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Implementation of a full-scale prehospital telemedicine system: evaluation of the process and systemic effects in a pre–post intervention study

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ABSTRACT

Objectives To review the implementation strategy from a research project towards routine care of a comprehensive mobile physician-staffed prehospital telemedicine system. The objective is to evaluate the implementation process and systemic influences on emergency medical service (EMS) resource utilisation.

Design Retrospective pre–post implementation study.

Setting Two interdisciplinary projects and the EMS of a German urban region.

Interventions Implementation of a full-scale prehospital telemedicine system.

Endpoints Descriptive evaluation of the implementation strategy. Primary endpoint: ground-based and helicopter-based physician staffed emergency missions before and after implementation.

Results The first research project revealed positive effects on guideline adherence and patient safety in two simulation studies, with feasibility demonstrated in a clinical study. After technical optimisation, safety and positive effects were demonstrated in a multicentre trial. Routine care in the city of Aachen, Germany was conducted stepwise from April 2014 to March 2015, including modified dispatch criteria. Systemic parameters of all EMS assignments between pre-implementation (April 2013 to March 2014) and post implementation (April 2015 to March 2016): on-scene EMS physician operations decreased from 7882/25 187 missions (31.3%) to 6360/26 462 (24.0%), $p<0.0001$. The need for neighbouring physician-staffed units dropped from 234/25 187 (0.93%) to 119/26 462 (0.45%), $p<0.0001$, and the need for helicopter EMS from 198/25 187 (0.79%) to 100/26 462 (0.38%), $p<0.0001$. In the post implementation period 2347 telemedical interventions were conducted, with 26 462 emergency missions (8.87%).

Conclusion A stepwise implementation strategy allowed transfer from the project phase to routine care. We detected a reduced need for conventional on-scene physician care by ground-based and helicopter-based EMS, but cannot exclude unrecognised confounders, including modified dispatch criteria and possible learning effects. This creates the potential for increased availability of EMS physicians for life-threatening emergencies by shifting physician interventions from conventional to telemedical care.

Trial registration number NCT04127565.

Strengths and limitations of the study

- The strength of the study is the description of different methods of implementation in a prehospital telemedicine system, with the transfer from project phase to routine care.
- We used real-life data from an emergency medical service (EMS) dispatch centre to evaluate the effect on EMS resource utilisation by implementation of a telemedical support system.
- This is the first study to examine effects the aforementioned implementation in an urban region.
- The limitation is that other influencing factors, such as adapted dispatch criteria, may have also influenced the results, which could not be calculated.
- Influences on patient outcomes could not be evaluated, another limitation of our findings.

INTRODUCTION

Emergency medical services (EMSs) face increasing emergency missions. Besides possible negative effects on patient outcome due to prolonged response intervals, there are economic consequences due to increased use and provision of resources.[1 2] As such, modern concepts must ensure a high quality of care without a steep increase in costs. Telehealthcare interventions have been spreading for acute and chronic medical conditions.[3–5] Despite rapidly increasing technological capabilities, barriers that restrict implementation still remain, which include legal, political and social issues.[6] There are barriers that must be justified by the behaviour of both medical staff and patients.[7] It is also well-known that in ST segment elevation myocardial infarction (STEMI) telemedical transmission of the 12-lead-ECG and consultation of a cardiologist lead to reduced intervals of myocardial reperfusion.[8 9] By using the telemedical procedure, in-hospital mortality in patients with STEMI can be reduced.[10] However, widespread use is lacking. Besides acute coronary syndromes, telemedical interventions in the prehospital phase and scientific data are rare, so that many projects are not transferred into routine care after cessation of project financing.[11 12] In acute stroke, studies have shown the feasibility of video transmission from the ambulance, but this technique has not been rolled out on a grand scale, while inter-hospital teleconsultation in acute stroke is implemented in more hospital systems and could be considered routine.[13–16] Overall, only a few EMS agencies use telemedical techniques.[12] In Germany, delegation of medications (eg, opioids) from physicians to ambulance personnel is regulated very strictly compared with other countries like Denmark.[17 18] To enable delegation of medications without physical presence of a physician on-scene, the responsible physician has to have a complete overview about the patient by German law, which can probably only achieved be telemedical virtual presence.

Against this background, we conducted two interdisciplinary research projects to develop and evaluate a comprehensive mobile teleconsultation system that supports on-scene paramedics from a remote site: this is with experienced physicians in all kinds of emergency medical situations. After technical and organisational development, and scientific evaluation, this system was implemented stepwise into routine care, financed by health insurance. In Germany, the EMS is generally financed by statutory health insurances and private health insurances after negotiation of needs and budget. The aim of the study was to evaluate the implementation strategy from the initial project idea to routine care, within a unique, physician-staffed telemedicine system. To evaluate systemic effects of this new concept in emergency care, the influence of implementation on EMS resources should be evaluated.

METHODS

Implementation strategy

The implementation process from the project idea (2006/2007) to routine care (2014–2016) was carefully dissected into all relevant steps and milestones. These steps were analysed descriptively with the respective rationale to be able to use the main results.

Organisational setup

In the city of Aachen, Germany (255 967 residents; December 2017), the EMS service is an integral part of the responsibilities of the fire department. Up to 11 emergency ambulances are run by the fire brigade and three EMS agencies. All emergency ambulances are staffed with 2-year trained paramedics. Two ground-based EMS physician units are run on a 24/7 basis to assist the ambulances if advanced life-support procedures (eg, rapid sequence induction) are necessary. All physicians are certified EMS physicians with at least 3 years of training in anaesthesia and critical care, as well as a certificate in advanced life support and prehospital trauma life support. If non-availability is due to duplicated events, physician-staffed units from adjacent districts or helicopter EMSs will be used as backup. All paramedics are trained on the telemedicine system, based on trained and published standard operating procedures.

Study design and evaluation of systemic effects

After two interdisciplinary research projects, transfer of telemedical procedures to routine care was considered possible.[19 20] To evaluate systemic influences of implementation into routine care, we compared EMS data of the 1-year pre-implementation period (April 2013–March 2014) with a similar interval after full implementation (April 2015–March 2016) in a pre–post intervention study: to assess EMS resource utilisation, the number of emergency missions carried out by on-scene EMS physicians was compared with the two periods as the primary outcome. The cumulative number of on-scene and telemedical interventions by physicians was analysed as a secondary outcome. Non-availability of EMS physicians due to overlapping emergency calls was analysed by the number of emergency missions by EMS physician units from adjacent EMS districts, including helicopter EMS. All EMS missions in the city of Aachen were included.

With full implementation, dispatch criteria were supported with an electronic list of symptoms and possible diagnoses (n=213 scenarios). In the pre-implementation period, it was at the discretion of the dispatcher to send an EMS physician unit whenever a situation was judged to be potentially life-threatening. Following implementation, 24/7 telemedical support was available, allowing structured adjustments of dispatch criteria by the EMS medical director. These emergency scenarios were not dispatched with an on-scene EMS physician as a general rule: acute stroke with the patient awake, painful conditions with the patient awake, mild dyspnoea, hypertensive urgency and terminated seizure. In the pre-implementation period, these conditions were dispatched with an on-scene EMS physician, although no electronic support was available.

Interaction of tele-EMS-physician and ambulance personnel

The paramedics on-scene—or in special situations the EMS-physician on-scene—decided if telemedical support was necessary based on standard operating procedures and based on personal assessment. After initiation of the call by the personnel on-scene they described the situation and they addressed questions to the tele-EMS physician in the telemedical centre. Automatically, all real-time vital parameters (numerical values and curves), all 12-lead ECGs and all still pictures taken with a smartphone were transmitted to the telemedicine centre from the start of the teleconsultation. After verbal consent of the ambulance personnel and the patient, the tele-EMS physician was able to start a real-time video transmission from a camera embedded into the ceiling of the ambulance. Short and direct communication rules should be used to allow structured and clear messages. Delegated medications had to be communicated clearly with substance name and dosage from the tele-EMS physician to the paramedics and they had to repeat substance name and dosage. After administration of the medication, they had to confirm it. Termination of the teleconsultation was decided jointly.

Legal framework

Delegation of medical procedures and medications to paramedics is regulated strictly in Germany. The responsible physician has to have a complete overview about the medical status of the patient. Therefore, trans-telephonic communication alone—which is routine in other countries like Denmark—is not sufficient if a broad spectrum of delegated medications should be achieved.[17 18] By using a multifunctional telemedical system which allows nearly a virtual presence via a functionalities like real-time video transmission, this legal barriers can be overcome.

Characteristics of telemedically supported emergencies in routine care

Data of telemedically-supported emergency missions were analysed descriptively in the post implementation period: type of emergency mission (emergency mission vs inter-hospital transfer), given delegated medications and medical severity. In a documented outcome, we reviewed the case to determine if a fatal outcome was a function of a telemedical intervention.

Data sources

We analysed the database of electronically documented telemedical interventions (Telemedical Documentation, P3 Telehealthcare, Aachen, Germany) and the database of the regional EMS dispatch centre (COBRA4, ISE, Aachen, Germany). Number of calls and telemedical supports, as well as conducted procedures, could be best evaluated this way. Patient data could not be connected between these systems.

Patient and Public Involvement

Patients were not involved in the design or implementation of this project. The public was informed by local media (newspaper, radio and local television), but had no influence on the project and study design.

Study registration

All cases were pseudonymised to ensure data privacy. Systemic data of the EMS dispatch centre contained no personal data, so there was no need for pseudonymisation. Study registration was done retrospectively at clinicaltrials.gov.

Statistical methods

Categorical data are presented as frequencies and percentages. Systemic parameters were compared with contingency tables, using the χ^2 test with Yate's correction. All statistical analyses were performed using GraphPad Prism V.7.0 (GraphPad Software, La Jolla, California, USA). Due to the exploratory nature of the study, p values <0.05 were considered significant.

RESULTS

Implementation process

The process of final implementation can be divided into three main phases: two research projects, followed by integration into health insurance-financed routine emergency care, standard for all conventional EMS services in Germany. We ensured that telemedical care was also financed this way. Table 1 outlines this process, including summarised research findings.[19–24] Local and national political stakeholders, health insurance companies and EMS providers at different levels (paramedics to EMS directors/stakeholders) were integrated from the first interdisciplinary workshop.[19] Iterative development with integration of end-users allowed for design and development, and continuous adaption of the technical system, including the organisational model. In the first research project, a mobile telemedicine system with multiple applications was first developed. General clinical and technical feasibility of prehospital teleconsultation and positive effects on stroke specific information transfer were shown.[14 25] Although the second project did not allow for a randomised controlled trial (RCT) due to practical, political and ethical concerns, the results of this prospective observational multicentre trial convinced political stakeholders and health insurances to transfer this concept to routine care in a model region (Aachen, Germany).[20 24 26] With routine care implementation, milestones of interim analyses and workshops were defined between the fire department, the related university (RWTH Aachen University, Germany) and the health insurances. Periodic quality reporting including review of data and screening for major events enabled data and patient safety monitoring, and continuous information by decision-makers and financiers. Clinical data for case review were extracted out of the electronic documentation system, technical performance was monitored using questionnaires about the technical performance based on the user's perspective.[27]

Technical development and capabilities in routine care

During the first project, the transmission unit was integrated into a backpack (2009), with a weight of 18 kg (self-development of research partners), while general technical development enabled miniaturisation and integration of a smartphone for system monitoring and photo transmission in the second project. Within 5 years, a stepwise professionalisation and miniaturisation saw a total weight of 1.7 kg and made the system viable for routine emergency medical care. Technical performance improved over time to a sufficient standard.[25 27] In routine care, the following technical capabilities evolved with a project related spin-off company (P3 Telehealthcare): two-way audio connection, real-time vital data transmission (numerical values and waveforms), 12-lead-ECG and still-picture transmission on-demand, as well as video streaming from in the ambulance. The connection between ambulances and the teleconsultation centre was accomplished by mobile transmission units (peeq-Box, P3

Table 1 Implementation strategy in steps and milestones

Phase	Process steps	Summary	References
Research Project (Med-on-aix) 2007–2010	1. Stakeholder workshops	Discussion and definition of requirements und expectations as well as misgivings; integration of data privacy experts	19
	2. Technical Design and development	Development of specification booklet by medical users; integration of users into all steps of technical development	19
	3. Mockup tests	Technical field tests with a precursor system	
	4. Legal opinion by expert	Legal opinion about the specific legal questions of mobile telemedical care and delegation of medical procedures to paramedics	
	5. Simulation study I	Improved guideline adherence in STEMI and major trauma in full-scale simulation	21
	6. Simulation study II (RCT)	Comparable quality of care between telemedically supported paramedics and on-scene physician teams.	22
	7. Development of economic models	Workshop-based with integration of politics, health insurances, technical partners and medical users.	
	8. Clinical feasibility study, prospective observational study	General feasibility was shown; video transmission in stroke and improvement of data transfer into the hospital were demonstrated.	14 25
	9. User survey	Interviews and questionnaire-survey of users. Future potential is seen but technical performance and usability were criticised.	28
Research project (TemRas) 2010–2013	10. Technical adaption	Iterative development cycles with integration of medical users. Miniaturisation of the technical system.	
	11. Technical field testing	Field testing by technicians and by emergency care providers.	29
	12. Development and execution of a training concept for providers	Parallel training concept for paramedics and future tele-EMS-physicians.	23
	13. Prospective multi-centre trial in 5 EMS districts over 1 year	Safety, feasibility and evaluation of quality of care in 425 telemedical emergency missions	20 24 26
	14. Integration of health insurances and discussion of results and economic potential	Discussion of the scientific results and portability into a routine care setting. Model calculation of costs and savings potential.	
Integration into routine emergency care 2014–2015	15. Agreement with health insurances about seed funding	Seed funding of a first real-life phase, limited depending on interim results.	
	16. Technical adaption	Technical adaption and further miniaturisation, integration of state-of-the-art monitor-defibrillator.	
	17. Integration and stepwise implementation into routine care (April 2014–March 2015)	Start with three equipped ambulances and 12.75 hour daytime service; 24-hour coverage after 3 months and stepwise integration of 11 ambulances within 1 year. Implementation of telemedical contents into the yearly training concept for paramedics. Evaluation of technical performance by end-users and assessment of quality of care. Scientific evaluation of guideline adherence.	27 31–33
	18. Discussion of interim results with politics, German health secretary and health insurances	Quarterly performance and quality reports. Discussion of interim results with health insurances, stakeholders and politics after 6 months in a workshop.	
	19. Full implementation since April 2015	Provision of 24/7 coverage, all ambulances technically equipped. Quarterly quality reports and real-time supervision of tele-EMS physicians. Scientific evaluation of guideline adherence.	31

EMS, emergency medical service; RCT, randomised controlled trial; STEMI, ST segment elevation myocardial infarction.

Table 2 Characteristics of telemedically supported missions after full implementation

Characteristics	Number (fraction)
Telemedically supported emergency missions	2347
Solely telemedically supported, without additional on-scene physician	2145/2347 (91.4%)
Telemedically supported cases with delegation of medication	1541/2347 (65.66%)
Cases with opioid delegation	497/2347 (21.18%)
Delegated single medications	4419 drug administrations in 1541 missions
M-NACA score of telemedically supported missions: n=2262/2347 missions scored (96.4%)	
M-NACA II—no hospital admission necessary	165
M-NACA III—transport to hospital required	1298
M-NACA IV—possible vital danger	613
M-NACA V—acute vital danger	180
M-NACA VI—successful cardiopulmonary resuscitation	1
M-NACA VII—death at scene	5
Telemedically supported inter-hospital transfers	315

M-NACA, modified National Advisory Committee of Aeronautics severity score.[37]

Telehealthcare) hooked to the monitor-defibrillator unit (C³, GS Stemple Elektromedizinische Geräte, Kaufering, Germany). In the ambulance, the transmission unit was connected to a wireless local network by a conventional in-car computer. Parallel, encrypted audio and data transmission from the emergency site, including en-route, were facilitated. In the teleconsultation centre, a physician responsible for telemedical consults was available. Context-sensitive documentation software provided checklists and algorithms of current international guidelines, and a technical display of all transmitted data (Telemedical Documentation, P3 Telehealthcare).

Systemic effects of telemedical support in routine care

Before the implementation of telemedical real-time support, 25 187 EMS assignments with emergency ambulances were conducted (April 2013–March 2014). Of these, 7882 (31.3%) were supported by an conventional on-scene EMS physician. After 1287 telemedical-supported missions during the first-year training and implementation phase (April 2014–March 2015), the system was fully implemented, enabling 24/7 availability. The total number of emergency ambulance missions increased to 26 462 after this (April 2015–March 2016). Of these, 2347 (8.87%) were supported telemedically, while their characteristics are summarised in table 2. The only National Advisory Committee of Aeronautics severity score (NACA) VI assignment was a consultation between the on-scene EMS physician and the physician at the telemedical centre for support, during a successful resuscitation of a 13-year-old child with known cardiac disease. In two of the NACA VII missions, the paramedics contacted the tele-EMS physician for termination of resuscitation due to latency and patient age, while the EMS-physician unit was en-route. In three other NACA VII cases, the EMS physician on-scene contacted the telemedical centre for organisational issues after the patient was pronounced dead. There were no other telemedically-supported missions in which the patient suffered cardiac arrest. Those supported by on-scene EMS physicians decreased from 7882 (31.3%, pre-intervention) to 6360 (24%, post intervention) for all cases, p<0.0001. The rate of ground-based EMS staffed units from neighbouring districts were used due to a shortage of resources, dropping from 234/25 187 (0.93%) to 119/26 462 (0.45%), p<0.0001. A helicopter-based EMS physician was summoned in 198 of the 25 187 (0.79%) cases pre-intervention, which decreased to 100 of 26 462 (0.38%) after implementation (p<0.0001). The total number of physician-guided prehospital interventions increased from 7882/25 187 (31.3% were only conventional on-scene care) to 8707/26 462 (32.9%, telemedical and conventional on-scene care) in the 1-year post implementation phase (p<0.0001).

DISCUSSION

Stepwise implementation with the integration of different end-users, politics, stakeholders and health insurers allowed for successful transfer from the research project phase to routine care in an urban model region. After implementation, utilisation of conventional on-scene care by EMS-physicians decreased significantly, but with the implementation of a telemedicine system, the dispatch criteria were modified und restructured, with the intention of reducing primary EMS physician unit alarms.

Although comprehensive scientific results were not available for discussion about continuation, continuous involvement of decision-makers and models for economic effects fostered commitment from financiers. Periodic quality reporting and further observational scientific evaluation in routine care enabled stable integration and expansion. While this continuous information strategy and the integration of decision-making barriers to implementation were overcome, an RCT was judged not to be possible by researchers during the described process. There was the unanimous opinion that an RCT would have created too many barriers within the framework of projects, which could have endangered the concept. Further, in the discussion with the ethics committee, an RCT was viewed critically due to the novelty of the system. However, these were more political than scientific reasons, but continuation of the project should not be endangered. For end-users, a satisfactory technical performance and usability were identified as key elements for implementation during user interviews and questionnaires.[28] Only in the course of the three phases we were able to meet user requirements.[25 27 29] While integrating new telemedical procedures, including expanded skills of paramedics, the users' perspectives differed noticeably between paramedics and physicians. In a Scottish project of mobile tele-ultrasound on-board ambulances, physicians feared distraction in key roles and assessed this as too difficult for paramedics; in contrast, paramedics felt valued, and assessed this new task as their role in prehospital care.[30] Although no relevant data were available, we reported similar concerns by physicians, although most paramedics felt valued with the new tasks. During routine care, positive effects on quality of care, as well as guideline adherence, were shown for acute coronary syndromes, pain reduction in trauma and non-trauma emergencies, and blood pressure management in hypertensive emergencies.[31–33] However, the process from research to implementation lasted one decade (table 1). This demonstrates that political decision-makers are not convinced with scientific results alone but require ideas and models that allow future economic potential. General technical and social development for mobile technologies accelerated the process in the last few years. The system's operation over the 1-year post implementation period would not be called economical, as the physician at the telemedical centre was not fully occupied. System operation was possible due to health insurance financing for a pilot region. With further expansion and integration of more EMS districts, the operation could be run economically. During all discussions with decision-makers, our aim was to expand the system after implementation in one model region. In other countries like Denmark, a 'telephone-only' consultation with an EMS-physician in charge is typical, but in Germany this would not have been permitted; this was due to delegation of measures and medications to the paramedics, as based on legal concerns.[17] The transmission of vital-data, ECG, still pictures and video from the ambulance allowed for a more detailed remote assessment compared with telephone consultation alone.

The frequency of telemedical interventions increased from the integration phase to the routine phase. In more than half of the telemedically-supported rescue missions, medications (including opioids) were delegated by the tele-EMS-physician to the paramedics on-scene. During routine care with all of its unadjusted influences and potential confounders, the process of telemedically-supported paramedic care proved its potential to reduce the number of on-scene interventions by EMS physicians. However, this cannot be explained by the implementation of the telemedical system alone. The EMS dispatch criteria were restructured and modified with the aim of reducing unnecessary primary alarms of EMS physician units. However, such dispatch criteria would likely not have been acceptable by personnel and patients, without availability of the telemedical system. Administration of opioids by paramedics is not allowed in Germany without its (telemedical) delegation by a physician. A reduced primary alarm ratio in painful conditions would have been unethical without the telemedical concept. Another factor that might have led to reduced EMS physician alarms was training effects of ambulance personnel. With improved performance in intravenous lines, analgesia and sedation over time, the paramedics could perform advanced care with telemedical support alone. However, these confounders probably influenced the number of EMS physician interventions and was not the result of the telemedical implementation system alone. Implementation with restructured dispatch criteria should ideally be called 'multi-interventions'. In similar situations, the effect cannot be attributed to a single intervention.[34] However, we also cannot exclude other confounders, given that no other structural changes were conducted in the EMS system (eg, number of ambulances or EMS physician units) besides modified dispatch criteria. The reduction of approximately 2500 on-scene manoeuvres in 1 year led to the significantly increased availability of ground-based physician intervention units, shown by the reduced need for neighbouring units and helicopter-based EMS. However, a significant increase in overall physician interventions was found by adding on-scene and telemedical interventions in the post implementation period. Although standard operating procedures existed for most common emergencies, a lower threshold for telemedical support, in contrast to summoning a physician-staffed EMS unit, has been our interpretation for this increase. A lower threshold of telemedical procedures may improve the quality of care but carries a risk of undermining the possible cost savings.

It must be acknowledged that during low acuity telemedical interventions, a parallel incoming call with high acuity can be answered, in contrast to similar on-scene interventions at different sites. Overall duration, and net time consumption of the physician, is significantly shorter with the physician in the telemedicine centre, compared with conventional on-scene care by EMS physicians.[31–33] Increased availability of limited resources of on-scene physicians is key to reducing response intervals, which can be lifesaving in life-threatening emergencies, such as major trauma or cardiopulmonary resuscitation.

LIMITATIONS

New technologies in certain work processes can lead to different behaviours of end-users. This study cannot determine if the use of the telemedical concepts was widespread for all EMS personnel or limited to some subgroups. No personal data about EMS personnel could be evaluated while following the ethics committee's statement. In a project about clinical decision support systems for paramedics, inequalities towards the technology were found.[35] Furthermore, our study was not designed to evaluate any medical outcomes or general safety of telemedical support, both of which are major limitations of this study. Thus, it is not clear if outcomes are changed by implementing a telemedicine system with modified primary dispatch criteria. No patient who received telemedical support suffered cardiac arrest during support or transport to the hospital. In addition, other confounders influencing the number of missions cannot be excluded with certainty. Detailed economic calculations were not possible, as the telemedicine system was financed for the city of Aachen during the study period, as a pilot region. Health insurances and project participants arranged future integration of more EMS districts, so that the function of a tele-EMS physician could be used more efficiently and economically. Only then, can a pre–post analysis of costs between regular and 'regular-plus' telemedically-supported EMS produce meaningful findings.

CONCLUSIONS

Transfer from research projects to health insurance-financed routine care was successful, using an implementation strategy accounting for political and economic aspects. Telemedical support for paramedics is an effective new element for prehospital emergency care, due to shifting missions from classic on-scene physician to telemedically-supported missions. Subsequently, the availability of physician-staffed EMS units increased significantly. This could lead to shorter response times in life-threatening situations/missions. In the future, remote telemedical support holds strong economic potential due to spatial independence and shorter workload time for the responsible physician. Yet, unrecognised confounders, with modified dispatch criteria and possible learning curves, could influence the reduced number of on-scene EMS physician missions. With more implementation to routine care, we achieved a prerequisite for future RCTs, comparing on-scene vs telemedical care in a model region.[36] Along with an RCT, could this question be addressed—regarding how telemedical support affects patient outcomes and whether telemedical support is generally safe.

Contributors SBer, JCB, SBec, MC, MF and RR made substantial contributions to the conception and design of the current study. All authors were mainly involved in project, study design, data analysis and publication of results of the mentioned research projects Med-on-aix and TemRas. SBer, MC and SBec performed data acquisition. The literature search was carried out by SBer, JCB, SBec, MF and RR. Data analysis and interpretation were conducted by all authors. Statistical tests were carried out by SBer, MF and MC. All authors made substantial contributions to the manuscript, while SBer and RR drafted the first complete version. All authors read and approved the final manuscript.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

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Provenance and peer review Not commissioned; externally peer reviewed.

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