

## A critical review on telemonitoring in heart failure

Olivier GURNÉ<sup>1</sup>, MD, PhD; Viviane CONRAADS<sup>2</sup>, MD, PhD; Luc MISSAULT<sup>3</sup>, MD, Wilfried MULLENS<sup>4</sup>, MD, PhD; Jean-Luc VACHIERY<sup>5</sup>, MD, PhD; Walter VAN MIEGHEM<sup>4</sup>, MD, PhD, Walter DROOGNE<sup>6</sup>, MD; Anne-Catherine POULEUR<sup>1</sup>, MD, PhD; Pierre TROISFONTAINE<sup>7</sup>, MD; Sandrine HUEZ<sup>5</sup>, MD; Eric NELLESENS<sup>8</sup>, MD; Béatrice PEPPERSTRAETE<sup>9</sup>, MD; Philippe BLOUARD<sup>10</sup>, MD; Johan VANHAECKE<sup>6</sup>, MD, PhD; David RAES<sup>11</sup>, MD for the Belgian Working Group on Heart Failure

<sup>1</sup>Cliniques Universitaires St Luc, Bruxelles, Belgium; <sup>2</sup>UZ Antwerpen, Edegem, Belgium; <sup>3</sup>AZ St Jan, Brugge, Belgium; <sup>4</sup>Ziekenhuis Oost Limburg, Genk, Belgium; <sup>5</sup>Hôpital Erasme, Bruxelles, Belgium; <sup>6</sup>UZLeuven, Leuven, Belgium; <sup>7</sup>CHR Citadelle, Liège, Belgium; <sup>8</sup>CHU Sart Tilman, Liège, Belgium; <sup>9</sup>CHU Brugmann, Bruxelles, Belgium; <sup>10</sup>Clinique St Luc, Bouge, Belgium; <sup>11</sup>GZA Sint Augustinus, Wilrijk, Belgium.

**Abstract** Morbidity and mortality remain high in heart failure despite considerable progress achieved with medical therapy and electrical devices. A multidisciplinary approach is actually strongly recommended. In order to provide optimal care to the ever-growing population of patients with heart failure, telemonitoring has been proposed as a modality to improve usual care. The aim of this review is to provide an overview of the existing evidence on telemonitoring in HF. Despite two major meta-analyses with favourable results, two recent, large, multicentre, randomized controlled trials, one with a sophisticated technical remote telemonitoring approach (TIM-HF) in stable chronic HF and the other with a comprehensive telephone-based interactive voice-response monitoring (Tele-HF) in patients recently hospitalized for heart failure, have been performed and both failed to demonstrate a clinical benefit for telemonitoring. Newer technologies or other modalities, such as collaboration between a general practitioner and a heart failure clinic facilitated by telemonitoring should be further evaluated. Dedicated telemonitoring for heart failure may be a practical adjunct in selective centres and patients, on top of usual care, including education and a multidisciplinary approach. However, prior to being accepted as a standard of care, more evidence from large, randomized clinical trials is required.

**Keywords** *Telemonitoring – heart failure.*

### INTRODUCTION

The successful management of chronic heart failure (HF) remains a challenge despite considerable progress achieved with medical therapy and electrical devices. Mortality and morbidity remain high, especially after hospitalization for an acute heart failure event. Moreover, the risk of death in these patients is about 25%<sup>1,2</sup> in the year following admission to the hospital/hospitalization. Early rehospitalization is more frequent during the first month (around 20%) and further compromises prognosis<sup>2</sup>. As a consequence, the impact on the budget

of Western health-care systems is substantial, as hospitalizations account for approximately 60-70% of all direct and indirect costs generated by HF<sup>3</sup>.

A multidisciplinary approach coordinating care along the continuum of HF and throughout the chain of care delivery, mainly through direct health-care providers and patient contacts, has been largely validated<sup>4,5</sup> and incorporated in both American and European guidelines<sup>6,7</sup>. However, these management strategies have tested multi-disciplinary approaches incorporating heart failure clinics. As a consequence, it is difficult to identify the incremental benefits of each separate component or the weight of each intervention in the global strategy.

In order to provide optimal care to the ever-growing population of patients with HF, telemonitoring, using several methods, has been proposed as a modality to improve care and/or replace direct physician-patient contact. Several non-invasive telemonitoring strategies have been reported with often conflicting results in terms of symptoms or quality of life. All of these studies have been conducted using regularly scheduled

#### Address for correspondence:

Olivier Gurné, MD, PhD, Cardiologie, Cliniques Universitaires St Luc, Université Catholique de Louvain, 10 Avenue Hippocrate, B-1200 Bruxelles, Belgium. E-mail: Olivier.gurne@uclouvain.be.

Received 13 February 2012; accepted for publication 28 March 2012.

structured telephone contacts between patients and health-care providers or using more sophisticated systems such as electronic transfer of physiological data with remote access technology via external, wearable or implantable electronic devices. In addition, most trials using telemonitoring have focused on patients with systolic dysfunction, following discharge after an exacerbation of HF. This manuscript intends to provide an overview of the existing evidence on telemonitoring in HF.

## AVAILABLE EVIDENCE FROM META-ANALYSES

Two major meta-analyses have been performed in the recent years and have shown favourable results. However, the quality and the methodology of the studies included were different and many only included a small number of patients.

The meta-analysis of Klersky et al.<sup>8</sup> was published in 2009 and included 6258 patients enrolled in 20 randomized controlled trials and 2354 patients from 12 cohort studies. The authors identified 3 different approaches of care. First, a usual care (UC) approach, which referred to in-person visits with the health-care provider without additional phone calls to or from the patients. Second, a telephone monitoring approach, including regularly scheduled structured telephone contacts between patients and health-care providers. Third, a technology-assisted monitoring approach with transfer of physiological data collected via remote (i.e. at the patient's home) external monitors or via cardiovascular implantable electronic devices. However, in the analysis of the data, the latter 2 approaches were collectively considered and analysed as "remote patient monitoring". Based on the meta-analysis, remote patient monitoring was associated with a significantly lower rate of deaths ( $-17\%$ ,  $P=0.006$ ) and hospitalizations for any reasons ( $-7\%$ ,  $P=0.030$ ). The strongest protective effect of remote patient telemonitoring was found when only hospitalizations for HF were considered:  $-29\%$ ,  $P<0.001$ . The decrease in events was less pronounced in the randomized controlled trials than in the cohort studies.

The meta-analysis of Inglis et al.<sup>9</sup> published in 2010 updated the meta-analysis of Clark<sup>10</sup> published in 2007 by the same group and included only randomized controlled trials. The investigators evaluated the aforementioned three different approaches, making the distinction between UC, structured telephone support if the monitoring and/or self-care management was delivered using simple telephone technology and telemonitoring if there was transmission of physiologic and other non-invasive data using digital/broadband/satellite/wireless or Bluetooth technology. The primary meta-analysis

included 25 studies, with 16 comparisons of structured telephone support to UC (5613 patients) and 11 comparisons of telemonitoring versus UC (2710 patients). Telemonitoring was effective in reducing the risk of all-cause mortality in patients with HF by 34% ( $P<0.0001$ ). A trend was observed with structured telephone support, but the effect size was not statistically significant ( $-12\%$ ,  $P=0.08$ ). Structured telephone support was effective in reducing the risk of all-cause hospitalization in patients with HF ( $-8\%$ ,  $P=0.02$ ), as was telemonitoring ( $-9\%$ ,  $P=0.02$ ). The effect of these interventions was more pronounced with HF-related hospitalizations, showing a reduction of  $-23\%$  ( $P<0.0001$ ) with structured telephone support and  $-21\%$  ( $P=0.008$ ) with telemonitoring.

Although supporting the use of telemonitoring, these meta-analyses have several significant inherent weaknesses due to their methodology. First, the combination of studies with different design and methodology has important drawbacks, even though some were controlled and randomized. In addition, most of these studies were performed over a prolonged period of time witnessing important improvements not only in medical treatment but also in electrical devices (resynchronization therapy, implantable defibrillators). In other words, temporal changes of standard of care might have affected the results. As an example, the first study was published in 1999 when beta-blockers were not used as consistently as they are today in patients with HF. Second, the management of HF patients has markedly changed with the progressive introduction of multidisciplinary care over the past 15 years. For example, education of the patient, an important aspect of such approaches, is now part of our daily practice, is recommended by scientific societies and many patients have access to information via educative booklets or specialized websites. As early as 2002, Krumholz et al.<sup>11</sup> identified education as a key point in global management of HF, leading a 37% reduction ( $P=0.004$ ) of readmission to the hospital for HF or for cardiovascular disease. It is likely that marked intensification of more conventional methods of delivering care brings advantages that will close the gap between structured telephone support and telemonitoring in comparison to a modern UC group. Third, inclusion criteria were very different across the trials included in the meta-analyses resulting in heterogeneous groups of patients for many variables, including for example time of patients after an acute event, age or severity of underlying systolic dysfunction. This bias in selection of population is a well-known weakness of meta-analyses that adds to the different methodologies and the different follow-up duration, which vary from study to study. Even the technology used varied markedly as

well as the parameters used to monitor patients. Fourth, it is well known that including small studies can distort results of meta-analyses<sup>12</sup>. It has indeed been suggested that small trials tend to report larger treatment benefit than larger trials and negative small trials are also often not published.

Since these meta-analyses, other trials have been published conducted in a more contemporary setting and including a larger number of patients, providing more statistical power to the findings in contrast to the historical trials included in the meta-analyses. For example, one of the old studies included in both meta-analyses<sup>8-10</sup>, the DIAL trial<sup>13</sup> included 1518 stable chronic HF patients in Argentina, who were enrolled between 2000 and 2001. Only those patients randomized to the active group received an education booklet, nowadays considered as usual care. In addition, intense telephone follow-up by trained nurses was offered to this group. Not surprisingly, the intervention resulted in a 29% reduction in the number of hospitalizations. One could also conclude that only the active group received optimal comprehensive care as suggested by our actual guidelines. Of note, patients enrolled in this particular study represented 24% of the patients of the randomized control trials included in the meta-analysis of Klerski et al<sup>8</sup>. Most of the other studies included in the latter meta-analysis enrolled a few hundred of patients, at most. A second example of studies included in the meta-analyses, the TEN-HMS<sup>14</sup> enrolled 426 high-risk patients in a three-arms study: a UC group (85 patients), a telephone support (173 patients) and a home telemonitoring arm (168 patients). The study was stopped prematurely due to a large difference in mortality rates between the 2 interventional groups versus the reference UC group (the 85 patients of whom the management plan was sent to their primary care physician who was asked to implement it according to modern standards of care). Patients randomly assigned to receive UC had a one-year mortality of 45%, significantly higher ( $P=0.032$ ) than those assigned to receive telephone support (27%) or home telemonitoring (29%). These data were included in the meta-analyses mentioned above<sup>8-10</sup> in favour of telephone support and telemonitoring. Nevertheless, there was no difference concerning the primary outcome of the TEN-HMS study, i.e. days lost because of death or hospitalization in acute medical/surgical beds for any reason between the 2 active arms.

Therefore, meta-analyses must be seen as hypothesis-generating, to be confirmed in well-conducted large randomized clinical trials with an appropriate design including a sensible protocol, well-predefined statistics, an adequate sample size and a long enough period of observation.

## CONTEMPORARY RANDOMIZED CLINICAL TRIALS

Since these meta-analyses, two large randomized trials have been performed recently, the Tele-HF<sup>15</sup> and the TIM-HF<sup>16</sup> trials.

The Tele-HF trial<sup>15</sup> included 1653 patients in 33 cardiology practices across the United States who had recently been hospitalized for HF. Patients were randomized to either telemonitoring (telephone-based interactive voice-response system) or UC. Clinicians were instructed to treat their patients in accordance with national guidelines and all patients received educational materials, even in the UC. The telemonitoring group was instructed to make daily calls to the system, with a series of questions about weight, general health and heart-failure symptoms. The primary end point (readmission for any reason or death from any cause within 180 days after enrollment) was not statistically different between the two groups: it occurred in 52.3% of the telemonitoring group and in 51.5% of the UC group. The system was free of charge for patients and considerable resources, which would be difficult to leverage outside a clinical trial, were dedicated to optimizing patient's engagement with the system. Nevertheless, 14% of the patients who were randomly assigned to undergo telemonitoring never used the system and only 55% of the patients were still using the system at least three times a week at the end of follow-up. This should be compared to small single-centre studies where a highly skilled and motivated nurse could achieve a higher compliance and better results and perhaps influence results of a meta-analysis when pulled together with others studies with the same design.

In contrast to Tele-HF, the TIM-HF trial<sup>16</sup> included 710 patients with stable chronic HF with systolic dysfunction and a history of decompensated HF within the 2 previous years (or a left ventricular ejection fraction  $\leq 25\%$ ). Patients were randomized between UC and remote telemedical management, based on a wireless Bluetooth device. Portable devices for ECG, blood pressure and body weight measurements, connected to a PDG device (personal digital assistant), sent automated encrypted transmission via cell phones to 2 telemedical centres which provided physician-led medical support 24 hours per day, 7 days per week. Median follow-up was longer in that study: 26 months compared to 6 months in Tele-HF. Of the 354 patients randomly assigned to receive telemonitoring, 81% were at least 70% compliant with the daily transfer of data to the telemedicine centres and had no break in information transfer for  $>30$  days. Despite this highly sophisticated system, remote telemedical management had no significant effect ( $-3\%$ ,  $P=0.87$ ) on all-cause mortality, the

primary end point, cardio-vascular death or HF hospitalization ( $-11\%$ ,  $P=0.44$ ), the first secondary end point. It should also be emphasized that medical treatment was quite optimal in this study performed in chronic stable patients, since 95% were on ACE-inhibitors or angiotensin receptor blockers, 92% on beta blockers and 64% on aldosterone antagonists. State of the art treatment may reduce the additional effect of telemonitoring and thus could reduce the likelihood of finding a positive effect in an optimally treated population. On the other hand, patients in Tele-HF recruited after a shorter time interval following an acute event, had a lower rate of guideline-mandated medications and a higher event rate, but again and in contrast to the findings of the meta-analyses, no significant effect was found. Comparable findings were seen in a smaller recent study performed in the United Kingdom, the Home-HF study<sup>17</sup>, which randomized 182 elderly patients comparing UC (but with one initial home visit by the study nurse) and telemonitoring. Primary outcome, days alive and out of hospital were similar in both groups.

Thus, these two recent, large, multicentre, randomized controlled trials, one comparing UC with a sophisticated technical remote telemonitoring approach (TIM-HF) in stable chronic HF in Germany<sup>16</sup> and the other comparing UC with a comprehensive telephone-based interactive voice-response monitoring (Tele-HF) in patients recently hospitalized for HF in United States<sup>15</sup> both failed to demonstrate a clinical benefit for telemonitoring. Despite potential criticism on these trials regarding patient selection (chronic versus recently hospitalized HF, elderly or younger patients, severe systolic dysfunction or moderate systolic dysfunction and even HF with preserved left ventricular systolic function), or regarding the parameters analysed in these studies or the modes of monitoring system used, either telephone based or true remote monitoring, it should be stressed that these 2 largest studies performed to date fail to demonstrate that this tool confers any improvement for the patient.

## NEWER MONITORING STRATEGIES

Newer telemonitoring strategies have been tested recently, based on implanted haemodynamic sensors. In the COMPASS-HF trial<sup>18</sup>, information was obtained from an implantable continuous haemodynamic monitor: briefly, the system resembles a single-lead pacemaker and the transvenous lead, positioned in the right ventricular outflow tract, has a sensor incorporated near its tip that allows to measure intracardiac pressure. Patients recently hospitalized with HF and in NYHA class III or IV were randomized to UC versus treatment,

guided by the haemodynamic information provided by the sensor. In this rather small trial (274 patients), such a sophisticated system led to a non-significant 21% lower rate of HF-related events.

In the recently presented CHAMPION trial<sup>19</sup> a haemodynamic sensor was implanted in the distal pulmonary artery. In this randomized controlled single-blind trial, 550 patients in NYHA class III HF were randomized between UC and treatment guided by the haemodynamic information from the sensor. The primary end point, HF hospitalizations at 6 months, was significantly decreased by 30% ( $P < 0.001$ ). Hospitalizations for HF at all days (mean follow-up of 15 months) was reduced by 38% ( $P < 0.0001$ ). Differences in patient selection with patients of the CHAMPION trial being less sick and being treated by heart failure physicians who mainly increased vasodilator therapy more in patients followed by the haemodynamic sensor, probably account for the positive result of the CHAMPION versus COMPASS-HF trial. Thus, even if the trial was positive, it is difficult due to the trial's design to distinguish any treatment effect from the monitor itself from the overall excellent care patients with the monitor received.

In the SENSE-HF trial<sup>20</sup>, the sensitivity and positive predictive value of implantable intrathoracic impedance monitoring to predict HF hospitalizations was studied prospectively in 501 patients. Subclinical fluid accumulation in the lungs over time is considered to precede episodes of overt decompensation. Accumulation of intrathoracic fluid decreases the impedance to electrical current passed across the lung. This impedance can be measured in a patient between a right ventricular lead and a device box (pacemaker or implantable defibrillators using the dedicated OptiVol<sup>®</sup> system). This could potentially be more sensitive than just monitoring body weight. In that study, this system had a low sensitivity and a low predictive value in the early period after implantation but the results markedly improved within the first 6 months. The advantage of this monitoring system, despite being invasive with the use of a pacemaker or an implantable defibrillator, is that it allows integration with other parameters that can be recorded by implantable electrical devices, such as heart rate variability, atrial fibrillation burden and patient activity, which could be more sensitive to predict HF worsening.

A less invasive monitoring system is currently evaluated in the MUSIC trial<sup>21</sup> where an adhesive device applied to the chest wall is able to record multiple physiological signals (ECG, heart rate variability, activity, posture, respiration rate, thoracic impedance, body temperature). However, so far no prospective results in HF are available for this device.

## DISCUSSION

This review underscores the need for a strict evaluation of telemonitoring as a disease-management system before its widespread adoption. Furthermore, the medical community should rigorously define which systems could be useful in specific patients groups and subsequently validate new technologies in well-designed large-scale trials. Regional differences in the way health-care systems are organized may affect the possible benefit of telemonitoring.

The cost-benefit ratio is an important issue since there is an incremental cost of using telemonitoring. However, this issue will be very difficult to appreciate due to the complexity of HF management and the diversity of health-care systems in different countries. Budgetary restrictions in health care may obstruct its application. Ethical considerations must also be discussed before adopting this disease-management strategy. Industry lobbying and political issues could also interfere with the decision-making process. Finally, it would be particularly unethical and even harmful if patients, physicians or other health-care providers would view telemonitoring as an alternative to multidisciplinary usual care, given the existing evidence for the latter.

Home telemonitoring enables patients to be actively involved in monitoring and managing their condition, shifting the focus of control towards the patients in their home. The heart of medical practice is the relationship between a care provider (physician, well-trained nurse, etc.) and a patient in the focus<sup>22,23</sup>. New technologies should be viewed as potentially useful adjuncts in selective subgroups and using specific parameters to be defined in good randomized controlled studies. They should not be the centre piece of redesigned health-care systems on top of UC. Technology should come second and the patient-centered relationship between patient and provider comes first.

In that view, data from a small recent randomized trial, TEMA-HF 1<sup>24</sup>, could be of interest. In that study, 160 patients following hospitalization for HF were randomized to UC or telemonitoring, with daily transmission of body weight, blood pressure and heart rate. All patients received a standard education course before discharge by a heart failure nurse. E-mail alerts were

sent to the general practitioner and heart failure clinic to intervene when pre-defined limits were exceeded. Per protocol, the general practitioner was asked to contact the patient and to adapt treatment if needed. The heart failure nurse contacted the patient by telephone within 1 to 3 days after the alert to verify whether the intervention was effective. A significant reduction in mortality was observed but only a trend in reduction in hospitalization for heart failure was seen. Thus, while confirmation of this kind of approach in larger trials is required as the study had multiple methodological limitations, this study shows that an intense collaboration between a general practitioner and a heart failure clinic can be facilitated by telemonitoring and this might lead to a clinical benefit in patients who first receive an education programme.

## CONCLUSION

Heart failure is a complex disorder for which integrated management is mandatory. A multidisciplinary approach, including education of the patients, has been proven to improve outcome to such extent that it is now fully included in the most recent guidelines of scientific societies, receiving the highest grade of recommendation based on the highest level of evidence<sup>6,7</sup>. This must be a priority before implementing any kind of telemonitoring.

Dedicated telemonitoring for heart failure may be a practical adjunct in selective centres and patients on top of usual care. However, it should never replace it as a standard of care because scientific evidence remains conflicting, insufficient and heterogeneous. A huge financial investment has already been made to finance clinical application of telemonitoring across the world. However, prior to being accepted as standard of care, which also means that some kind of reimbursement by health-care providers would be implemented, more evidence from large randomized clinical trials is required, especially concerning cost-efficacy analysis<sup>25</sup>, before even considering spending money on a promising tool that is still awaiting a clear demonstration of its benefit.

**CONFLICT OF INTEREST:** none declared.

## REFERENCES

1. Cleland JG, Swedberg K, Follath F, Komajda M, Cohen-Solal A, Aguilar JC, Dietz R, Gavazzi A, Hobbs R, Korewickij J, Madeira HC, Moiseyev VS, Preda I, van Gilst WH, Widimsky J, for the Study Group on Diagnosis of the Working Group on Heart Failure of the European Society of Cardiology, Freemantle N, Eastaugh J, Mason J. The EuroHeart Failure survey programme - a survey on the quality of care among patients with heart failure in Europe Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003; **24**: 442-63.
2. Harjola VP, Follath F, Niemen MS, Brutsaert D, Dikstein K, Drexler H, Hochadel M, Komajda M, Lopez-Sendon JL, Ponikowski P,

- Tavazzi L. Characteristics, outcomes and predictors of mortality at 3 months and 1 year in patients hospitalized for acute heart failure. *Eur J Heart Failure* 2010; **12**: 239-48.
3. Lee WC, Chavez YE, Baker T, Luce BR. Economic burden of heart failure: a summary of recent literature. *Heart Lung* 2004; **33**: 362-71.
  4. McAlister F, Stewart S, Ferrua S. Multidisciplinary strategies for the management of heart failure patients at high risk for admission. A systematic review of randomized trials. *J Am Coll Cardiol* 2004; **44**: 810-9.
  5. Göhler A, Januzzi JL, Worrell SS, Osterziel KJ, Gazelle GS, Dietz R, Siebert U. A systematic meta-analysis of the efficacy and heterogeneity of disease management programs in congestive heart failure. *J Cardiac Fail* 2006; **12**: 554-67.
  6. Hunt SA, Abraham WT, Chin MH, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American College of Chest Physicians; International Society for Heart and Lung Transplantation; Heart Rhythm Society. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *Circulation* 2005; **112**: e154-235. of heart failure). *Circulation* 2005; **20**: e154-e235.
  7. Dikstein K, Cohen-Solal A, Filipatos G, McMurray JGG, Ponikowski P, Poole-Wilson PA, Strömberg A, van Veldhuisen DJ, AQtar D, Hoes SW, Keren A, Mebazaa A, Nieminen M, Priori SG, Swedberg K; ESC Committee for Practice Guidelines (CPG). ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur Heart J* 2008; **29**: 2388-442.
  8. Klerski C, De Silvestri A, Gabutti G, Regoli F, Auricchio A. A meta-analysis of remote monitoring of heart failure patients. *J Am Coll Cardiol* 2009; **54**: 1683-94.
  9. Inglis SC, Clark RA, McAlister FA, Ball J, Lewinter C, Cullington D, Stewart S, Cleland JG. Structured telephone support of telemonitoring programmes for patients with chronic heart failure. *Cochrane Database Syst Rev*. 2010; **8**: CD007228.
  10. Clark RA, Inglis SC, McAlister FA, Cleland JG, Stewart S. Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and metaanalysis. *BMJ* 2007; **334**: 942-51.
  11. Krumholz HM, Amatruda J, Smith GL, Mattern JA, Roumanis SA, Radford MJ, Crombie P, Vaccarino V. Randomized trial of an education and support intervention to prevent readmission of patients with heart failure. *J Am Coll Cardiol* 2002; **39**: 83-9.
  12. Nüesch E, Trelle S, Reichenbach S, Rutjes AWS, Tschannen B, Altman DG, Egger M, Jüni P. Small study effects in meta-analyses of osteoarthritis trials: meta-epidemiological study. *BMJ* 2010; **341**: c3515-23.
  13. GESICA investigators. Randomised trial of telephone intervention in chronic heart failure: DIAL trial. *BMJ* 2005; **331**: 425-9.
  14. Cleland JG, Louis AA, Rigby AS, Janssens U, Balk HM; TEN-HMS Investigators. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death: the Trans-European Network-Home-Care Management System (TEN-HMS) Study. *J Am Coll Cardiol* 2005; **45**: 1654-64.
  15. Chaudhry SI, Mattern JA, Curtiss JP, Spertus JA, Herrin J, Lin Z, Phillips JA, Hodshon BV, Cooper LS, Krumholz HM. Telemonitoring in patients with heart failure. *NEJM* 2010; **363**: 2301-9.
  16. Koehler F, Winkler S, Schieber M, Sechtem U, Stangl K, Böhm M, Boll H, Baumann G, Honold M, Koehler K, Gelbrich G, Kirwan BA, Anker SD; Telemedical Interventional Monitoring in Heart Failure Investigators. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the telemedical interventional monitoring in heart failure study. *Circulation* 2011; **123**: 1873-80.
  17. Dar O, Riley J, Chapman C, Dubrey SW, Morris S, Rosen SD, Roughton M, Cowie MR. A randomized trial of home telemonitoring in a typical elderly heart failure population in North West London: results of the Home-HF study. *Eur J Heart Fail* 2009; **11**: 319-25.
  18. Bourge RC, Abraham WT, Adamson PB, Aaron MF, Aranda JM Jr, Magalski A, Zile MR, Smith AL, Smart FW, O'Shaughnessy MA, Jessup ML, Sparks B, Naftel DL, Stevenson LW; COMPASS-HF Study Group. Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure: the COMPASS-HF study. *J Am Coll Cardiol* 2008; **51**: 1073-9.
  19. Abraham WT, Adamson PB, Bourge RC, Aaron MF, Costanzo MR, Stevenson LW, Strickland W, Neelaguru S, Raval N, Krueger S, Weiner S, Shavelle D, Jeffries B, Yadav JS; CHAMPION Trial Study Group. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. *Lancet* 2011; **377**: 658-66.
  20. Conraads VM, Tavazzi L, Santini M, Oliva F, Gerritse B, Yu CM, Cowie M. Sensitivity and positive predictive value of implantable intrathoracic impedance monitoring as a predictor of heart failure hospitalizations: the SENSE-HF trial. *Eur Heart J* 2011; **32**: 2266-73.
  21. Anand IS, Greenberg BH, Fogoros RN, Libbus I, Katra RP; MUSIC investigators. Design of the Multi-Sensor Monitoring in Congestive Heart Failure (MUSIC) study: prospective trial to assess the utility of continuous wireless physiologic monitoring in heart failure. *J Cardiac Fail* 2011; **17**: 11-6.
  22. Havranek EP. Improving the outcomes of heart failure care. Putting technology second. *J Am Coll Cardiol* 2005; **45**: 1665-6.
  23. Desai AS, LW Stevenson. Connecting the circle from home to heart-failure disease management. *NEJM* 2010; **363**: 2364-7.
  24. Dendale P, De Keulenaer G, Troisfontaines P, Weytjens C, Mullens W, Elegeerts I, Ector B, Houbrechts M, Willekens K, Hansen D. Effect of a telemonitoring-facilitated collaboration between general practitioner and heart failure clinic on mortality and rehospitalization rates in severe heart failure: the TEMA-HF 1 (TElemonitoring in the MAnagement of Heart Failure) study. *Eur J Heart Fail* 2012; **14**: 333-40.
  25. Seto E. Cost comparison between telemonitoring and usual care of heart failure: a systematic review. *Telemed J E Health* 2008; **14**: 679-86.