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eHealth solutions for therapy management in oncology

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Practice points

- Cancer treatment is increasingly taking place in an outpatient setting, due to the growing usage of oral and subcutaneous medications. This is leading to new challenges for patients and providers.
- Challenges can include achieving appropriate patient-physician communication, lack of adherence and potential side effects and their impact on quality of life (QoL) and other patient-reported outcomes (PROs). eHealth technologies offer an opportunity to address some of these challenges.
- eHealth covers diverse types of technologies, including computers, smartphones and video conferences. There is
 also a considerable number of applications and services specifically relevant to oncology care, including video
 tumor conferences, video or web conferences between patients and professionals, web-based cancer aftercare
 guides, telephone-led follow-up interviews or patient education systems.
- The inclusion of eHealth solutions in the process of gathering PROs has the capability to improve overall well-being, enable better patient-clinician communication and lower symptom distress.
- eHealth solutions also have the potential to support clinical decision-making, via the ongoing, systematic collection of symptom data.
- At present, eHealth is underutilized in cancer care, for a number of reasons, including regulatory, technological and organizational questions.
- The PreCycle study is an upcoming multicenter, randomized Phase IV intergroup trial to evaluate the impact of an eHealth-based PRO assessment on QoL in patients with hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer treated with palbociclib and an aromatase inhibitor or palbociclib and fulvestrant. The study will be the largest randomized eHealth study in oncology with more than 1000 patients, and it is hoped it will provide data that will allow us to assess the impact of an eHealth-supported therapy management on QoL.

In an outpatient setting, some challenges of cancer treatment include continuous patient-physician communication, lack of adherence, potential side effects and their impact on quality of life and other patientreported outcomes. These challenges in the support of disease management can be overcome by the introduction of eHealth applications. Though the market of eHealth applications is fast growing, many applications lack evidence regarding their effectiveness, safety and utility. Only few prospective randomized trials have been conducted, so far. Results of these studies univocally show a gain in health-related quality of life, in the examined eHealth applications. It remains unclear if procedural and cost efficacy are affected by eHealth applications. The upcoming PreCycle study will be the largest randomized eHealth study in oncology.

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Increasingly, cancer treatment is taking place in an outpatient setting [1]. The trend toward oral agents over intravenous administration and the growing number of oral and subcutaneous medications for oncological and hematological diseases lead to new challenges for patients and providers [2,3]. Some of the challenges include continuous patient–physician communication, lack of adherence, potential side effects and their impact on quality of life (QoL) and other patient-reported outcomes (PROs) [3–5]. New eHealth technologies can provide solutions

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that are able to overcome these issues and provide unique opportunities [2,5,6], because the ability to assess PROs in real-time enables quick clinical decision-making and intervention [7].

Eysenbach defines eHealth as "an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterizes not only a technical development but also a state-of-mind, a way of thinking, an attitude and a commitment for networked, global thinking, to improve healthcare locally, regionally and worldwide by using information and communication technology" [8].

In the last years, the number of innovative eHealth solutions for chronic diseases has increased. There have been several developments regarding electronic tools to support patients during their cancer therapy [6,9–12]. Herein, eHealth covers diverse types of technologies, including computers, smartphones and video conferences [9].

Specific to cancer care, there is a considerable number of applications and services directed at medical knowledge management and clinical decision support for professionals, like video tumor conferences [13,14], video or web conferences between patients and professionals [15,16], web-based cancer aftercare guides [17,18], telephone-led follow-up interviews or patient education systems, which provide information and enhance patient knowledge [19-22]. In order to optimize the support of the patients, it is necessary to realize that the patient often plays a key role in providing care for himself. Patient-centered care has taken center stage in discussions about quality provision of healthcare. It supports patients in the management of their illness and related symptoms and involves them as an active part of their own care [23–25]. Advances in technology have significantly increased electronic PROs (ePRO) data collection capabilities and options in clinical trials. Hence, electronic monitoring of PRO has proven to show substantial potential in the involvement of patient-centric care [6].

PROs are important means of evaluating and recording the different patient-related activities, being reported by the patient himself. Therefore, the use of PROs has become increasingly interesting in the clinical practice. It allows symptom control, evaluation of physical functioning, mental health and patient-reported QoL.

The inclusion of eHealth solutions in the process of gathering PROs has the capability to improve the overall well-being, enables better patient-clinician communication and lower symptom distress [5,6,26-28]. Also, this kind of monitoring provides a systematically collected symptom data [29,30] and, thus, eventually supports clinical decision-making to improve symptom management [31], which could save a lot of care provider's time during clinical visits [6,11], might reduce the number of office visits [32] and could enhance adherence [33]. Nevertheless, these solutions have to be adapted to different kinds of settings or phases of cancer therapy. By now, only a few studies report significant improvements, most studies focus on acceptability and feasibility [7].

Unmet needs & ongoing challenges

Despite the existence of many e-solutions, eHealth is still underutilized in cancer care. Probably, this underutilization depends on many different issues like regulatory, technological and organizational questions including the lack of scientific validation. An ePRO system has the potential to enhance care coordination and the two-way communication between the patient and physician. However, the patients may fear that an eHealth solution could replace clinical visits [34], and prohibit direct feedback, and reminders from the attending physician that could eventually limit the patient's interest in self-reporting and adherence to the eHealth solution [29].

Additionally, the implementation of an ePRO system requires significant resources and experience as well as special user training [6]. In addition, primary ongoing challenges for eHealth solutions are concerns of the patients [3,34] and governance, regarding privacy and data security, and regulatory issues [9,35,36]. Regarding the ability to support new models of care, the full potential of eHealth is only reached if high degrees of pervasiveness, interoperability and an embedment into a broader information system would be achieved [9,37]. Although there are promising solutions and interventions, most of the published applications show a lack of evidence regarding their effectiveness, safety and utility [10]. There is a need of high-quality clinical trials with large sample sizes to demonstrate evidence [33,38] and determine optimal interventions [12,31]. Once these issues are solved, eHealth will become an essential part of future oncological management [3].

Research on eHealth in cancer treatment support

In 2013, a study was published about the effects of an interactive health communication application for cancer patients in illness management and symptom control. Ruland *et al.* defined that an interactive health communication is an internet-based application that allows cancer patients to monitor their symptoms and problems and immediately transfer this information to the health provider [25]. Additionally, this platform provides individually

tailored information, supports self-management and connects patients with expert cancer nurses. Back then, an electronic forum for inter-patient communication was introduced, as well. The authors compared parameters like symptom distress, depression and health-related QoL in breast and prostate cancer patients, who either had access to the health platform or only received uniform resource locators (URLs) of general cancer-related websites. The results were favorable for the health platform in most of the measured items [25].

Denis *et al.* conducted a national multi-institutional Phase III prospective randomized trial in high-risk lung cancer patients that compared web application follow-up and clinical routine assessment with CT scan [39]. In the experimental arm (patients using the web application), the web application automatically triggered physicians visit, based on dynamical analysis of the weekly self-reported symptoms. At the American Society of Clinical Oncology (ASCO) Annual Meeting 2016, Denis *et al.* concluded that overall survival in patients with lung cancer using a web-application-guided follow-up has been improved compared with standard modalities [39]. The authors also hinted that web-application-based support might improve QoL and be more cost-effective than standard follow-up.

Assessing changes in health-related QoL over 6 months, Basch *et al.* conducted a trial among 766 patients receiving routine outpatient chemotherapy for advanced solid tumors [31]. So far, this is the largest published study about eHealth in oncology patients. In the PRO group, patients received weekly email prompts to report 12 common symptoms between visits. In case of severe or worsening symptoms were reported, nurses received email alerts. Otherwise, the treating physicians received symptoms print out at visits. Among the PRO group, health-related QoL improved among significantly more participants and worsened among fewer participants.

Patients receiving intervention were less frequently admitted to the emergency room or hospitalized and remained on palliative chemotherapy longer. Even more, the 1-year survival and the quality-adjusted survival was increased in the PRO group. Surprisingly, for patients lacking prior computer experience, benefits were greater. It is important to add that the majority of patients reported severe symptoms during the study and was consequently reassessed in the clinic in response to the email alerts. Basch *et al.* concluded that symptom reporting of patients during cancer care was associated with a variety of clinical benefits. They also mentioned limitations in this randomized trial. The generalizability of this study is limited because of the design. It was conducted in an urban, tertiary care cancer center and only English-speaking patients were included. Further trials are needed to confirm these findings in more diverse settings and populations. Another limitation is the utilization of the EuroQol EQ-5D Index that measures health-related QoL in a more generalized manner, compared with an analysis, which is based on particular symptoms. Additionally, a substantial number of the participants were lost to follow-up, due to treatment dropout or death. A lack of personal reminders and insufficient time were named as the most common barriers for the mostly elderly patients. To overcome these, it is necessary to systematically involve clinical staff in the process to provide active feedback and reminding patients. However, the end point data were not overly affected by missing data [31].

Partially contrary, a randomized trial in 102 patients with TNM stage I–III breast cancer showed that health questionnaires might indeed improve reporting and detecting symptom assessment, but would not effectively reduce the number of clinic visits [30]. The study compared standard care with individualized survivorship care, based on online health questionnaires at 3-month intervals and self-reported systems, monitored by a nurse practitioner. Over an 18-month period, there were no statistically significant differences noted between the two groups with regard to oncology-related appointments, medical tests or number of physician visits [30]. While there is virtually univocal favor for eHealth applications regarding a gain in health-related QoL, procedural and cost efficacy may or may not be altered by the introduction of eHealth in supportive cancer care.

PreCycle: impact of eHealth-support on QoL in metastatic breast cancer patients treated by palbociclib & endocrine therapy

The PreCycle study is an upcoming multicenter, randomized Phase IV intergroup trial to evaluate the impact of an eHealth-based PRO assessment on QoL in patients with hormone receptor positive, HER2-negative, locally advanced or metastatic breast cancer treated with palbociclib and an aromatase inhibitor or palbociclib and fulvestrant. The study will be the largest randomized eHealth study in oncology with more than 1000 patients. Patients will be randomized 2:1 for CANKADO active versus CANKADO inform. CANKADO is an eHealth treatment supportive service including a high-density observation of PRO. The CANKADO active arm will receive a fully functional CANKADO-based eHealth treatment support system, whereas CANKADO inform will be a CANKADO-based eHealth service with no further functions other than a personal login, documentation of daily drug intake and text description. The primary study objective is to assess the impact of an eHealth-supported therapy management on QoL. CANKADO is a freely accessible tool, which can be used without additional costs by patients and healthcare professionals.

Discussion & conclusion

To date the market of eHealth applications has been very complex. A recent systematic analysis of cancer-related smartphone applications pointed out that the majority of applications targeted on breast cancer [10]. It appears that specific tumor entities are more likely to be targeted by eHealth applications. This observation might reflect that classical campaigns also focus on highly affine target groups in common cancer patients.

Regarding the purpose of the application, significant shares of the analyzed application predominantly focus on raising awareness about cancer or providing educational information about cancer-supporting fundraising efforts, assisting in early detection, promoting a charitable organization, supporting cancer prevention or social support. Only 11 out of 295 analyzed applications mainly support disease management, like the applications mentioned in this review [10].

In conclusion, there is an emerging count of cancer-related eHealth applications that have the potential capacity to assess symptoms and indicators of disease, to provide fast between-visit interventions if needed, and to promote desired behavior changes. Introduction of eHealth is a convenient way for patient-health provider interaction, to gain patient-related outcomes and to potentially improve supportive cancer care, at relatively low cost. Because many applications lack evidence on their utility, clinical efficacy and safety, future research needs to focus on these issues.

Future perspective

The PreCycle study will enlighten the impact of an eHealth-supported therapy management on QoL in breast cancer patients. Future work is also necessary to further explore different aspects of eHealth in supportive cancer care. For example, it would be important to determine which patient subgroups may benefit the most from this type of health communication intervention. It is also unclear if eHealth applications are helpful regarding a reduction of patient visits, medical overtesting and overall treatment costs.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

- 1. Ventura F, Ohlen J, Koinberg I. An integrative review of supportive e-health programs in cancer care. *Eur. J. Oncol. Nurs*. 17(4), 498–507 (2013).
- Castelnuovo G, Mauri G, Simpson S, Colantonio A, Goss S. New technologies for the management and rehabilitation of chronic diseases and conditions. *Biomed. Res. Int.* 2015, 180436 (2015).
- Harbeck N, Wuerstlein R, Schinkoethe T. Improved patient management using eHealth tools: potential and pitfalls. Breast Cancer Manage. 4(1), 1–5 (2015).
- Potential and pitfalls of using eHealth in breast cancer management.
- 4. Duman-Lubberding S, Van Uden-Kraan CF, Jansen F *et al.* Feasibility of an eHealth application 'OncoKompas' to improve personalized survivorship cancer care. *Support. Care Cancer* 24(5), 2163–2171 (2016).
- Kearney N, Mccann L, Norrie J et al. Evaluation of a mobile phone-based, advanced symptom management system (ASyMS) in the management of chemotherapy-related toxicity. Support. Care Cancer 17(4), 437–444 (2009).
- 6. Bennett AV, Jensen RE, Basch E. Electronic patient-reported outcome systems in oncology clinical practice. *CA Cancer J. Clin.* 62(5), 337–347 (2012).
- Review on the electronic measurement of patient-reported outcomes in cancer management.
- Breen S, Ritchie D, Schofield P *et al.* The Patient Remote Intervention and Symptom Management System (PRISMS) a telehealth-mediated intervention enabling real-time monitoring of chemotherapy side-effects in patients with haematological malignancies: study protocol for a randomised controlled trial. *Trials* 16, 472 (2015).
- 8. Eysenbach G. What is e-health? J. Med. Internet Res. 3(2), E20 (2001).

- Lewis J, Ray P, Liaw ST. Recent worldwide developments in eHealth and mHealth to more effectively manage cancer and other chronic diseases – a systematic review. Yearb. Med. Inform. 10(1), 93–108 (2016).
- Recent systematic review on worldwide developments in eHealth to effective cancer management.
- 10. Bender JL, Yue RYK, To MJ, Deacken L, Jadad AR. A lot of action, but not in the right direction: systematic review and content analysis of smartphone applications for the prevention, detection, and management of cancer. J. Med. Internet Res. 15(12), e287 (2013).
- 11. Jensen RE, Snyder CF, Abernethy AP et al. Review of electronic patient-reported outcomes systems used in cancer clinical care. J. Oncol. Pract. 10(4), E215–E222 (2014).
- 12. Kuijpers W, Groen WG, Aaronson NK, Van Harten WH. A systematic review of web-based interventions for patient empowerment and physical activity in chronic diseases: relevance for cancer survivors. *J. Med. Internet. Res.* 15(2), e37 (2013).
- 13. Donnem T, Ervik B, Magnussen K *et al.* Bridging the distance: a prospective tele-oncology study in Northern Norway. *Support. Care Cancer* 20(9), 2097–2103 (2012).
- 14. El Saghir NS, Keating NL, Carlson RW, Khoury KE, Fallowfield L. Tumor boards: optimizing the structure and improving efficiency of multidisciplinary management of patients with cancer worldwide. *Am. Soc. Clin. Oncol. Educ. Book* 2014, E461–E466 (2014).
- Katz MH, Slack R, Bruno M et al. Outpatient virtual clinical encounters after complex surgery for cancer: a prospective pilot study of 'TeleDischarge'. J. Surg. Res. 202(1), 196–203 (2016).
- Hennemann-Krause L, Lopes AJ, Araujo JA, Petersen EM, Nunes RA. The assessment of telemedicine to support outpatient palliative care in advanced cancer. *Palliat. Support. Care* 13(4), 1025–1030 (2015).
- 17. Willems RA, Bolman CA, Mesters I, Kanera IM, Beaulen AA, Lechner L. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial. *Psychooncology* 26(2), 222–230 (2016).
- Kanera IM, Willems RA, Bolman CA et al. Use and appreciation of a tailored self-management eHealth intervention for early cancer survivors: process evaluation of a randomized controlled trial. J. Med. Internet Res. 18(8), e229 (2016).
- Cnossen IC, Van Uden-Kraan CF, Eerenstein SE *et al.* An online self-care education program to support patients after total laryngectomy: feasibility and satisfaction. *Support. Care Cancer* 24(3), 1261–1268 (2016).
- Song L, Rini C, Deal AM *et al.* Improving couples' quality of life through a web-based prostate cancer education intervention. *Oncol.* Nurs. Forum 42(2), 183–192 (2015).
- Ryhanen AM, Rankinen S, Siekkinen M, Saarinen M, Korvenranta H, Leino-Kilpi H. The impact of an empowering Internet-based Breast Cancer Patient Pathway program on breast cancer patients' clinical outcomes: a randomised controlled trial. *J. Clin. Nurs.* 22(7–8), 1016–1025 (2013).
- 22. Baker TB, Hawkins R, Pingree S *et al.* Optimizing eHealth breast cancer interventions: which types of eHealth services are effective? *Transl. Behav. Med.* 1(1), 134–145 (2011).
- Hagglund M, Bolin P, Koch S. Living with lung cancer patients' experiences as input to eHealth service design. Stud. Health Technol. Inform. 216, 391–395 (2015).
- 24. Lubberding S, Van Uden-Kraan CF, Te Velde EA, Cuijpers P, Leemans CR, Verdonck-De Leeuw IM. Improving access to supportive cancer care through an eHealth application: a qualitative needs assessment among cancer survivors. *J. Clin. Nurs.* 24(9–10), 1367–1379 (2015).
- 25. Ruland CM, Andersen T, Jeneson A *et al.* Effects of an internet support system to assist cancer patients in reducing symptom distress: a randomized controlled trial. *Cancer Nurs.* 36(1), 6–17 (2013).
- Interesting study that allows cancer patients to monitor their symptoms and problems and immediately transfers this information to the health provider.
- Judson TJ, Bennett AV, Rogak LJ et al. Feasibility of long-term patient self-reporting of toxicities from home via the Internet during routine chemotherapy. J. Clin. Oncol. 31(20), 2580–2585 (2013).
- 27. Berry DL, Blonquist TM, Patel RA, Halpenny B, Mcreynolds J. Exposure to a patient-centered, web-based intervention for managing cancer symptom and quality of life issues: impact on symptom distress. J. Med. Internet Res. 17(6), e136 (2015).
- 28. Cleeland CS, Wang XS, Shi Q *et al.* Automated symptom alerts reduce postoperative symptom severity after cancer surgery: a randomized controlled clinical trial. *J. Clin. Oncol.* 29(8), 994–1000 (2011).
- 29. Basch E, Iasonos A, Barz A et al. Long-term toxicity monitoring via electronic patient-reported outcomes in patients receiving chemotherapy. J. Clin. Oncol. 25(34), 5374–5380 (2007).
- Wheelock AE, Bock MA, Martin EL et al. SIS.NET: a randomized controlled trial evaluating a web-based system for symptom management after treatment of breast cancer. Cancer 121(6), 893–899 (2015).
- Large breast cancer trial that shows eHealth questionnaires might improve reporting and detecting of symptoms.
- 31. Basch E, Deal AM, Kris MG *et al.* Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. *J. Clin. Oncol.* 34(6), 557–565 (2016).
- Largest published trial on eHealth in oncology patients. Significant improvements in health-related quality of life.

- 32. Johansen MA, Henriksen E, Horsch A, Schuster T, Berntsen GK. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of randomized controlled trials. Part 1: state of the art. *J. Med. Internet Res.* 14(5), e118 (2012).
- 33. Linn AJ, Vervloet M, Van Dijk L, Smit EG, Van Weert JC. Effects of eHealth interventions on medication adherence: a systematic review of the literature. *J. Med. Internet Res.* 13(4), e103 (2011).
- 34. Steele Gray C, Miller D, Kuluski K, Cott C. Tying eHealth tools to patient needs: exploring the use of eHealth for community-dwelling patients with complex chronic disease and disability. *JMIR Res. Protoc.* 3(4), e67 (2014).
- Mohammadzadeh N, Safdari R, Rahimi A. Cancer care management through a mobile phone health approach: key considerations. Asian Pac. J. Cancer Prev. 14(9), 4961–4964 (2013).
- Schepers SA, Sint Nicolaas SM, Haverman L et al. Real-world implementation of electronic patient-reported outcomes in outpatient pediatric cancer care. Psychooncology 26(7) 951–959 (2016).
- 37. Nasi G, Cucciniello M, Guerrazzi C. The role of mobile technologies in health care processes: the case of cancer supportive care. J. Med. Internet Res. 17(2), e26 (2015).
- Agboola SO, Ju W, Elfiky A, Kvedar JC, Jethwani K. The effect of technology-based interventions on pain, depression, and quality of life in patients with cancer: a systematic review of randomized controlled trials. J. Med. Internet Res. 17(3), e65 (2015).
- Denis F, Lethrosne C, Pourel N et al. Overall survival in patients with lung cancer using a web-application-guided follow-up compared with standard modalities: results of Phase III randomized trial. J. Clin. Oncol. 34(18 Suppl.), doi:10.1200/JCO.2016.34.18_suppl.LBA9006 (2016) (Epub ahead of print).
- Most recent results of an eHealth study in cancer care. Improved overall survival in patients with lung cancer using a web-application-guided follow-up.