

The OPTIMIZER smart system for managing heart failure

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is the OPTIMIZER smart system. It is a programmable cardiac stimulation device for people with chronic heart failure. The system is for people who still have symptoms after having optimal drug treatment, when cardiac resynchronisation therapy is not suitable. It can be used when patients have a normal QRS interval (less than 120 ms) in New York Heart Association class II to IV, with a left ventricular ejection fraction of 25% to 45%.
- The **innovative aspect** is that it is the only device that uses cardiac contractility modulation therapy.
- The intended **place in therapy** would be in addition to drug therapy in people with chronic heart failure.

- The **main points from the evidence** summarised in this briefing are from 6 studies (1 randomised controlled trial, 1 case-control study, 3 observational studies and 1 retrospective analysis) including 633 adults. The studies show that the OPTIMIZER smart system could be more effective than drug therapy alone in patients with heart failure.
- **Key uncertainties** around the evidence or technology are that there is only 1 comparative study, which was unblinded. Also, none of the studies were done in the NHS.
- The **cost** of the OPTIMIZER smart system is £17,000 per unit (excluding VAT). The **resource impact** would be greater than standard care.
- NICE's interventional procedures guidance on cardiac contractility modulation device implantation for heart failure recommends that this technique appears safe, but it should be used in the context of research.

The technology

The OPTIMIZER smart system (Impulse Dynamics) is a programmable cardiac stimulation device for patients with chronic heart failure who have symptoms after having optimal drug treatment, when cardiac resynchronisation therapy is not suitable. The system has 3 components: a programmable implantable pulse generator with a rechargeable battery and implantable leads, a charger and an OMNI programmer.

The implantable pulse generator is implanted in the chest and connected to 2 standard pacemaker leads that go through veins into the right ventricle. The leads sense ventricular activity and give out cardiac contractility modulation (CCM) signals. An optional additional lead can sense atrial activity. Unlike a pacemaker or a defibrillator, the OPTIMIZER system is designed to control the strength of contraction of the heart muscle rather than the rhythm. Pulses are given at regular intervals in the day. This increases the contraction strength and the pumping capacity of the heart, which can improve a person's exercise ability and physical and emotional quality of life.

The portable OMNI programmer allows doctors to change the OPTIMIZER signal parameters according to individual patient needs. The implantable pulse generator needs weekly recharging at home for about 40 to 60 minutes. The rechargeable battery should work for 15 years.

Innovations

The OPTIMIZER is currently the only device available that uses CCM therapy, which does not influence the heart rhythm. Instead, it delivers CCM electrical pulses that stimulate the heart, increasing the contraction strength and the pumping capacity of the heart. After these signals, the heart muscle contractility increases with no increased oxygen consumption. The OPTIMIZER can be a treatment option for patients who still have symptoms of heart failure after drug therapy when other cardiac implantable electronic devices are not suitable.

Current care pathway, population, setting and intended user

Treatments for chronic heart failure include cardiac rehabilitation, drugs to improve heart function, cardiac resynchronisation therapy and cardiac transplantation. NICE has published a guideline on chronic heart failure in adults. NICE's technology appraisal guidance on implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure states that cardiac resynchronisation therapy is not recommended for people with a normal QRS interval (less than 120 ms) in New York Heart Association (NYHA) class II to IV with a left ventricular ejection fraction (LVEF) of 35% or lower. According to the company these are the people who would be eligible for, and benefit from, the OPTIMIZER smart system. Currently the only option for these people is to continue with conventional drug treatment.

Over 920,000 people are estimated to have heart failure in the UK (Conrad et al. 2018). The company estimates that there would be about 10,920 people eligible for the OPTIMIZER smart system (on NYHA class II to IV and normal QRS). It would expect around 2,100 people per year to get the device implanted. If the focus is on people with LVEF of 35% and above (for which the company feels there are data showing the strongest clinical effect), there would be 655 devices implanted per year.

Patients who can have the OPTIMIZER system might also need an implantable cardioverter defibrillator (ICD) or might already have 1 implanted. However, there are not expected to be many of these people in the UK. The company has confirmed that this has no effect on CCM treatment and does not prevent implantation of the OPTIMIZER. The system is designed to work alongside any ICD device, and does not interrupt the ICD.

NICE's interventional procedures guidance on cardiac contractility modulation device implantation for heart failure states that although the evidence on CCM device implantation for heart failure raises no major safety concerns, the evidence on efficacy is inadequate in quantity and quality. Therefore, it recommends that CCM device implantation should only be done in the context of research.

The following guidance are relevant to this care pathway:

- Cardiac contractility modulation device implantation for heart failure (2019) NICE interventional procedures guidance 655
- Chronic heart failure in adults (2018) NICE guideline NG106
- Implantation of a left ventricular assist device for destination therapy in people ineligible for heart transplantation (2015) NICE interventional procedures guidance 516
- Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (2014) NICE technology appraisal guidance 314

Costs

An economic evaluation study by Maniadakis et al. (2015) outlined the costs associated with the OPTIMIZER smart system and standard care. It is expected that the device would be used in addition to standard care.

Technology costs

Table 1 Unit costs for the OPTIMIZER smart system

Description	Cost
The OPTIMIZER smart system	£17,000
Leads (n=2)	£395
Other hospital costs (staff)	£245
Other hospital costs (capital)	£120
Other hospital costs (consumables and tests)	£95

Other hospital costs (hospital care)	£510
Total implantation cost	£18,365

Costs of standard care

Drug therapy for heart failure is estimated to cost £1,362 over the patient's lifetime.

Economic studies

Maniadakis et al. (2015) modelled the management of chronic heart failure. This model outlined the cost effectiveness of the OPTIMIZER smart system and drug therapy compared with drug therapy alone for treating heart failure in people with normal QRS when drug therapy has not controlled symptoms adequately. The time horizon was over a patient's lifetime, with 4-week cycles. The results showed OPTIMIZER with drug therapy had a total mean lifetime cost of £37,467 and drug therapy alone had a total mean lifetime cost of £16,885. In the model, people who had the device and drug therapy gained 5.26 quality-adjusted life years (QALYs) compared with 4.0 in the drug therapy alone arm. There was an incremental increase of 0.96 life years gained in favour of OPTIMIZER. The incremental cost per QALY gained was £16,405. The authors did a sensitivity analysis, which showed that at a £30,000 per QALY threshold, the likelihood of the device and drug treatment being cost-effective was 99.8% and was 97% at £25,000 per QALY.

Resource consequences

The OPTIMIZER smart system is currently used in a small number of NHS trusts in England. The device could be implemented using existing infrastructure, using existing cardiac catheter laboratories to implant it. Clinical teams who implant cardiac devices would need minimal additional training to be able to implant the OPTIMIZER, which is very similar to that of other cardiac devices such as a pacemaker. The company offers free training and field clinical specialists to help with advice during device implantation.

Regulatory information

The OPTIMIZER smart system is a CE-marked class III medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Heart failure is most common in older people. Therefore, older people are most likely to use this technology, and age is a protected characteristic under the Equality Act (2010). This technology is not suitable for people under 18.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Six studies are summarised in this briefing including 633 patients. Table 2 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

There is an ongoing multicentre prospective observational registry on the OPTIMIZER smart system that has provided a number of publications. This evidence is helpful to see the technology's potential, particularly improvement in exercise tolerance and quality of life. However, none of the evidence includes UK patients and there is only 1 comparative study, which was unblinded. A well-conducted blinded randomised controlled trial would help increase certainty about efficacy. The studies include a cross section of patients with different severities of disease. These might represent real world populations more accurately, but the studies do not clearly define when associated drug treatments are used, which could substantially affect the results.

Table 2 Summary of selected studies

Anker et al. (2019)

Study size, design and location	Observational study n=140. Multicentre study in USA and Europe. Patients with a NYHA class III or IV, QRS duration less than 130 ms and LVEF between 25% and 45% were enrolled.
Intervention and comparator(s)	The OPTIMIZER smart system. No comparator.
Key outcomes	Results were presented in 3 groups: <ul style="list-style-type: none"> • the whole cohort (LVEF 25% to 45%) and split into patients with: <ul style="list-style-type: none"> • LVEF 35% to 45%, QRS 130 ms or lower, NYHA class III or higher • LVEF 25% to 35%, QRS 130 ms or higher, NYHA class III or higher. The results showed a reduction of 75% in hospital admissions ($p<0.0001$) in the 25% to 45% LVEF group and by a similar rate in the 35% to 45% group. MLWHFQ and NYHA class improved in all 3 groups, ($p<0.002$). Three-year survival was compared with predicted survival (SHFM) for each patient. The mortality rate was 17.2% for the whole cohort, 20.6% in the 25% to 35% LVEF group, which was similar to the predicted rates. The mortality rate in the 35% to 45% LVEF group was better than predicted (88.0% compared with 74.7%, $p=0.046$).
Strengths and limitations	No control group. The patients were recruited from a separate large prospective observational study. Inclusion was voluntary and approximately 70% agreed to enrol in this study, which may have introduced selection bias.
<u>Abraham et al. (2018)</u>	
Study size, design and location	RCT, n=160 patients with NYHA functional class III or IV symptoms, QRS duration less than 130 ms, and EF 25% to 45%. Location: USA and Europe.
Intervention and comparator(s)	The OPTIMIZER smart system (n=74). Comparator: continued medical therapy (n=86).

Key outcomes	Patients in the OPTIMIZER group had improved peak VO ₂ (increase 0.84 ml O ₂ /kg/min), NYHA functional class ($p<0.001$), 6-min hall walk ($p=0.02$) and a reduction in the MLWHFQ score ($p<0.001$) compared with the control group. Cardiovascular death and heart failure hospital admissions was reduced from 10.8% to 2.9% ($p=0.048$). There were 7 device-related adverse events.
Strengths and limitations	The treatment arm was unblinded, which could have introduced bias.
<u>Muller et al. (2017)</u>	
Study size, design and location	Prospective observational study n=143 with LVEF less than 45%. Location: USA and Germany (24 sites).
Intervention and comparator(s)	The OPTIMIZER smart system. No comparator.
Key outcomes	Results were presented in 3 groups (the whole cohort and split into patients with LVEF less than 35% and LVEF 35% or higher). Of the 143 patients, 106 patients (74%) completed the 24-month follow-up. NYHA and MLWHFQ improved in all 3 groups. LVEF in the entire cohort improved at 6 (2.5%), 12 (2.9%), 18 (5.0%), and 24 (4.9%) months. Overall survival at 2 years was 86.4% (95% CI 79.3 to 91.2%). Of the 18 deaths, 7 were considered to be cardiovascular related. Serious adverse events (n=193) were seen in 91 subjects and similarly distributed between groups with LVEF less than 35% and LVEF 35% or higher, and according to the authors were similar to other device trials for heart failure. The authors reported that there were an insufficient number of subjects who had follow-up data for 6-min walk or peak VO ₂ assessment to enable a comparative analysis.
Strengths and limitations	No control group.
<u>Kloppe et al. (2016)</u>	
Study size, design and location	Retrospective observational study n=68 with NYHA class II or III symptoms and normal QRS duration. Location: Germany.

Intervention and comparator(s)	The OPTIMIZER smart system (mean follow-up 4.5 years, range 0.25 to 10.3 years). No comparator.
Key outcomes	Results were compared with predicted survival (SHFM) pre-implant for each patient. There were 16 deaths during the follow-up period, 6 were cardiovascular related. Mortality rates (Kaplan–Meier analysis) at 1 year (0% compared with 6.1%), 2 years (3.5% compared with 11.8%) and 5 years (14.2% compared with 27.7%) were lower with the OPTIMIZER smart system compared with those predicted by SHFM ($p=0.007$).
Strengths and limitations	A retrospective observational study. Other factors such as drug therapy were not assessed, which could have influenced the results.
<u>Liu et al. (2016)</u>	
Study size, design and location	Case-control study n=41 with NYHA class III symptomatic heart failure and EF less than 40%. Location: Hong Kong.
Intervention and comparator(s)	The OPTIMIZER smart system (mean follow-up 75 months). No comparator.
Key outcomes	The results showed that all-cause mortality for the entire cohort was significantly reduced in the OPTIMIZER group 41% compared with the control 71% ($p=0.001$). Subgroup analysis showed that the all-cause mortality of OPTIMIZER patients with an EF of less than 25% did not significant differ compared with the control, however patients with a EF between 25% and 40% had a significant survival benefit ($p<0.001$). Admission rates were also significantly reduced for OPTIMIZER in the EF 25% to 40% subgroup ($p=0.001$).
Strengths and limitations	There were 6-year follow-up data but the sample size was relatively small.
<u>Kuschyk et al. (2015)</u>	
Study size, design and location	Single site retrospective analysis n=81 with symptomatic heart failure and reduced LVEF. Location: Germany.

Intervention and comparator(s)	The OPTIMIZER smart system (mean follow-up 34.2 months, range 6 to 123 months).
Key outcomes	The results showed significant improvements in NYHA class ($p=0.001$), LVEF ($p=0.001$), NT-proBNP levels ($p=0.001$). Quality of life measured by MLWHFQ also improved. Mortality rates appeared to be lower than estimated compared with the predicted rate calculated using a MAGGIC score.
Strengths and limitations	Small single-centre retrospective analysis. Drug therapy was administered at the discretion of the treating clinician and not assessed as part of the study, which could have had an effect on the results.
Abbreviations: EF, ejection fraction; LVEF, left ventricular ejection fraction; MAGGIC, meta-analysis global group in chronic heart failure; MLWHFQ, Minnesota Living With Heart Failure questionnaire; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; peak VO ₂ , peak oxygen uptake; RCT, randomised controlled trial; SHFM: Seattle Heart Failure Model.	

Recent and ongoing studies

- Evaluation of the safety and efficacy of the 2-lead OPTIMIZER smart system. ClinicalTrials.gov identifier: NCT03339310. Status: active, not recruiting. Estimated study completion: November 2019. Indication: ejection fraction 25% or higher and less than or equal to 45%. Device: the OPTIMIZER smart system.
- CCM in heart failure with preserved ejection fraction. ClinicalTrials.gov identifier: NCT03240237. Status: recruiting, estimated study completion March 2019. Indication: ejection fraction 50% or higher (HFpEF) who have New York Heart Association (NYHA) class II or III symptoms despite appropriate medication. Device: the OPTIMIZER smart system.

Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not

represent NICE's view.

There were 3 of 4 specialists who were familiar with or had used this technology before.

Level of innovation

Specialist commentators indicated that this technology is innovative and novel, with no other technology providing the same function. One expert stated that it is a novel concept, extending the use of existing technologies such as pacing leads against a new target for treatment.

Potential patient impact

The OPTIMIZER system could benefit patients with heart failure who are still highly symptomatic after optimal drug treatment. Patients with a narrow QRS when cardiac resynchronisation therapy is not suitable, have a potential new treatment option alongside optimal drug treatment. As well as offering a new treatment option, the OPTIMIZER system could improve heart failure symptoms and exercise tolerance.

Potential system impact

The OPTIMIZER system could improve heart failure symptoms, which could reduce hospital admissions.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Shaumik Adhya, consultant cardiologist, did not declare any interests.
- Dr Zachary Whinnett, consultant cardiologist, implants OPTIMIZER in NHS practice.
- Dr Neil Sulke, consultant cardiologist, did not declare any interests.
- Professor G Andre Ng, professor of cardiac electrophysiology, consultant cardiologist and electrophysiologist. Lead investigator on INOVATE-HF and ANTHEM-HFrEF trials sponsored by LivaNova.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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