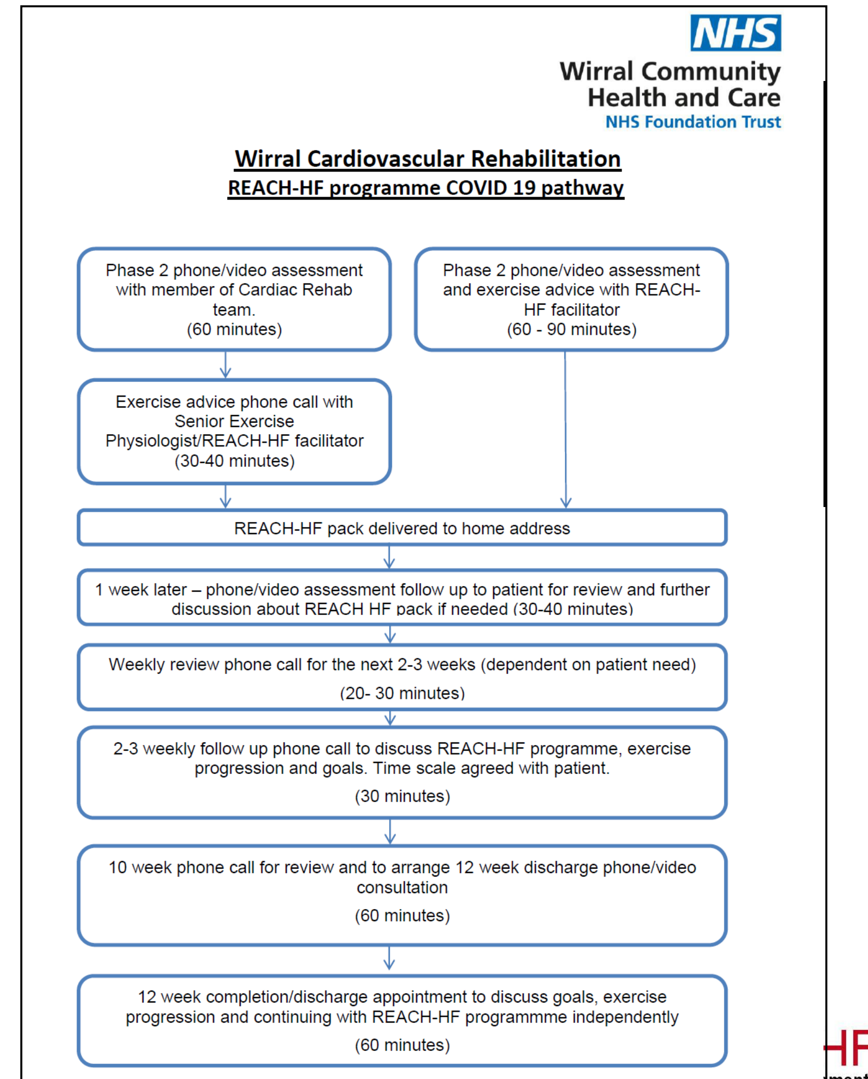
- **Thank you! and any questions?**

Back up slides


Enrollment
Assessed for eligibility (n= xxx)
Excluded (n= xxx)
Not meeting inclusion criteria (n= xxx)
Declined to participate (n= xxx)
Other reasons (n= xxx)
Randomised
(n = 520 HFpEF
patients & caregivers)
Allocation
Allocated to intervention (n= 260 patients, n caregivers)
REACH-HF + usual care
Received allocated intervention (n= xxx)
Did not receive allocated intervention (give reasons)
(n= xxx)
Allocated to control (n= 260 patients, n caregivers)
Usual care only
Received allocated intervention (n= xxx)
Did not receive allocated intervention (give reasons)
(n= xxx)
Follow-Up
4 and 12 months
Lost to follow-up (give reasons) (n= xxx)
Discontinued intervention (give reasons) (n= xxx)
Lost to follow-up (give reasons) (n= xxx)
Discontinued intervention (give reasons) (n= xxx)
Analysis
Analysed (n= xxx)
Excluded from analysis (give reasons) (n= xxx)
Analysed (n= xxx)
Excluded from analysis (give reasons) (n= xxx)

Repurposing REACH-HF with COVID-19

- **Facilitator training**
  - ➢ Switch to 2-day web-based course
  - ➢ May-Nov 2020: 103 trainees (physios, CR nurses, HF nurses & exercise physiologists) across 20+ sites in the UK
  - ➢ Further courses for 2021 by NHS Lothian
- **Delivery without home visit(s)**



in Chronic Heart Failure

FAQs

- What if our Trust/hospital/CR team don’t allow home visits?
- Can we access (baseline) ISWT outcome results from trial participants?
- Is GCP training required for all site staff (including REACH-HF facilitators)?

What is our Trust/hospital/CR team don't allow home visits?

- Know from HFrEF trial and HFpEF pilot that initial (and final) F2F meeting with patient (& caregiver) = KEY
- Options
  1. Have the patient/caregiver come into centre for 1st (& last) visit
  2. 1st (& last) visit by skype/teams?
  3. 1st (& last) vist by phone

Can we access ISWT outcome results from trial participants?

- Yes (assuming sites are able to do ISWT)
- We will communicate this to each site research team so that they liaise with you on this

Is GCP training required for all site staff (including REACH-HF facilitators)?

- Our sponsor, NHS Greater Glasgow & Clyde have advised…Yes!

- Contact your local site research team/trust who will provide details on completing GCP training (several online modules available)

Next Steps

- Please **do liaise with your site research team**
  - Link between patient (caregiver) recruitment and referral to REACH-HF team = KEY
- Site investigator (web) meetings
  - **Aimed at site research teams** but you may want to attend
  - Dates in July/August – please check with your site research team
- MHO send out **updated version of Manuals** (mid Aug)
- Participant recruitment planned to begin Sept 2021…**you go live!**

Contact us

- If you have any questions about the trial, don’t hesitate to contact us at….

REACH-HFpEFproject@glasgowctu.org

- Any questions about the intervention delivery please contact us at heart.manual@nhslothian.scot.nhs.uk