Beszámoló Prof. Dr. Kásler Miklós miniszter úr számára a Közép-Kelet Európai Onkológiai Akadémia 2020-2021-es tevékenységéről

A daganatos megbetegedések, mint az egyik vezető halálok fontosságára tekintettel a közép-kelet európai régió határokon átívelő szakmapolitikai, epidemiológiai, onkológiai oktatási, képzési, klinikai és alapkutatási valamint onkológiai ellátási együttműködését intézményesítendő Prof. Dr Kásler Miklós emberi erőforrás miniszter úr kezdeményezésére, 2019 június 12-én 21 ország egészségügy miniszterei illetve államtitkárai közös állásfoglalásban nyilvánították ki együttműködési szándékukat és a Közép-Kelet Európai Onkológiai Akadémia (Central-Eastern European Academy of Oncology, CEEAO) megalapításának szükségességét.
Az aláíró országok az alábbiak voltak: Magyarország, Azerbajdzsáni Köztársaság, Belarusz Köztársaság, Bosznia és Hercegovina, Bolgár Köztársaság, Horvát Köztársaság, Kazah Köztársaság, Grúzia, Lett Köztársaság, Litván Köztársaság, Montenegró, Moldáv Köztársaság, Észak-macedón Köztársaság, Lengyel Köztársaság, Románia, Oroszországi Föderáció, Szerb Köztársaság, Tádzsik Köztársaság, Üzbég Köztársaság és Türkmenisztán.
A nemzetközi szakmapolitikai rendezvényt 1st Regional Conference on Partnership and Cooperation in Oncology címmel kétnapos szakmai konferencia követte, több száz résztvevővel. Az összesen három napos rendezvény helyszíne a Várkert Bazár volt.

Ezt követően az Emberi Erőforrás Minisztériumnak irányításával az Országos Onkológiai Intézet szakértői csoportja létrehozta a CEEAO Szervezeti Működési Szabályzatát, a CEEAO Alapító Okiratát és Kurrikulumát.

2020 január 23-án a Magyar Parlament Vadásztermében a Magyar Kormány részéről Prof. Dr Kásler Miklós emberi erőforrás miniszter, Prof. Dr Horváth Ildikó államtitkár és Dr Lőrinczi Zoltán államtitkár jelenlétében hivatalosan megalapította a Közép-Kelet Európai Onkológiai Akadémiát és a Közép-Kelet Európai Onkológiai Akadémia Alapítványt.
A tagországok mindegyike két akadémikust delegál a CEEAO-ba. A CEEAO elnökének Dr med habil Mátrai Zoltánt az Országos Onkológiai Intézet Daganatsebészeti Központ központvezető főorvosát választották, elnökhelyetteseknek Prof. Dr Andrej Dimitrievics Kaprint, az Orosz Föderáció Egészségügyi Minisztériumának Országos Orvosi Radiológiai Kutatóközpontjának főigazgató főorvos, az Orosz Tudományos Akadémia tagját és Dr Vickó Ferencet, Szerbia egészségügyi államtitkárát. Magyarországot akadémikusként Prof. Dr Polgár Csaba az Országos Onkológiai Intézet főigazgató főorvosa képviseli a szervezetben.
A CEEAO munkájának szakmai támogatására elismert nemzetközi szakemberekből álló Tudományos Tanácsadó Testület jött létre.
A CEEAO hivatalos megalapítását 2nd Conference of the Central-Eastern European Academy of Oncology címmel sikeres regionális szakmapolitikai konferencia követte, melynek helyszíne a Festetics Palota volt.

A CEEAO hivatalos megalapítását követően létrejött a CEEAO Kuratóriuma, melynek elnöke Prof. Dr Ottó Szabolcs onkológus, valamint a CEEAO Alapítvány Igazgatósága, amelynek igazgatója Dr Csuka Orsolya onkológus kutató, az Országos Onkológiai Intézet fejlesztési igazgatója lett. Felállt a CEEAO Felügyelőbizottsága, amelynek elnöke Dr Lőrinczi Zoltán államtitkár, majd később Prof. Dr Kollár Lajos elnök úr lett.

A megalapítást követően elkészült a CEEAO magyar, orosz és angol nyelvű honlapja https://ceeao.org/ és a szervezet megkezdte munkáját. A CEEAO tevékenységére sajnos a Covid-19 pandémia szintén negatív hatással volt.

A CEEAO szakmaspecifikus profilja a Central-Eastern European Breast Cancer Surgical Consortium (CEEBCSC) 1st International Congress and Scientific Workshop of the Central-Eastern European Breast Cancer Surgical Consortium címmel 2019 június 13-14 tartotta első nemzetközi konferenciáját.
A konferencián jelent meg hivatalosan a Mátrai Zoltán, Gulyás Gusztáv, Kovács Tibor, Kásler Miklós, Principles and Practice of Oncoplastic Breast Surgery című angol nyelvű korszerű emlősebészeti szakkönyve a Medicina Kiadó Zrt. gondozásában, amely azóta az európai emlősebészeti szakvizsga hivatalosan ajánlott szakirodalma.

2019 szeptember 23-27. Prof. Dr Andrej Kaprin alelnök úr meghívására Prof. Dr Polgár Csaba főigazgató főorvos úr és Dr Mátrai Zoltán elnök úr részt vettek a 2nd International Forum of Oncology and Radiology című nemzetközi onkológiai fórumon Moszkvában, amelyet az Orosz Föderáció elnöke, Vlagyimir Vlagyimirovics Putyin nyitott meg.

A 2020 június 25-28. White Nights Oncological Conference 2020, Szentpétervár, Oroszország
A CEEBCSC II. Nemzetközi Konferenciája az orosz fél rendezésével (NN Petrov Research Institute of Oncology, Szentpétervár.

Az Országos Onkológiai Intézet és a NN Petrov Reseach Institute of Oncology között havi rendszerességgel történik a korszerű telemedicina alkalmazásával multidiszciplináris onkológiai ülés. A web felületet az orosz fél alakította ki, az üléseket átlagban több mint 200 végpontról érik el, különböző országokból, de a tudományos előadások felvételeit bármikor el tudják érni a kódszóval rendelkező regisztrálók.
https://live.niioncologii.ru/CEEBCSC200919
https://live.niioncologii.ru/ceebcsc251019
https://live.niioncologii.ru/ceebcsc221119
https://live.niioncologii.ru/ceebcsc201219
https://live.niioncologii.ru/ceebcsc280220

A CEEBCSC a standardizált európai emlősebészeti szakvizsga és akkreditációs program (Projekt BRESO) alapító tagszervezete az European Society of Surgical Oncology (ESSO), a European Society of Breast Cancer Specialists (EUSOMA), a Division of Breast Surgery of the European Board of Surgery of the UEMS (DBS), a European Breast Cancer Coalition (Europa Donna), a European School of Oncology (ESO), a European Breast Cancer Research Association of Surgical Trialists (EUBREAST), a European Commission Initiative on Breast Cancer (ECIBC), *a* Group for Reconstructive and Therapeutic Advancements (G.Re.T.A) mellett. A BRESO projektben olyan szervezetek társultak még, mint az European Society for Radiatiotherapy and Oncology (ESTRO), a European Society for Medical Oncology (ESMO), a European Society of Breast Imaging (EUSOBI), a EUPath, European Society of Pathology (ESP).
https://breastsurgeoncertification.com/
A BRESO Projekt keretén belül azóta megjelent az Egyesült Államok szakmai elvárásaival harmonizált Európai Emlősebészeti Kurrikulum, aminek szerzői között a CEEBCSC és a CEEAO elnöke is szerepel.

Kovacs T, Rubio IT, Markopoulos C, Audisio RA, Knox S, Kühn T, Mansel R, Matrai Z, Meani F, Nava M, Wyld L; BRESO Structure Working Group Theoretical and practical knowledge curriculum for European Breast Surgeons. Eur J Surg Oncol. 2020 Feb 8. pii: S0748-7983(20)30046-9. doi: 10.1016/j.ejso.2020.01.027.
https://www.ncbi.nlm.nih.gov/pubmed/32075718

A CEEBCSC az orosz partnerrel nagy forgalmú közösségi információs médiaportált üzemeltet, amin szakmai híreket közlünk, több mint 700 nemzetközi követővel
https://www.facebook.com/CEEBCSC/

2020 augusztus 27-29. A CEEBCSC az International Breast Symposium Düsseldorf (IBSD), a világ egyik legrangosabb emlőráksebészeti kongresszusának stratégiai partnere lett. A nemzetközi együttműködés 2021-ben (2021 június 24-26) is folytatódik. http://www.breast-symposium.com/

European Breast Cancer Research Association of Surgical Trialists (EUBREAST) együttműködés, hogy a tudományosan legmagasabb értékű, előretekintő, összehasonlító klinikai vizsgálatokat a régió országaiban elterjesszük. A CEEBCSC hivatalos együttműködő partnere az EUBREAST-nek. https://www.eubreast.com/?Coperations

2020 április 22-25. Prof. Dr Andrej Kaprin alelnök úr meghívására Prof. Dr Polgár Csaba főigazgató főorvos úr és Dr Mátrai Zoltán elnök úr részt vettek a XIth Congress of Oncologists and Radiologists of CIS nemzetközi online konferencián. Az előadások témái a magyarországi

Covid helyzetben történő onkológiai ellátás és a CEEAO szerepe a regionális együttműködésekben volt.

2020 július 1. Towards a cancer mission in Horizon Europe: recommendations címmel Prof. Dr Kásler Miklós EMMI miniszter úr és Prof. Dr Nagy Péter az Országos Onkológiai Intézet tudományos igazgatójának társszerzőségével jelent meg angol nyelvű átfogó közlemény Mol Oncol. 2020 Aug;14(8):1589-1615. doi: 10.1002/1878-0261.12763. tizennégy ország, vezető centrumának szakmai és szakmapolitikai képviselőitől a Horizon Europe rákprogramról. A szakmai szervezetek álláspontját képviselő European Academy of Cancer Sciences (EACS) a cikkben deklarálja, hogy a régiónkban együttműködő partnereként a CEEAO-t tekinti. https://pubmed.ncbi.nlm.nih.gov/32749074/

2020 szeptember 21-25. Prof. Dr Andrej Kaprin alelnök úr meghívására Prof. Dr Polgár Csaba főigazgató főorvos úr és Dr Mátrai Zoltán elnök úr részt vettek a 3rd International Oncology and Radiology Forum „for Life" organized by the Association of Oncologists Of Russia nemzetközi online konferencián. Az előadások témái a magyarországi Covid helyzetben történő onkológiai ellátás és a CEEAO szerepe a regionális együttműködésekben volt. https://ceeao.org/events/3-rd-international-oncology-and-radiology-forum-for-life-organized-by-the-association-of-oncologists-of-russia-2/

2020 október 5. Az Országos Onkológiai Intézet és a Saint-Petersburg Oncocentre online konferenciája a Cooperation between the Saint-Petersburg Oncocentre and the National Institute of Oncology online konferenciája, ahol előadásként a CEEAO regionális munkájának bemutatása is megtörtént.

2020 október 31. A Mátrai Z, Gulyás G, Kovács t, Kásler M. Principles and Practice of Oncoplastic Breast Surgery (Medicina Kiadó Zrt) című angol nyelvű korszerű emlősebészeti szakkönyv orosz nyelvű ünnepélyes kiadása Szentpéterváron. https://kormany.hu/hirek/az-emlorak-korszeru-sebeszete-cimu-szakkonyv-mar-orosz-forditasban-is-megjelent?fbclid=IwAR3xnivY6sY6TfOjGzt1CTA6U0_WCRbG78mM9J9zEHXfdHR68hAjMjanHcM

2020 november 11. A CEEAO szervezésében az Országos Onkológiai Intézet Dermato-onkológiai Centrumának, Prof Dr Liszkay Gabriella osztályvezető asszony tudományos elnökletével Current Advances in the Complex Treatment of Skin Tumours nemzetközi online továbbképzés történt, több mint 380 résztvevővel.

https://ceeao.org/events/current-advances-in-the-complex-treatment-of-skin-tumours-international-online-workshop/

2020 december 3-6. A CEEBCSC társ szervezője a 4th International Annual Conference of the Asian Society of Mastology – ASOMACON 2020 rendezvénynek, külön tudományos szekcióval, magyar és orosz szakemberek előadásaival.

2020 december 10-11. A CEEAO elnöke nyitja meg online megjelenéssel az International Conference of Cancer Care in Kazakhstan. from Past to the Future. The 60th Anniversary of Kazakh Institute of Oncology and Radiology konferenciát.

2021 február 6. XXVII. Szent Agáta Mammológus Nap, nemzetközi online konferencia a CEEAO és az Országos Onkológiai Intézet szervezésében, magyar, orosz, kazah, lengyel és azerbajdzsáni előadókkal. 175 magyar és 135 külföldi résztvevővel.
https://ceeao.org/events/xxvii-st-agatha-mammologist-day/

2021 február 6-7. A CEEBCSC az Asian Society of Mastology-val indiai Jaipur Breast Course társszervezője, szakmai előadásokkal.
http://ceebcsc.org/news/jaipurbreastcourse/

2021-ben a CEEAO a magyar, 2020 augusztusában elfogadott IV. Emlőrák Konszenzus Konferencia szakmai anyagát alapul véve regionális emlőrák onkológiai konszenzust hoz létre, hogy meghatározza a nők leggyakoribb rosszindulatú daganatának, az emlőráknak a minimálisan elvárható szakmai standardjait. A hiánypótló projekt alapjául szolgáló szakmai dokumentum angol és orosz nyelvre történő fordítása megtörtént. A folyamatban lévő nyelvi lektorálást követően a CEEAO akadémikusainak segítségével, kétkörös egyeztetés után konszenzus konferencián véglegesítődik a szakmai szöveg, Budapesten.

2021 július 30-31. Az eredetileg 2020. májusra szervezett és a Covid-19 pandémia miatt halasztani kényszerülő klinikai kutatási, transzlációs kutatási, regionális onkológiai szervezetek együttműködésével és regoinális onkológiai centrumok networking-jával foglalkozó CEEAO – Országos Onkológiai Intézet- Magyar Onkológusok Társasága által rendezett nemzetközi konferencia. A konferencia célja a kelet-nyugat tudományos kapcsolódás és együttműködés, valamint az onkológiai társaságok integrálódása a CEEAO-ba és a régió nagy onkológiai központjainak együttműködése, Magyarország és az Országos Onkológiai Intézet központi szerepével. A konferenciára tervezetten 140 meghatározó szakember érkezik a régióból és Nyugat-Európából, valamint az Egyesült Államokból. A visszaigazolt résztvevők között említendőek pl. *az* International Agency for Research on

Cancer, IARC, European Academy of Cancer Sciences, European Society of Medical Oncology (ESMO), European Society of Surgical Oncology (ESSO), European Society of Therapeutic Radiology and Oncology (ESTRO), Oncoplastic Breast Consortium (OPBC), Central Eastern European Breast Cancer Surgical Consortium (CEEBCSC), International Breast Cancer Study Group (IBCSG), Austrian Breast and Colorectal Cancer Study Group (ABCSG), European Organisation for Research and Treatment of Cancer (EORTC), Breast International Group (BIG), Breast Surgical Oncology Project (BRESO), European Society of Breast Cancer Specialists (EUSOMA)

2021-ben a már megkezdett a fiatal onkológiai betegeket érintő onkológiai fertilitás prezervációs tudományos program és konszenzus kialakítását tervezzük. A magyar és angol illetve orosz nyelvű kérdőívek a CEEAO tagországainak és az akadémikusoknak már kiküldésre kerültek, csakúgy, mint a Magyar Onkológiai Társaság tagjainak. A hiánypótló program szakmai vezető Dr Novák Zoltán az Országos Onkológiai Intézet osztályvezető főorvosa. A terv ősszel jelenléti konszenzus konferencia Budapesten.

A CEEAO Tudományos Tanácsadó Testületének tagjaként Dr Liszkay Gabriella professzor asszony „Bőrtumorok komplex onkológiai kezelése” címmel idén ismét online workshopot szervez és nemzetközi szerzőkkel angol, orosz nyelvű hiánypótló szakkönyv kiadását tervezi a melanoma malignum bőrtumorok sokszakmás korszerű kezeléséről.

A CEEAO 2021 március 23-án online közgyűlést tart, az idei szakmai programok megvitatására, pontosítására és további tervek meghatározására.

2021-ben a CEEBCSC orosz, lengyel, román, szlovén, cseh, szlovák és ukrán partnereivel az európai emlősebészeti akkreditációs vizsgára felkészítő online képzési programot indít angol és orosz nyelven.

2021 szeptember 24-25. Kijev, Ukrajna a CEEBCSC 3. nemzetközi konferenciája.

Budapest, 2021.03.01.

Dr Mátrai Zoltán

Molecular Oncology

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Towards a cancer mission in Horizon Europe: recommendations

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16 Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands
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18 Cancer Prevention Europe, Lyon, France
19 Dutch Cancer Society, Amsterdam, the Netherlands
20 French National Cancer Institute (INCa), Boulogne Billancourt, France
21 Swiss Institute for Experimental Cancer Research (ISREC), Federal Institute of Technology in Lausanne (EPFL), Lausanne, Switzerland
22 Swiss Cancer Center Leman (SCCL), Lausanne, Switzerland
23 German Cancer Aid, Bonn, Germany
24 Stockholm School of Economics, Stockholm, Sweden
25 Institute of Health and Society, University of Oslo, Oslo, Norway
26 Association of European Cancer Leagues (ECL), Brussels, Belgium
27 Ministry of Human Resources, Budapest, Hungary
28 SIOPE Head Office, Brussels, Belgium
29 NIHR Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, UK
30 The Swedish Cancer Society, Stockholm, Sweden
31 EORTC Headquarters, Brussels, Belgium
32 Federation of European Academies of Medicine, Brussels, Belgium
33 Organisation of European Cancer Institutes (OECI), Brussels, Belgium
34 National Institute of Oncology, Budapest, Hungary
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Keywords
cancer mission; cancer research/care/prevention continuum; comprehensive cancer centres; European healthcare systems; patient empowerment; science policy

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A comprehensive translational cancer research approach focused on personalized and precision medicine, and covering the entire cancer research–care–prevention continuum has the potential to achieve in 2030 a 10-year cancer-specific survival for 75% of patients diagnosed in European Union (EU) member states with a well-developed healthcare system. Concerted actions across this continuum that spans from basic and preclinical research through clinical and prevention research to outcomes research, along with the establishment of interconnected high-quality infrastructures for translational research, clinical and prevention trials and outcomes research, will ensure that science-driven and social innovations benefit patients and individuals at risk across the EU. European infrastructures involving comprehensive cancer centres (CCCs) and CCC-like entities will provide researchers with access to the required critical mass of patients, biological materials and technological resources and can bridge research with healthcare systems. Here, we prioritize research areas to ensure a balanced research portfolio and provide recommendations for achieving key targets. Meeting these targets will require harmonization of EU and national priorities and policies, improved research coordination at the national, regional and EU level and increasingly efficient and flexible funding mechanisms. Long-term support by the EU and commitment of Member States to specialized schemes are also needed for the establishment and sustainability of trans-border infrastructures and networks. In addition to effectively engaging policymakers, all relevant stakeholders within the entire continuum should consensually inform policy through evidence-based advice.

1. Introduction

Recently, the European Academy of Cancer Sciences (EACS) and several European organizations and cancer centres joined forces to define common goals for the implementation of a mission-oriented approach to cancer in Horizon Europe, initially proposed by Celis and Pavalski in 2017 [1–3]. The aim is 'to have an impact on society at large by uniting countries to substantially reduce the enormous cancer burden in the European Union (EU) and improve the health-related quality of life of patients by promoting cost-effective, evidence-based best practices in cancer prevention, treatment, and care'. As highlighted previously, the main goal is to 'achieve a 10-year cancer-specific survival for ¾ of the adult patients diagnosed in year 2030 in Member States with a well-developed healthcare system. Because cancer mortality provides a timelier assessment of progress also capturing advances in both therapeutics and prevention, it will be important to document the expected declining trends of age-standardized mortality in each EU country' [1,2]. The objectives of the mission must be mindful of the needs of the European patients and citizens at large, by bringing maximum value for public investment, and to ensure that health technologies developed by funding

Abbreviations
AI, Artificial intelligence; CCC, Comprehensive Cancer Centre; CCCoE, Comprehensive Cancer Centre of Excellence; CEEAO, Central-Eastern European Academy of Oncology; CPE, Cancer Prevention Europe; EACR, European Association for Cancer Research; EACS, European Academy of Cancer Sciences; EC, European Commission; ECPC, European Cancer Patient Coalition; EMBO, European Molecular Biology Organization; EORTC, Organisation for the Research and Treatment of Cancer; ESMO, European Society for Medical Oncology; ESSO, European Society of Surgical Oncology; ESTRO, European Society Radiotherapy and Oncology; EU, European Union; OECI, Organization of European Cancer Institutes; SIOPE, European Society of Paediatric Oncology.

through the mission are available to those who need them for a fair and affordable price.

This goal can only be achieved by integrating and bridging the entire continuum of cancer research, prevention and care, which spans from basic, epidemiological and preclinical research to clinical, prevention, implementation and survivorship research. Particular attention should be paid to the gap between research and cancer care, and research and prevention. Different disciplines are involved in this endeavour each with their own specific emphasis. These include the following: (a) cancer biology (basic and preclinical research); (b) identification of healthy individuals at risk of developing cancer (primary prevention); (c) early cancer detection (secondary prevention); (d) cancer patient treatment and research (clinical); and (e) support for cancer survivors (tertiary prevention). Assessing progress in these areas requires different methodological approaches [4–6]. Outcomes research for both therapeutic interventions and the effectiveness of public health interventions and health services will be critical for progress assessment. This will require adequate resources, multidisciplinary expertise, access to large, high-quality data sets including patient records, suitable analysis tools and coordinated collaborative projects. Taken together, all the above elements are essential for achieving science-driven medical and social innovations and their resulting intervention trajectories, all tailored to the individual needs of patients [2].

The latter goal emphasizes the need to create integrated, networked and geographically distributed infrastructures that can entail Comprehensive Cancer Centres of Excellence (CCCoEs) meeting the Excellence standards of the EACS [7], Comprehensive Cancer Centres accredited by the Organisation of European Cancer Institutes (OECI), cancer research and clinical centres and technological platforms. CCCs are crucial to establish closer links between research and healthcare systems [8,9]. By integrating cancer care and prevention with research and education, CCCoEs and CCCs are well-positioned to boost innovation and deliver state-of-the-art comprehensive multidisciplinary cancer care. Only a few designated CCCs do incorporate paediatric care as paediatric cancer patients often also require specific expertise only available in children hospitals. Nevertheless, further concentrating paediatric oncology in centres with the necessary critical mass can boost innovation and effectiveness of the treatment of children with cancer. Across Europe, the integration of cancer research and clinical care for children and adolescents needs to address the exquisite circumstances of this patient population, as has been demonstrated in the successful launch of the European Commission (EC) supported Paediatric Cancer Expert Reference Network (https://paedcan.ern-net.eu/). Geriatric patients, which constitute a much larger group, are best served by CCCs that have specific programmes focussed on the specific needs of elderly patients.

In this update, which accommodates the input of many European cancer organizations, we provide a more detailed view of the infrastructural requirements to promote excellence in cancer research. We also emphasize consensus priority areas to realize the cancer mission objectives and outline recommendations for engaging professionals and institutions throughout Europe.

2. Infrastructures to support cancer research of excellence

We want to emphasize that creativity, originality, curiosity and a visionary foresight among individual scholars or teams of investigators remain the engine for innovation and discovery. However, these investigators need to be embedded in infrastructures of sufficient critical mass. This is essential for effectively linking basic, translational, clinical and prevention cancer research with care, as well as for driving innovation across the whole cancer research/care/prevention continuum. Such infrastructures would provide researchers access to essential technology platforms, resources and patients.

Multidisciplinary/professional patient-centred institutions are best positioned to (a) support basic and translational research, (b) link research with the healthcare systems including prevention organizations, (c) offer pharmaceutical and biotechnology industries strategic partnerships, (d) generate intellectual property and engage in profitable technology transfer, (e) provide training, capacity building and mobility of researchers and clinicians across Europe, (f) facilitate the communication and dissemination of information and finally (g) provide the best care for patients (Fig. 1A). Networks of such institutions, accessible to research teams across Europe, will be essential to achieve the goals. Specialized academic medical/cancer research centres are critical especially for primary prevention research and intervention research [10]; their particular target population of healthy individuals and their research often based on observational rather than intervention studies, with links to basic research, epidemiology, public health and social and human sciences.

We propose three networked research infrastructures accessible to research teams from across Europe that

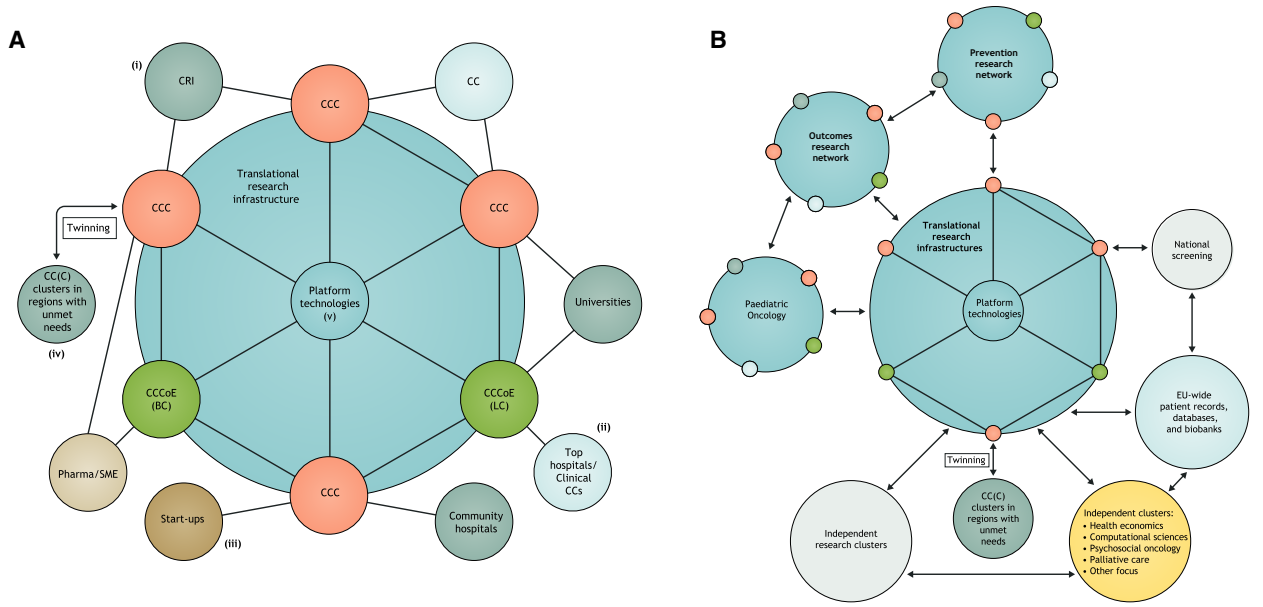

Fig. 1. Research networks provide cancer researchers with sufficient critical mass of research infrastructures, patients, samples, technology and expertise. (A) Paradigm of a translational research network. Multidisciplinary, patient-centred institutions, such as CCCs and CCCoEs, each having a broad research scope, interact closely. For example, they collaborate on specific research items (indicatively, on breast cancer (BC), or lung cancer (LC)) and share platform technologies, thereby forming the core components of a translational research infrastructure. CCCs and CCCoEs are best positioned to: (i) support basic and translational research through crosstalk with cancer centres (CCs) and cancer research institutes (CRIs), as well as linking to academic research at universities, for example, research on (bio)chemistry, engineering, genetics, molecular and cell biology, tumour biology, immunology; (ii) exchange data to improve care for patients both at top clinical hospitals and community hospitals; (iii) work closely with start-ups and offer pharmaceutical and biotechnology industries strategic partnerships; (iv) provide training, capacity building and mobility of researchers and clinicians across Europe through twinning programmes; (v) generate intellectual property and engage in profitable technology transfer, facilitating the communication and dissemination of information. (B) Infrastructures involve interacting networks. These networks too are based on the close collaboration among researchers in CCCs, CCCoEs, clinical CCs, universities and other research organizations (see also panel A). The three suggested types of infrastructures (translational research, clinical and prevention trials, and outcomes research) may in addition include structures addressing specific research requirements. An already-established paediatric oncology network exemplifies how innovative research and clinical strategies can be delivered, based on strong collaboration across European centres. In the context of a cancer mission, all networks would establish cross-border relationships with each other, and also with existing independent research clusters and professional clusters focusing, for example, on health economics, computational sciences, psychosocial oncology or palliative care. In addition, strong links to national screening facilities, and EU-wide patient records, databases and biobanks can be established and maintained.

will be essential to achieve the goals. The three infrastructures should focus on translational research, clinical and prevention trials, and outcomes research (Fig. 1B).

2.1. Infrastructure for translational research

Translational research bridges basic/preclinical research with clinical and prevention research, builds on inventions and innovation from basic/preclinical research, and has a direct impact on therapeutic and prevention research [1,3]. This should result in proof of principle clinical/prevention trials that, if successful, subsequently require research for effective implementation in the healthcare system.

A comprehensive infrastructure for translational research linked to clinical research will require:

- A robust basic cancer research programme.
- Close interactions between innovative basic/preclinical research, molecular and digital pathology, a variety of omics technologies and immunotyping facilities for patient stratification.
- A bidirectional translational research structure.
- Data acquisition tools and structured databases with possibilities for computational analyses relevant for both therapeutics and prevention studies.
- Reduced fragmentation of oncology data sources through a well-functioning European Health

Data Space with focus on the integration of real-world data sources and harnessed quality-of-life data; data safety, open science and FAIR principles (findable, accessible, interoperable and reusable). Harmonized interoperability standards, data sharing.
- Innovative imaging technologies, with a focus on novel molecular and functional imaging.
- Facilities and expertise to develop and implement cell-based and other biological therapies.
- High-quality pharmacology.
- Biobanks with associated patient records.
- Capacity for 'proof-of-concept' clinical/prevention trials.
- Longitudinal sampling routines (tumour biopsies/consecutive biopsies and liquid biopsies).
- Interaction with clinical-trials consortia or networks to develop practice-changing clinical trials.

2.2. Infrastructure for clinical and prevention trials

'Proof-of-principle' studies may serve as a starting point for further clinical and prevention research, including the assessment of its utility in health care or prevention, and patient-reported outcomes. Well-developed clinical trial structures, as well as advanced diagnostic methods, such as state-of-the-art molecular pathology, omics technologies and pharmacology to stratify patients, are crucial.

Due to a large number of tumour subgroups, the traditional clinical trials methodology built on the phase I–IV trial concept are gradually being superseded by new more sophisticated stratification methods [11–14]. Moreover, there are increasing possibilities to follow therapy response using innovative imaging technologies, consecutive tumour biopsies and/or liquid biopsies [15]. Such biopsies permit treatment adjustment to the changing biology of the tumour. However, it will be essential to monitor closely whether these more advanced and potentially costly interventions improve patient outcome; implementation research can determine this.

Implementation research needs to include health economics of therapeutic interventions and prevention programmes for early detection on large patient populations, to inform on their clinical utility, benefits and harms to patients and the healthcare system at large. In addition, patients' experiences during new treatment approaches have to be considered. The patient's gender and age are also parameters that need to be carefully weighed in clinical trial designs. Paediatric oncology is an obvious example, but this equally holds for elderly patients. Given the ageing population, age may be considered as an essential parameter in the implementation (adaptation of therapeutic strategies, importance of supportive care, presence of comorbidities and frailties) and evaluation (health-related quality of life) of clinical and prevention trials.

By contrast, as primary prevention mostly addresses harmful exposures and behaviours, research is observational and often requires hundred thousands of individuals in multinational study series to draw firm conclusions. Implementation of protective measures and secondary prevention effectiveness and efficacy can be evaluated in field trials, with the individual or sometimes even communities, serving as observational units [5]. Tertiary prevention, although involving the cancer patient, usually follows the individual well beyond the time they are in contact with a cancer hospital.

A comprehensive infrastructure for clinical and prevention trials will require:

- Availability of sufficiently large numbers of diverse patient groups for clinical research to develop personalized/precision cancer medicine, in case of prevention trials access to large numbers of healthy subjects.
- Molecular pathology including multi-omics technologies and immunotyping for stratification of patients and healthy subjects for distinct treatment arms.
- State-of-the-art infrastructure for early clinical trials, next-generation clinical trials, practice-changing clinical trials and implementation research.
- Follow-up monitoring/treatment adaptation by repeated biopsies and functional/molecular imaging technologies.

Comprehensive cancer centres and CCCoEs (Fig. 2) often fulfil many of these requirements as far as the clinical trial trajectory is concerned. They are further complemented with clinical research networks, many in collaboration with Organisation for the Research and Treatment of Cancer (EORTC), an organization that will play a significant role in this infrastructure. However, CCCs currently lag behind in implementation research, which we consider an essential aspect that needs to be addressed. Prevention research is not sufficiently covered in most CCCs and also requires distinct infrastructures which might vary depending on the nature of the trial. Clearly, it has to include strong

epidemiology, biostatistics, data acquisition capacity and advanced computational capabilities. IARC fulfils a critical international role in this latter domain, and Cancer Prevention Europe (CPE) is expected to make critical EU-focused contributions.

2.3. Infrastructure for outcomes research

Evidence of the effectiveness of therapeutics and prevention strategies is essential for the assessment of clinical utility, cost-effectiveness and prioritization [16]. In addition to showing effectiveness in clinical and prevention trials, evidence of effectiveness in day-to-day clinical practice is required. For therapeutics, data from quality-assured clinical registries are indispensable for evaluating effectiveness. Outcomes research in therapeutics addresses questions related to all aspects of the clinical pathway, including treatment optimization, side effects of treatments, long-term follow-up with assessment of health-related quality of life, rehabilitation and survivorship, as well as attention to social aspects. This should preferably be a collaborative effort between clinicians, researchers and epidemiologists. For prevention, outcomes can be measured using data from population-based registries for cancer incidence and mortality.

Areas of research that need special attention for patients living with cancer are rehabilitation, psycho-oncology, sequelae prevention and supportive care for palliative oncology, as well as survivorship [17]. Since around half of all cancer patients in the EU will ultimately need palliative care (nearly all patients that die

Fig. 2. Overview of Accredited CCCs and Cancer Centres in Europe.

from cancer), this area requires specific attention. Outcomes research has to differentiate between: (a) supportive care when cure is no longer possible but life extension with a good health-related quality of life still is a reasonable goal and (b) palliation at the end of life. Patients with rare cancers and in specific vulnerable age ranges, that is, children and the elderly will need more tailored regimes.

A network of CCCs with consistently structured clinical registries will be instrumental for collecting the necessary data and formulating research questions. By stimulating collaborations between CCCs, the critical mass will be in place for effective outcomes research. The EACS plans together with OECI to identify the criteria for designation of CCCoEs and CCCs, which will be instrumental for Outcomes Research.

A comprehensive infrastructure for outcomes research will require:

- Extensive collaboration among clinicians, epidemiologists and other researchers in CCCoEs, CCCs, clinical cancer centres, universities and other research organizations. Use of networks within networks, an infrastructural model designed by Cancer Core Europe, will be essential for high-quality outcomes research.
- Competencies in epidemiologic theory, biostatistics, bioinformatics, artificial intelligence (AI)—including big data and machine learning—as well as communication technology, which should become an integrated part in many aspects of cancer research, treatment and prevention.
- Well-structured databases with preclinical, clinical and socio-economic data, and data from observational studies (patient registries/databases). These databases, preferentially deposited in EU-controlled data centres, should allow linkage to randomized data platforms. Eligible patients can be invited to participate. State-of-the-art computational tools need to be linked to the databases.
- Pan-European databases on patients with rare cancers. Outcomes research on rare cancers is difficult to achieve in individual countries due to the limited number of cases. The European Reference Networks can play here an important role (https://ec.europa.eu/health/ern/networks_en).
- Complete and updated national cancer registries. The NORDCAN database provides an example of easily accessible data on cancer incidence and death (https://www-ep.iarc.fr/NORDCAN/English/frame.asp).
- Comprehensive and updated national cause of death registries.
- Transparent data-sharing policies. This is a critical prerequisite to perform effective outcomes research.

2.4. Infrastructure models

The models of the infrastructures suggested above can be based on the structures of some existing networks and some key recommendations listed below. CCCs such as those accredited by the OECI [9], the German Cancer Aid [18], or CCCoEs designated by the EACS with focus on translational research [7] will be key components of the three infrastructures. These centres are well-positioned to form networks, both nationally and internationally, and some indeed have done so, both within and beyond national boundaries. Networks composed of CCCoEs, CCCs, cancer research institutes and clinical centres with well-developed integrated basic, preclinical and clinical research, as well as relevant technical platforms, will be important elements of the infrastructures (Fig. 1B). Institutional collaborations will enable the recruitment of sufficiently large patient cohorts, access to biological materials and technological resources, as well as the establishment of sustainable large-scale research programmes. Cancer Core Europe is an example of a translational cancer research consortium for therapeutics [19–21], and CPE an example of a network for prevention research [5,22]. These consortia share common interests, and their close interaction will be crucial to explore the biology underlying known and new causes of cancer. Such interactions can result in new prevention programmes and diagnostic technologies to detect malignant disease at an early stage, thereby permitting treatment that is more effective.

The network model of infrastructures adopted by Cancer Core Europe is based on institutional collaborations (legal entity) among seven large cancer centres across Europe, most of which are CCCs [19–21]. The German Cancer Research Consortium (DKTK) is a national entity linking eight CCCs; moreover, within the frame of the German National Decade against Cancer, a German consortium of six National Centres for Tumour diseases is under development to structure the clinical part of the research continuum as well as a National Cancer Prevention-Development Strategy. Another prime example of a national network is the Cancer Research UK network of 15 translational research centres, which are funded to the tune of €230 million a year (https://www.cancerresearchuk.org/funding-for-researchers/our-research-infrastructure/our-centres) on top of competitive grant funding. A

further example of a national legal entity linking 20 Cancer Centres in France is Unicancer (http://www.unicancer.fr/en/patients/unicancer-charter) furthering translational and clinical research, and clinical improvements. An additional example is the collaborative initiative taken by paediatric oncologists through the European Society of Paediatric Oncology (SIOPE; https://siope.eu/encca/).

2.5. Recommendations for creating the three types of infrastructures for innovative cancer research

2.5.1. Create networks of CCCs and CCCoEs

Today around 35 CCCs are accredited in Europe, 22 by the OECI and 13 by the German Cancer Aid; two CCCoEs are already certified by the EACS (Fig. 2). It is essential to have at least one CCC in each country acting as a nucleus from which expertise and best practices are disseminated within the country, and some larger Member States might need 10 or more CCCs. Newly accredited CCCs, generated through supportive partnership arrangements, should result in networks of CCCs/CCCoEs and other centres (both within Member States and across borders) to innovate and perform high-quality multidisciplinary cancer research and provide high-quality cancer care, including health-related quality of life and survivorship research. They may also conduct prevention research and offer prevention services depending on how health care is organized in each country. CCCoEs, on the other hand, should provide advanced infrastructural facilities. To increase the number of CCCs, institutions that have capabilities to become a CCC or an accredited clinical centre need to be incentivized by establishing funding opportunities to reach the standards required for formal accreditation by the OECI [23]. Countries that do not have CCCs are recommended to establish at least one CCC, through appropriate funding instruments (e.g. cohesion funds).

2.5.2. Generate incentives for 'twinning' a CCC or clinical centre with an established CCCoE or equivalent high-quality centre, to facilitate the training of specialists and researchers

The aim is to increase the knowledge and skills of cancer professionals and to promote research collaborations, thereby boosting healthcare innovation (Fig. 1). 'Twinning' could be initiated from clinical centres (or individuals working in these locations) that aspire to accreditation, or from established CCCs that want to reach out to raise the standards of centres elsewhere. The funding mechanism should be flexible and avoid unnecessary bureaucracy. Examples are already in place: The German Cancer Research Centre (DKFZ, Heidelberg) has twinned with the Athens CCC (http://www.accc.gr/), and the Swedish Karolinska Institute (KI, Stockholm) is in discussion about expanding an existing formalized collaboration with the National Institute of Oncology NIO, Budapest, into a twinning partnership (https://onkol.hu/kutato-osztalyok/?lang=en and https://onkol.hu/department_of_selenoprotein_research/?lang=en). Experiences acquired through these collaborations could help the development of new 'twinnings'. Cancer Core Europe is supporting this development, and the engagement of the recently established Central-Eastern European Academy of Oncology (CEEAO) could play a strategic role in this endeavour (https://hungarytoday.hu/kasler-central-eastern-european-academy-of-oncolog/). The OECI, the EACS and the European Association of Cancer Research (EACR) will be of critical importance in the areas of training and education.

To make an impact, however, the infrastructures need to be sustainable. Only then, a number of such collaborative entities can be created and the inclusion of institutions in all EU Member States secured. The ERA-NET TRANSCAN (https://www.era-learn.eu/network-information/networks/transcan-2), for example, offers a strategy to support international translational cancer research collaborations and will greatly benefit from the proposed infrastructures. Developing and expanding infrastructures will require open access to knowledge, transparent access rules to data, commitment from all Member States, alignment of European and national funding sources, as well as instalment of strong governance and management.

3. Research portfolio: areas of priority

The cancer mission aims to apply and expand present knowledge to reduce cancer incidence and mortality and to improve health-related quality of life by promoting affordable, evidence-based best practices in cancer prevention, treatment and care. Coordinated multidisciplinary research in the consensus areas highlighted below, supported by the networked infrastructures described above, will be necessary to achieve the mission goals.

3.1. Basic and preclinical research

Basic research is essential to enlighten our understanding of the molecular mechanism underlying cancer [24]

Box 1

Recommendations for basic and preclinical research.

- Encourage multidisciplinary projects (cancer biology, chemistry, immunology, radiobiology, engineering, computational science, public health).
- Promote high risk–high return projects.
- Promote research in poor prognosis cancers.
- Engage researchers from all EU countries.
- Use ERC funding paradigms to select the most promising bottom-up proposals.
- Facilitate participation of small and medium enterprises and industry.

and is the engine that fuels innovation in both prevention and therapeutics [1,25]. Our recommendations (Box 1) may help maximize the potential of basic and preclinical research which provide the basis for speeding up the translation of discoveries into clinical and potentially preventive applications that impact patients' lives and benefit society at large.

A number of research areas are expected to have a bearing on the innovation of prevention and therapeutics research. Research towards identification of new causes of cancer through unravelling mechanisms of carcinogenicity, the biology underlying premalignant and malignant lesions, identification and validation of biomarkers for detecting premalignant disease, and elucidation of the role of ageing and comorbidities in the emergence and progression of malignant clones is expected to result in new preventions strategies. In addition, for development of therapeutics with a focus on medical oncology, the following are vital: prediction of antitumour effects and side effects of treatment; development of technologies to stratify patients for treatment; innovation of precision pharmacological monitoring; mechanisms underlying drug and immunotherapy resistance, and how to overcome them; as well as characterization and manipulation of the tumour microenvironment. Innovation in imaging and radiation therapy is dependent on basic/preclinical research [26]. Involvement of computational sciences will gain more in-depth insight into cancer biology and clinical/prevention cancer research.

3.2. Primary prevention

Primary prevention research has provided recommendations to decrease, for example, tobacco smoking, alcohol consumption and exposure to UV radiation by the sun or UV devices and to maintain a normal body weight [27]. Figure 3 puts the preventable fraction of cancers through primary prevention in the context of the increasing European cancer burden. However, implementation is often inadequate [5]. For some preventive measures known to be successful, there are political and societal barriers delaying or even hampering implementation; notably, cigarette smoking remains responsible for almost half of all preventable cancer cases in Europe [22]. For many other known harmful exposures or unhealthy behaviours, the most effective and efficient preventive strategies are not yet identified. Consequently, implementation research is essential to augment the effectiveness of such programmes. Such research should address awareness in society, particularly concerning attitudes and lifestyles, as well as the role of authorities in regulating the consumption of harmful substances and exposure to environmental carcinogens. Additional research areas, such as public health, sociology, and behavioural science, have to be integrated into this research. If behavioural change is the goal of the preventive measures, it is essential to include expertise in these areas (Box 2).

Box 2

Recommendations for primary prevention.

- Support implementation research to enhance the effectiveness and efficacy of prevention programmes that address well-known risk factors (tobacco, UV exposure, alcohol consumption, overweight) and if effective would substantially reduce cancer incidence throughout the EU.
- Support continued aetiological research to uncover new causes of cancer, genetic predisposition and the influence of behavioural and environmental factors.
- Support population health intervention research to develop operational strategies and policies in cancer prevention, for example new primary prevention strategies (vaccination, medical) that are less expensive and easy to implement, independent from the expenditure on health
- Promote research to elucidate the individual and societal cognitive processes behind successful behavioural preventative interventions and to address the socio-economic and commercial determinants of health.care in a particular country.
- Promote behavioural/nudging, area-based/territory-based/community-based intervention research linked to prevention, by engaging scientists from disciplines less represented in cancer research today, such as behavioural, communication and social sciences.
- Overall funding for prevention research must increase substantially, and new areas of research must be included.

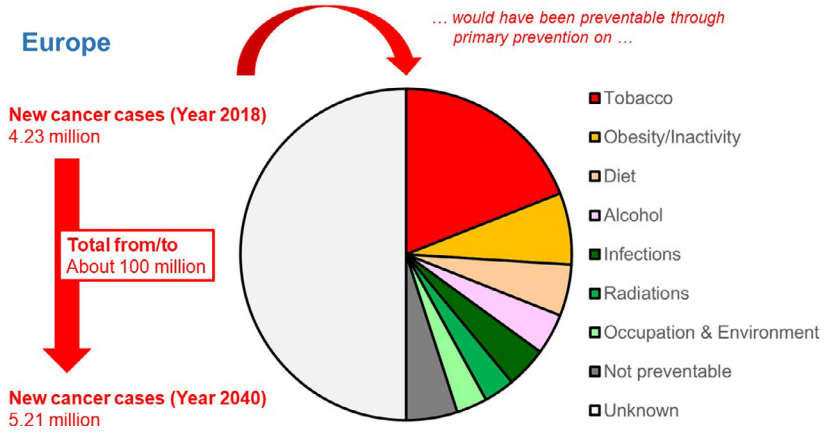

Fig. 3. Newly diagnosed patients with cancer estimated for the year 2018 and projected for the year 2040 for Europe (UN definition), the predicted new cancer burden for the total period from 2018 to 2040, and the preventable cancer burden in 2018 had primary prevention against the listed established causes of cancer been rigorously implemented [22] (Source: J. Schüz—Modifiable risk factors and prevention: overview of current knowledge and main challenges; European Code against Cancer initiative. Health Working Group; Environment, Public Health and Food Safety (ENVI) Committee of the European Parliament, 18/2/2020: https://www.europarl.europa.eu/cmsdata/196417/Schuz_modifiable%20risk%20factors.pdf).

Prevention research should involve identification of causes of cancer and individuals at high risk (exposure and genetic predisposition) using epidemiological research coupled with mechanistic studies, including interactions of risk factors. Research is needed to reduce carcinogenic exposures (environment, workplace) and addiction to carcinogenic substances as well as to uncover underlying biological and social mechanisms. Behavioural research linked to changing lifestyle patterns that increase cancer risk and long-term side effects of treatment and offering active primary prevention (e.g. vaccination, novel targets for medical prevention) is other relevant research areas. Implementation research should be structured and optimized (Box 2).

3.3. Early detection for prevention and treatment

The distinction between early benign disease and premalignant disease likely progressing to invasive/metastatic disease is still difficult [28]. Identification of early markers, obtained from early lesions or liquid biopsies, that predict progression to malignant disease, will be extremely valuable for effectively eliminating malignant disease early. In addition, combining early detection with the identification of individuals at high risk, based on lifestyle and/or genetic predisposition, will enhance the innovation and effectiveness of screening and early detection programmes [29]. Programmes of early detection will be critical particularly within primary- and community care, linked to the expertise and data in specialist centres within networks. The impact of the COVID-19 crisis has already shown large falls in symptomatic presentations to primary care, and screening [30]; (https://www.bbc.com/news/health-52985446). This fragility points to the need for targeted presymptomatic interventions offered to individuals based on risk profile.

Box 3

Recommendations for early detection.

- Critically evaluate currently applied early detection methods and their target populations, and select and promote/disseminate those with proven benefit for broader implementation in the EU.
- Promote biological characterization of premalignant disease that progress to invasive and metastatic cancer.
- Stimulate biomarker discovery and development of diagnostic technologies for early detection of lesions that are likely to progress to cancer.
- Support the development of innovative low-cost devices, methods, and programmes that permit effective early detection with high specificity.
- Develop the concept of prevention screening based on relevant early detection.
- Provide support for their industrial production, testing and validation for use in daily practice.
- Encourage implementation research of early detection programmes, assess participation and analyse factors that affect compliance.
- Analyse clinical effectiveness and health economics of early detection programmes.

Significant research initiatives are already devoted to identify the specific characteristics of early lesions and to develop new diagnostic methods [31]. However, much remains to be learned, and it will require substantial efforts to develop valid predictive diagnostic assays for early detection of malignant disease. Once promising methods are available, well-structured implementation research will be needed to evaluate their effectiveness in screening programmes. Assessment of clinical effectiveness combined with health economics is critical. The outcome of early detection and treatment has to be compared to the outcome of treatment following manifestation of clinical symptoms. This type of information will be necessary to prioritize early detection programmes within the EU and to assure that the most effective screening programmes are rolled out first. In addition, swift access to medical care is essential for individuals experiencing symptoms that warrant further examination. More research on the impact of healthcare systems on early detection is needed. We also need effective approaches to make the population more aware of early signs of disease. Our recommendations for early detection are summarized in Box 3.

3.4. Development of new therapies

The number and proportion of academia-initiated clinical trials (including diagnostics, medical and clinical oncology, radiation therapy, translational associated research, surgery and multimodal treatment) should increase with the specific aim of improving survival and health-related quality of life, with particular emphasis on precision medicine and age/gender-specific aspects. New functional and molecular imaging technologies should be evaluated for effectiveness in clinical trials.

Methodologies for predicting treatment outcomes, both positive and negative, are essential for personalized/precision cancer medicine and already receive ample attention in medical oncology, with focus on anticancer agents and immunological treatments [32,33]. Targeting multiple tumour driving pathways by combinations of targeted drugs applied concurrently or in a specific order may increase the efficacy of treatment by circumventing mechanisms of primary or acquired resistance [34]. Expanding molecular pathology by multiomics technologies to identify tumour drivers and conducting high-throughput functional *in vitro* screens in cells carrying the same lesions might lead to new combination therapies and offer opportunities for drug repurposing [35].

Immunological interventions with checkpoint inhibitors, antibodies, vaccination programmes and cell therapies show ample promise [36–40]. In addition, developments in radiobiology and radiophysics have boosted innovation in radiation therapies; for example, novel fractionated radiation regimens, use of different sources (photons, protons and light ions), or combination with other treatments offer new perspectives [41–45]. Surgical treatment is moving towards technologies with improved preservation of organ function and integration with both radiation therapy and medical anticancer treatment [41,46]. Predicting the best possible intervention will increasingly be guided by big data analyses requiring the contribution of machine-learning algorithms and computational sciences [47].

Early clinical research delivers proof-of-concept outcomes that might have practice-changing potential. However, it requires further studies to assess their potential value for the health care. For wide implementation in the healthcare system, clear criteria need to be defined for outcomes. Clinical effectiveness has to be assessed in regular practice by collecting real-life data through implementation research. Survival benefits linked to information on side effects and health-related quality of life should illustrate the added value compared to current standard treatment. Outcomes of the implementation research should serve as the new gatekeeper when randomized comparative clinical trials cannot be used. Our recommendations for development of new therapies are summarized in Box 4.

3.5. Psychosocial oncology, rehabilitation, and survivorship research

Psychosocial oncology, rehabilitation, and survivorship are closely related areas. As the recommendations for each of these areas show substantial overlap, we describe the relevant issues of each first and then provide an overarching set of recommendations (Box 5).

3.5.1. Psychosocial oncology research

Psychosocial interventions have shown improvement in emotional and social functioning and health-related quality of life in a large meta-analysis [48]. Psychosocial oncology is an essential component within the entire clinical trajectory. Technologies to identify patients at risk for psychological distress and to select the most appropriate intervention strategy need further development. Psychosocial oncology can also play a vital role in addressing lifestyle problems as part of prevention programmes, including tertiary prevention as a part of rehabilitation. Psychosocial interventions encompass many research areas such as behavioural science (psychology), epidemiology, public health science, nursing research, sociology and biostatistics.

Box 4

Recommendations for development of new therapies.

- Increase support to academia-initiated clinical trials (including diagnostics, drug development, radiation therapy, associated translational research, surgery and multimodal treatment).
- Encourage and support research in drug repurposing to find new applications of well-established and widely available generic medicines.
- Adopt existing and create new innovative investigator-initiated trial concepts such as Drug Rediscovery Protocol or basket studies, exploring new engagement paradigms with the pharmaceutical industry.
- Support treatment optimization research to identify the optimal dosage and duration of existing treatments, both for the benefit of patients and to guarantee the sustainability of healthcare systems.
- Improve stratification methods of patients using multi-omics, novel complex multilayer biomarkers based on systems biology models.
- Develop methodologies for predicting treatment outcomes (*in silico* studies).
- Stimulate development and application of new functional and molecular imaging technologies (including radiomics).
- Increase support to already-established multicentre platforms for early drug development.
- Develop new sophisticated *in vitro* and *in vivo* functional screening methods (e.g. Interspaced clustered regularly short palindromic repeats/Cas9 based in preclinical models, i.e. Patient-derived xenografts or organoids) to identify new therapeutic paradigms.
- Support the development of academic cell therapy entities (e.g. Chimeric antigen receptor T cells cell production) to boost further innovation in less toxic immunotherapy approaches.
- Promote integration of advanced computational methods (AI, machine learning) with clinical research.
- Structure implementation research in therapeutics to effectively introduce practice-changing therapies.

Communication with patients and relatives is critical, given the new diagnostic and treatment modalities aimed at personalized/precision cancer medicine [49]. Information for the patients will increase in complexity, making it essential to develop tools to ensure that patients fully understand the options available for informed choices in the context of shared decision-making. Communication with patients is also complicated by the often-conflicting information patients collect from the internet. With the diversification of treatments and growing number of cancer patients with chronic disease, the demand for information will continue to grow.

Developing guidelines and standards for psychosocial care should be an integral part of implementation research for evaluating programme effectiveness; which patients are offered the interventions and how do they perceive the intervention. A range of demographic, cultural/ethnic, social, clinical and intervention-related characteristics can influence the relative effectiveness of psychosocial interventions. Thus, it is important to further develop and test tailored psychosocial interventions that fit the needs of specific subgroups of patients as well as individual patients [48,50]. Research is also needed to identify the psychosocial needs of patients and their families along the entire continuum from diagnosis through treatment and into the survivorship phase.

Although there are a number of well-researched, psychometrically sound and widely used measures for monitoring the symptom burden, psychosocial needs and quality of life of patients with cancer, additional work is needed [51,52]. This work could take advantage of available and emerging technologies, such as the use of mobile devices to detect problems at relevant points in time, and eHealth interventions that make psychosocial interventions more accessible to a larger number of patients at lower costs. A promising development is the use of modern test theory, and particularly item-response theory models and computer-adaptive testing to refine the assessment of patient-reported outcomes at the individual patient level.

Despite a large number of publications, further trials are needed to evaluate the health-related quality of life assessment protocols. Methodological development should focus on new study designs that take advantage of the Internet and wireless acquisition of physical and psychological data. The complexity of assessing health-related quality of life is increasing with the clinical trials methodology weighting more towards personalized/precision cancer medicine [53,54]. The latter is a motivation to conduct more research to develop relevant questionnaires.

3.5.2. Rehabilitation research

Rehabilitation is of vital importance for the outcome after cancer treatment [17]. Rehabilitation should focus

Box 5

Recommendations for psychosocial oncology, rehabilitation, and survivorship research.

- Support methodological development for assessment of health-related quality of life.
- Develop tools to enhance communication with patients and shared decision-making (e.g. increasing patients' access to their medical records via patient portals, development and testing of decision aids for selecting from available treatments).
- Establish international collaboration for developing survivorship-specific patient-reported outcomes in order to monitor the physical and psychosocial health and health-related quality of life of individuals in the post-treatment period. This is a prerequisite for establishing effective programmes to address the individual needs of cancer survivors (e.g. return to work, fertility, sexuality, reconstruction surgery, dental health, cognitive functioning, fear of recurrence, etc.).
- Develop, test and implement apps and wearable devices for effective follow-up monitoring and appropriate interventions.
- Support research to create a comprehensive overview of the negative consequences of a cancer diagnosis and treatment on physical, mental and social health in the short and the long term.
- Develop prediction models for side effects of treatments.
- Support long-term follow-up programmes notably for paediatric and young cancer patients to conduct large-scale, longitudinal, observational studies in distinct cohorts of cancer survivors to better understand their problems and needs.
- Establish and assess outcomes of guidelines to facilitate return to social health, enable reintegration in the workforce and alleviate financial and legal constraints (e.g. life insurance, mortgage).
- Identify health and social inequalities in the cancer survivorship population.
- Initiate research on the economic consequences cancer survivors and their relatives are facing. This should include both direct and indirect costs.
- Evaluate the need for and effectiveness of survivorship care models used in various healthcare systems.
- Conduct research to better understand the causes of differences and discrimination in the survivorship experience between countries and cultures, including financial services such as loans and mortgages.

on three areas: physical, mental health affected by psychological consequences of diagnosis and treatment and, finally, social health (e.g. as influenced by professional reintegration, altered family relationships and financial constraints). High age, comorbidities and frailty [55] are important risk factors for the development of side effects; examples of adverse long-term effects of disease and intervention are treatment-induced cardiotoxicity, neurotoxicity, impaired fertility and sexual problems, cognitive impairment and fatigue. Identification and prediction of side effects and psychological complications can assist in the choice of therapy and therefore represent essential research areas. The latter also holds for identification of the needs for supportive care and psycho-oncological assistance. Research is needed to identify the most effective and efficient intervention strategies for returning to work [10].

For timely detection of complications, long-term follow-up is necessary. Patient-reported outcomes could prove very useful in this regard. Outcomes research should be used for reversed translation to research and design innovative rehabilitation strategies.

3.5.3. Survivorship research

The goal to achieve 10-year cancer survival for 75% of patients by 2030 poses a major medical, socio-economic, legal, as well as a political challenge. We need to articulate the most relevant stigmas associated with cancer and convey the message that cancer is no longer a death sentence with cancer survivors having the right to return to a normal life upon recovery.

Cancer survivorship is strongly influenced by the side effects of treatment with a significant impact on patients, the healthcare system and society overall. Long-term adverse effects have consequences for patients' physical, mental and social health. A review by the former EACS Taskforce on Cancer Survivorship was recently published [56] where survivorship was defined as the phase after active cancer treatment. Survivorship research—the last component of the cancer research continuum and an integrated part of the translational research—has a bearing on the evaluation of multiple outcomes, including symptom burden, functional health, health-related quality of life and socio-economics. Information collected from surviving

cancer patients may help identify and reduce long-term side effects of treatment and improve rehabilitation and psychosocial services.

Closer cooperation between clinicians and patients in multidisciplinary and interdisciplinary survivorship research is needed at a Pan-European level to identify socio-economic inequalities, including disparities among the EU Member States and in particular the Central and Eastern European (CEE) countries. Reintegration in the workplace and social life, as well as equal rights to take out loans and mortgages, is essential study areas. New legal rules that protect cancer survivors against economic discrimination need to be articulated and proposed to the legal authorities.

The increasing cancer survivorship has initiated discussions about the necessity of specialized cancer survivorship clinical structures within or outside the CCCs, to address the need for infrastructures/facilities for long-term follow-up and support of cancer survivors [17]. Long-term follow-up is particularly relevant for paediatric and young cancer patients. The development of patient-reported outcomes surveys tailored to the cancer survivor population is required to ensure that chronic physical and psychosocial health needs can be addressed in an effective and timely manner [57].

3.6. Palliative oncology

Supportive care is multidisciplinary and must accommodate the patient's needs. With cancer increasingly becoming a chronic disease following continuous or intermittent treatments, supportive palliative care is crucial until end-of-life palliation. Improved therapies translate in life prolongation, but also cause side effects that need recognition, as the overall goal is life prolongation while maintaining a good health-related quality of life.

Emerging evidence suggests that early integration of palliative and oncological care improves symptom control, health-related quality of life and even entails a significant life prolongation [58–60] and higher satisfaction among caregivers [61]. Currently, there is a need to establish supportive care teams or home care teams with expertise not only in caring for the dying patient, but also to address problems, symptoms and side effects associated with palliation among patients surviving for months or years [62]. Our recommendations for palliative oncology are detailed in Box 6.

Development and validation of health-related quality of life assessment methodologies—including psychosocial or existential aspects relevant to patients with severe complications of late-stage cancer—are urgently needed. Advances in preclinical research might also help to mitigate symptoms, especially in patients with pain or cancer cachexia.

3.7. Paediatric oncology

Across Europe, there are more than 35 000 new paediatric cancer cases annually and > 6000 children and adolescents dying from cancer each year. Two-thirds of the almost half a million childhood cancer survivors in Europe live with the long-term effects of treatment, which can be severe, affecting their daily lives and socio-economic participation [63]. While there are interactions across the age spectrum, childhood cancers have a unique set of challenges compared to adult cancers, including the specific types of cancers, the underpinning biology, the clinical pathways, the long-term physical and psychosocial impact and, crucially, the long-term support of a sick child by their family.

Childhood cancer accounts for 20% of childhood deaths after infancy and is the leading cause of child mortality from disease in Europe [64]. The European paediatric oncology community already has an extensive track record in the successful delivery of innovative research and clinical strategies from strong collaborative research networks that have markedly improved outcomes. The improvements in the diagnosis and treatment of childhood cancers over the past four decades were built on a strong foundation of cross-border, multidisciplinary, international research, more recently supported by EU Framework funding programmes.

These established, integrated research and clinical networks are well-positioned to deliver a further ambitious and integrated programme of international research. The launch of the European Reference

Box 6

Recommendations for palliative oncology.

- Increase research efforts to evaluate the optimal organization of supportive care because emerging cancer treatments often permit a substantial life prolongation.
- Integrate supportive care teams or home care teams into oncological care; implementation should depend on proven clinical effectiveness.
- Promote development and assessment of educational programmes teaching palliative care professionals how to recognize and mitigate potentially life-threatening side effects resulting from specific treatments (targeted drugs, immunotherapy).

Network for Paediatric Oncology (ERN PaedCan) in March 2017 heralded the start of a framework for national healthcare systems to cooperate in the care of children with cancer. International cooperation is essential in the complex and rare disease setting that characterizes childhood cancers. The ERN PaedCan infrastructure enables access to state-of-the-art diagnostics and treatment and facilitates cross-border exchange of disease-specific expertise. Further building on this infrastructure will reduce the current inequalities in childhood cancer health care, while also providing a scaffold to integrate research networks (Box 7).

In 2015, SIOPE, in partnership with the patient advocate groups Childhood Cancer International-Europe and Unite2Cure, published a detailed long-term strategic plan focused on health care and research initiatives to increase survival and the quality of life for children and adolescents with cancer in Europe by 2025 [65]. This strategic plan is evolving to keep pace with emerging innovations and should become part of a European mission to beat cancer. Focus on innovative therapies including precision medicine, next to further research in the biology of paediatric tumours, is an important goal. In addition, equal access to the standard of care and specific attention to teenagers and young adults is an important goal as well as more attention for survivorship issues.

Box 7

Recommendations for paediatric oncology

- Support of paediatric cancer projects by investment in research and innovation to specifically combat childhood cancer and reduce disparities.
- Invest in an integrated programme of research to realize the seven key objectives of the SIOPE strategic plan:

  i Innovative therapies
  ii Precision medicine in health care
  iii Increase biology knowledge of paediatric tumours
  iv Increase equal access to standard care, expertise and clinical research
  v Address the needs of teenagers and young adults
  vi Improve the quality of survivorship
  vii Understanding the causes of paediatric cancers and addressing prevention where possible.

3.8. Geriatric oncology

Cancer is a group of diseases mainly affecting individuals at an advanced age, with diagnosis usually above 60 years and death above 70 years. Ageing and cancer are both associated with the accumulation of mutations in DNA [66], and, among other changes, ageing affects the hematopoietic clonal heterogeneity (designated either as ARCH for age-related clonal haematopoiesis or as CHIP for clonal haematopoiesis of indeterminate significance).

Clones defined by mutations in proto-oncogenes and tumour suppressor genes accumulate in most tissues with ageing, including skin [67], oesophagus [68,69], liver [70], colon [71], lung [72] and many others [73]. In the oesophagus, for example, a strong positive selection of clones carrying mutations in distinct cancer genes was identified. With ageing, these clones cover much of the epithelium, with *NOTCH1* mutations affecting up to 80% of cells. Surprisingly, their prevalence is higher in normal tissue than in oesophageal cancers [68].

Widespread positive selection of mutant clones may contribute to tissue ageing by negatively affecting tissue function. Toxic exposures will further increase the mutational burden, as observed in the bronchial epithelium of tobacco smokers [72] and hepatocytes of cirrhotic patients [70]. Furthermore, cells might also become senescent [74]. And although no longer capable to divide, these cells can create an inflammatory environment promoting tumour progression [74].

Currently, many research questions are linked to mutation load and ageing, as well as senescent cells that accumulate during ageing and are associated with a distinct secretory phenotype. These age-related changes undoubtedly also influence cancer therapy. Therefore, more information is needed regarding the relationship between ageing and cancer (Box 8). We also need to understand how ageing affects treatment feasibility and efficacy and to what extent cancer and cancer treatment accelerate ageing. Targeting senescent

Box 8

Recommendations for geriatric oncology.

- Support basic research aiming at understanding the links between ageing and cancer.
- Support clinical research in elderly to optimize treatment.
- Develop instruments, for example frailty scales relevant for oncologic patients, and methods of data collection for assessment of health-related quality of life in geriatric cancer patients, with an eye for their often-extensive comorbidities.

cells may become a therapeutic strategy to either prevent or treat cancer as well as to mitigate other chronic diseases (Box 8).

High age and comorbidities are regularly exclusion criteria in clinical trials. As a result, we often lack evidence on treatment benefits among older patients. There is a need for clinical trials that analyse dose escalation and de-escalation, combinations therapies, the impact of comorbidities and the influence on health-related quality of life (Box 8).

3.9. Outcomes research

Outcomes research is essential for assessing the degree to which the goals and objectives of a cancer mission are achieved (Box 9). We need to select robust methods to follow the expected reduction in mortality and increase in long-term survival. We also need methods to compare outcomes of EU countries and monitor whether inequalities indeed decrease. Outcomes research linked to health economics is fundamental for priority setting with an important role for patients/patient organizations. Lead-time bias due to early detection and overdiagnosis of nonlethal cancer has to be taken into consideration when survival benefits are analysed. Interpretation of trends in cancer patient survival is indeed challenging and never straightforward [75]. There is a need to define time frames for short-term (5 years) and long-term goals. Increases in the 10-year survival rate among patients diagnosed through 2030 will be impossible to assess until 2040.

Outcomes research has been a missing element in large parts of translational studies (see the chapter on infrastructures). CCCs should contribute with quality-

Box 9

Recommendations for outcomes research.

Different domains of cancer need definition of distinct outcome parameters. No outcome will be relevant to all. The main domains are cancer therapeutics and prevention.

1) Cancer therapeutics

a) Short-term

- Assess clinical effectiveness of innovations—in combination with health economics analyses as a 'gate keeper' before implementation into the healthcare system.
- Monitor the percentage of patients in clinical trials and compare outcomes for patients in and outside clinical trials.
- Study short-term overall survival to mitigate effects of lead-time bias and possible overdiagnosis.

b) Long-term

- Study 5- and 10-year overall patient survival to mitigate effects of lead-time bias and possible overdiagnosis.
- Study 5- and 10-year cancer overall mortality and cancer-specific mortality (rate of death of cancers in the population, stratified by age and gender, and other relevant risk factors).
- Assess all-cause mortality (although new treatments may not reduce all-cause mortality, all-cause mortality should be used as an endpoint to ensure that harms of the new treatment do not affect other causes of death).
- Determine health-related quality of life after 5, 10 years and longer.

2) Prevention

a) Short-term

- Assess population receptivity to prevention interventions.
- Assess the potential impact of intervention programmes on the prevalence of behavioural risk factors for cancer, such as smoking, alcohol consumption, obesity (of the whole population) as a function of intervention programmes.
- Monitor the percentages of patients and individuals included in behavioural research and in prevention trials or other studies aiming at reducing the cancer burden.

b) Long-term

- Assess trends in cancer incidence, cancer mortality and overall mortality.
- Study effects of cancer prevention strategies on mortality in the population.

assured and consistently structured clinical registries to monitor assessment of clinical effectiveness of implementation, including documentation of reproducibility of research outcomes in clinical practice. Outcomes research is also needed to demonstrate the effectiveness of prevention initiatives. The OECI has started programmes for the development of outcomes research, and health services research, within its constituent CCCs. In addition, the German Cancer Research Consortium has an expanding clinical database bringing together the information of eight of the leading German CCCs.

Implementation of personalized/precision cancer medicine requires scientific evidence on an increasing number of subgroups based on new molecular pathology/genomics diagnostic technologies. Even for common tumours, the large number of subgroups will offer challenges similar to those in studies of rare cancers; for future studies to be informative, international collaboration will often be a prerequisite, so that patient numbers are sufficiently large for reaching statistically robust conclusions.

Outcomes research should be classified into short-term and long-term assessment for cancer care, including therapeutics (Box 9). Benefits of prevention, on the other hand, can be meaningful to assess only as a long-term effect, although short-term outcomes may guide quality assurance and acceptability in the population. Valid outcomes research requires high-quality data (see above) and the ultimate outcomes are cancer incidence, mortality and overall survival of cancer patients.

Many population screening programmes to detect and prevent cancer early may result in healthy individuals undergoing unnecessary tests and treatments [76]. Early detection screening, such as prostate and breast cancer screening, increases the recorded incidence of cancer [77,78]. Prevention screening such as cervical and colorectal cancer screening increases the incidence of precursors (cervical intraepithelial neoplasia for cervix and colorectal polyps for colorectal cancer) but decreases the incidence of invasive cancer. Efforts should be made to improve the prognostic value of cancer screenings and reduce the burden for the individual: to do more good than harm—'less tests less treatments'.

3.10. Health economics

New possibilities for cancer prevention, diagnosis and therapies usually come from findings resulting from public and private investments in medical research [16]. Their numbers rise rapidly, making informed choices necessary. This leads to an increased interest in clinical and cost-effectiveness research. The impact on population health depends on what one pays for in the different European healthcare systems. Current data reveal significant differences in inputs and outputs, and this is reflected in the performance measures [79]. Health economics studies the unavoidable choices between different alternatives when resources are limited. European healthcare systems differ with respect to available resources for cancer care and how those resources are used, but they share the same objectives of improving outcomes for cancer patients. Development and sharing information for making the best use of available options given limited resources for cancer care are a common interest.

The objective of a mission-oriented approach to cancer research in Europe is to improve health outcomes for cancer patients through the development and introduction of new methods for prevention, early diagnosis and treatment of the disease, using surgery, radiotherapy and cancer medicines. Health economics includes the study of the efficiency and equity of resource allocation to and within cancer care. A key point in the translational research process is when decisions are to be made about pricing and reimbursement for the introduction of a new method or drug in clinical practice in different countries. Decision-makers, including public payers, clinicians and patients, should have accurate information about clinical effectiveness, costs and overall value of the new method/drug to decide about use and payment. These decisions are not only important for improving outcomes for patients and healthcare efficiency, but also for the research community in prioritizing investments in the development of new methods.

Often robust data on clinical effectiveness and value for patients of new methods compared to existing alternatives are lacking. For example, the number of new cancer medicines increases fast. But there is rather limited information from clinical trials on outcome parameters, as compared to alternative treatments [80]. Follow-up studies in clinical practice have serious shortcoming in terms of data on patient characteristics and methodology and thus not fulfilling their potential to contribute to evidence generation and improvements over time [81]. The latter is a problem that cannot be mitigated by more sophisticated health technology assessment methods. The potential consequence is the introduction and regular use of methods and medicines that have little or no value, or a delay in the introduction of new treatment regimens that do improve outcomes for patients.

At present, we have also incomplete information about cost-effectiveness of resources used to treat

cancer [82]. Data are lacking about the resources spent for different types of cancer care and for different groups of patients and how this affects outcome.

Therefore, decision-makers, including public payers, clinicians and patients, need better information about the potential clinical effectiveness and value of the new method in order to make decisions about their use and reimbursement. Health economics needs to be included as an integral component of the translational research pathway. Therefore, research including aspects of SES (socio-economic status) is important in order to promote equal access to cancer care. Without public reimbursement through taxes or public health insurance, appropriate cancer care is not affordable for the general public. The pricing and budget impact of cancer medicines on the healthcare system poses a particular challenge and requires close monitoring of objective benefits and costs and patients should be involved in health economics research at all levels. Our recommendations for health economics implementation are summarized in Box 10.

Box 10

Recommendations for health economics.

- Make the collection of data for an assessment of cost-effectiveness a mandatory part of all clinical research projects aimed at developing new preventive or therapeutic methods within the cancer mission.
- Evaluate already existing methods (in fact deferred maintenance) as a validated reference.
- All applications for clinical research grants should include a statement of how the project will contribute to the objectives of the mission, and a plan for how the impact should be assessed.
- Support the development of a database carrying the relevant information to appraise cost-effectiveness of preventive and therapeutic innovations.
- Support the advancement of methods that assess the social value of cancer care beyond aggregate gains in length and quality of life of patients, that are relevant for decisions about allocation of resources for cancer; severity of disease condition; necessity of intervention; prevalence of the condition; and impact on caregivers and dependents of patients.
- Install a task force that continuously evaluates and reports on the cost-effectiveness of new innovations in prevention and therapeutics, as information to healthcare systems to decide on adoption and reimbursement. The task force should also assess if the cancer mission research programme achieves its objectives.

3.11. Big data and computational science

EU-wide population databases will be indispensable for answering some of the questions listed above, including comparative research between geographically distinct regions in Europe. This requires consistency in institutional clinical registries that need to be based on standardized patient records with genomic/molecular marker information, providing opportunities for specific studies such as Outcomes Research and Health Economics Research as outlined above. Assessment is needed of the value, validity and reliability of voluntary patient-reported data uploaded to a single EU digital centre and its compatibility with privacy and 'droit d'oublier' requirements. There is also much work to be done on how to aggregate detailed datasets for research purposes, while guaranteeing patient anonymity. Work is also needed to develop AI paradigms for mining data to identify new correlations and meaningful algorithms (improvements in predicting response, relapse and side effects). Sophisticated diagnostic methods and algorithms to interpret them are needed to select the most promising cancer therapy for individual patients (e.g. to avoid the commonly observed selection of resistant clones [83–85]. Our recommendations on big data and computational science are summarized in Box 11.

Box 11

Recommendations for big data and computational science.

- Stimulate introduction of AI/machine-learning approaches in multiple areas: image analysis, whole-genome sequencing, patient-reported outcome information, clinical record datasets, lifestyle parameters, prevention measures and early detection.
- Define the core data records that should be collected from every patient, complemented with predefined disease-specific and patient-specific records, on the assumption that certain data stay in the treating institution unless that patient gives permission for wider use.
- Explore whether patient-initiated data sharing provides an option to create large well-accessible and reliable datasets without violating existing privacy rules.
- Offer practical training courses focussed on acquiring new computational skills relevant for research and clinical care.
- European data protection policies need to prevent the misuse of data without restricting the use of data.

4. Patient empowerment

The primary focus of patient empowerment is on improving the healthcare systems, so that the patient is at the centre of shared decision-making.

The cancer mission aims at covering the entire research continuum. By definition, translational cancer research has a focus on patients and individuals at risk and strives to improve all aspects associated with the consequences of a cancer diagnosis. In traditional research, patient participation was largely limited to being the subject of research. Currently, there is a significant cultural shift that increasingly ensures that real-life experiences of patients are considered when determining priorities in research areas [86].

Patients that actively participate in research focused on unmet needs develop increased self-confidence, and a more robust advocacy voice, making them feel more empowered, valued and respected. Early patient involvement in research offers opportunities for identifying and influencing research questions and defining meaningful study endpoints. Patient empowerment, as far as cancer research is concerned, is mostly related to unmet needs of patients.

Comprehensive cancer centres integrate care, prevention, research and education enabling innovation in multidisciplinary care. Patient perspectives are important, and since assigning priorities to projects is unavoidable, patients should be represented in CCC boards, while CCC leadership also establishes formal interactions with patient organizations.

The integration of patient advocacy in the full spectrum of childhood cancer research and multidisciplinary care is exemplified by the partnership between ERN PaedCan and the CCI-Europe, the primary patient and survivorship organization in Europe. CCI-E representatives are core members of the Network's Oversight Committee, as well being intrinsic to the implementation of the ERN's objectives at the national level.

It will be necessary to involve patients' representatives in the governing bodies of all consortia and infrastructures mentioned earlier in this article. Similarly, patients and patient organizations should have a role in the different project areas suggested above (Box 12).

5. Specialist education

Education must cover all components of the cancer research/care/prevention continuum and be accessible to researchers and cancer specialists from all EU countries to reach the goals of the mission on cancer [87]. Leading European cancer organizations [EACR, EACS, European CanCer Organisation, ECPC, European Molecular Biology Organization (EMBO), EORTC, European Society for Medical Oncology (ESMO), European Society of Surgical Oncology,

Box 12

Recommendations for patient empowerment.

- Support primary and secondary prevention with a focus on individuals with modifiable risk.
- Involve patients and patient organizations in prioritizing therapeutic research areas.
- Support rehabilitation research, and research focussing on health-related quality of life issues (supportive care, psychosocial oncology, palliative care and survivorship) including patients and families for shared decision-making.
- Involve patients and patient advocacy organizations in prioritizing research areas in outcomes research and health economics. This should also include assessment of the socio-economic impact on patients and their families (/households/relatives/dependents and caregivers), and the identification of patient groups particularly vulnerable to impairments of their socio-economic situation due to cancer and cancer care.
- In areas where research focuses on how to decrease present inequalities, patients and patient organizations should be enabled to play a pro-active role.
- Shared decision-making should ensure that all medical and social consequences of a cancer diagnosis are considered.
- Education is a prerequisite to reach the goals of the mission. Both European Cancer Patient Coalition (ECPC), Association of European Cancer Leagues and SIOPE have extended educational programmes for patients, relatives and the public. Increase collaborations with CCCs and consortia of research centres will be necessary to further expand the educational activities.
- Communication and diffusion of information are vital to bring science and technology to society and to emphasize their importance for generating science-driven and social changes that impact the lives of patients. The mission governing body, cancer patient organizations, national cancer societies, universities and hospitals, policymakers as well as the press, should broadly disseminate the information.

European Society Radiotherapy and Oncology, Federation of European Biochemical Societies and SIOPE] regularly organize conferences and support educational courses. In addition, Cancer Core Europe organizes an annual Summer School for Translational Cancer Research, the OECI focus on the comprehensiveness of cancer care and the ECPC on education centred on patients and their relatives. Trainings in cancer prevention are currently organized irregularly and would benefit from a more systematic approach, both reaching out to medical and public health professionals.

An inventory of educational activities within the EurocanPlatform project revealed an impressive amount of educational activities in 23 participating cancer research centres (https://cordis.europa.eu/project/id/260791/reporting). Making courses accessible to students and professionals from all Member States will increase knowledge and promote networking. Exchange of researchers will foster new research collaborations in consortia of cancer centres. Furthermore, the twinning of centres can greatly help in disseminating expertise and establishing a critical research culture. Implementing our recommendations as outlined above and summarized in Box 13 will decrease inequalities across EU countries and facilitates capacity building. Specific educational programmes targeting the next generation of leaders will support sustainability and increase interaction between research centres as exemplified by Cancer Core Europe.

6. Inequalities in research

Emphasizing the link between cancer outcomes and research activities, the EC recognized that increasing the quality and quantity of research capacities is needed to improve outcomes for cancer patients with specific attention to high-risk individuals in the Member States (https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/SPH_VisionPaper_02062016.pdf) [88].

Box 13

Recommendations for specialist education.

- Establish recurrent educational and scientific conferences prepared by the organizations mentioned above.
- Organize theoretical training courses.
- Create a new European comprehensive culture of education, training and lifelong learning.
- Extend the reach of educational courses by arranging participation also through the internet.

To reduce disparities with the primary aim to improve patient survival as well as the health consciousness in the Central and Eastern EU region, Prof Miklós Kásler, Minister of Human Capacities, Hungary, took the lead in bringing 21 countries together. His initiative resulted in the foundation of the CEEAO, within which institutions join forces in fighting cancer in a population encompassing 260 million people. In January 2020, the governing council and the scientific advisory board of CEEAO were elected at its general assembly in the Hungarian Parliament. The organization aims at harmonizing cancer control plans in the region with a focus on cancer care, prevention and education. As an example of a well-functioning consortium within the region under the umbrella of CEEAO, the wide-ranging, coherent activities of Central-Eastern European countries within the Central-Eastern European Breast Cancer Surgical Consortium are worth mentioning. The ERN PaedCan has already achieved at least one 'node' per country in Central/Eastern Europe for development of paediatric oncology.

Despite the presence of excellent basic and clinical research in some areas, translational research activities largely suffer from insufficient funding and limited collaborative activities in the Central and Eastern EU region [89]. For example, a dedicated cancer research fund is not available in many countries. In addition, the number of clinical trials (in particular early clinical trials and investigator-initiated trials) is lagging in this region [90]. Hence, innovation in prevention, early detection and treatment could have a significant impact on cancer incidence and survival in many Central and Eastern European countries. To this end, tighter collaboration between clinical and basic research activities should be enabled primarily by strengthening the scientific activities of accredited cancer centres.

Our recommendations for addressing inequalities in cancer research are summarized in Box 14. As noted above, the OECI's and EACS's accreditation and designation programmes should serve as primary quality control of translational cancer research and its integration into high-quality patient care in Europe. CCCs accredited for their care, research and education should play a central role in fulfilling the aims of the cancer mission. In parallel, the accreditation programme intrinsic to the ERN PaedCan is driving quality for research for cancer in children and young individuals. These entities constitute the powerhouses not only of high-quality cancer research in Europe; they also provide the best opportunity and model for a strong interaction between research and multidisciplinary health care, a pivotal element to ensure that innovations benefit patients.

Box 14

Recommendations for addressing inequalities in cancer research.

- Strengthen Central-Eastern European cancer centres with effective utilization of OECI's Accreditation and Designation programme, and EACS's Designation of Excellence (DoE) programme via collaboration with the CEEAO.
- Extend and strengthen the Paediatric Cancer Expert Reference Network to be accessible to children with cancer throughout Europe. Promote concentration of paediatric cancer research and care where feasible.
- Support cancer research activities that address region-specific issues in cancer care, prevention, research and training within Europe.
- Open dedicated calls for proposals in the Central-Eastern EU region to decrease inequalities in basic, clinical and translational cancer research.

Out of the 40 OECI accredited centres, 22 hold the CCC designation and 18 are designated as clinical 'Cancer Centres' (CC), which represent recognized, high-quality clinical centres, although with significantly less research output. Inequalities become immediately evident by the geographic distribution of these accredited cancer centres because out of the 40 OECI accredited centres, there is only one OECI accredited CCC and five accredited CCs in the Central-Eastern EU region (Fig. 2). The ERN PaedCan unites 57 Full Members from 18 countries and a further 12 Affiliated Partners from eight countries (Fig. 4).

7. Relationship between the cancer mission and Europe's Beating Cancer Plan

The decision to support European cancer activities with both a European Beating Cancer Plan (https://ec.europa.eu/health/non_communicable_diseases/cancer_en) and a cancer mission is timely and strategically relevant. There are apparent inequalities both within and among EU countries concerning cancer treatment, or care, and cancer prevention. For example, access to early detection programmes, advanced diagnostic methods, immunotherapy, precision medicine, state-of-the-art surgery, radiation therapy, functional/molecular imaging or rehabilitation is highly variable. The EU project European Network for Cancer Research in Children and Adolescents (https://siope.eu/activities/eu-projects/encca/) also demonstrated significant inequalities in paediatric oncology between EU countries. The Europe's Beating Cancer Plan will be valuable to coordinate national cancer plans to make better use of evidence-based cancer treatment/care and prevention. The latter will mitigate inequalities by supporting national programmes for equal access to cancer patients and survivors.

8. Concluding remarks

A comprehensive translational cancer research approach that is focused on personalized/precision medicine and covers the entire cancer research-prevention-care continuum has the potential to achieve in 2030 the goal of a 10-year cancer-specific survival for 75% of the patients diagnosed in EU Member states with a well-developed healthcare system. Expected effects of primary prevention on incidence and mortality is a more long-term goal to be assessed by age-standardized mortality monitoring. Concerted actions across this continuum that spans from basic and preclinical research through clinical and prevention research to outcomes research, as well as the establishment of high-quality networked infrastructures will pave the way not only to clinical innovation, but also to the mitigation of economic and social inequalities across European countries.

Here, we propose the establishment of three types of infrastructures focusing on translational research, clinical and prevention trials, and outcomes research. These infrastructures, embodied in CCCs or CCC-like entities, will provide researchers with access to a critical mass of patients, biological materials and technological resources, bridging research and health care. The latter will warrant that future scientific and social innovations benefit cancer patients across the healthcare systems in Europe.

We prioritized 13 research areas to achieve a balanced research portfolio, namely: basic and preclinical research; primary prevention; early detection for prevention and treatment; development of new therapies; psychosocial oncology, rehabilitation, and survivorship research; palliative oncology; paediatric oncology; geriatric oncology; outcomes research; health economics; big data and computational science. We have worked together to provide recommendations for each of the above areas; these recommendations will be, in our view, important for achieving key targets. We also offer suggestions as to how to strengthen patients' empowerment, improve specialist education, and decrease present inequalities in cancer research within the EU.

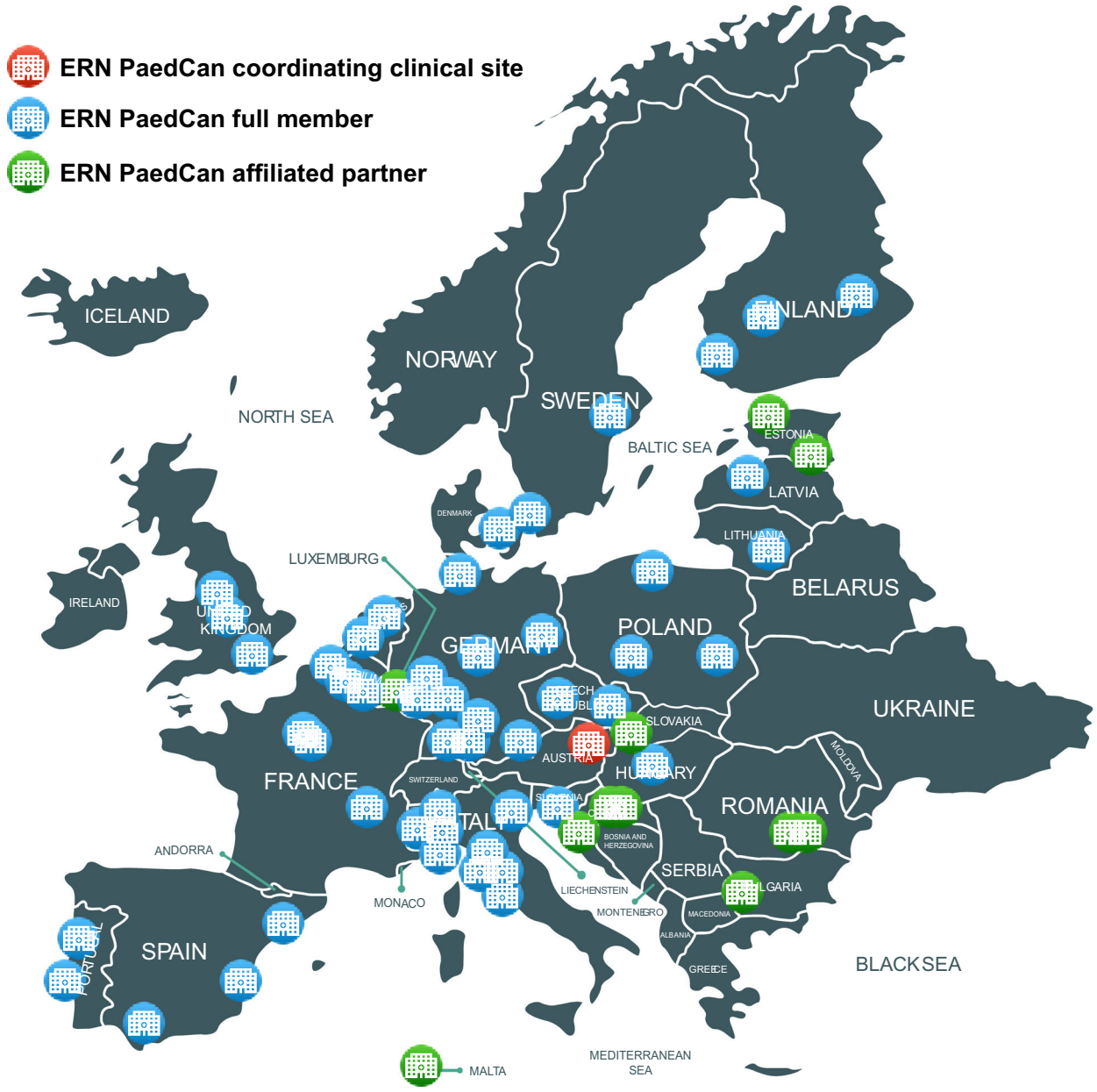

Fig. 4. ERN PaedCan Network for paediatric cancer. Distribution of members over Europe.

Meeting key objectives will require further harmonization of EU and national priorities and policies, improved research coordination at the national, regional and EU level, as well as more efficient and flexible funding mechanisms. It is also crucial to ensure the sustainability of trans-border infrastructures and networks, for example through long-term support directly by the EU, or other schemes to which Member State countries commit. It will require political will and perseverance to bridge the gaps in science, society and policy that affect cancer treatment and care [91]. Science policy is often developed in isolation [91]; therefore, it will be crucial to engage policymakers and to ensure that all the relevant stakeholders along the entire research–care–prevention continuum speak with a single voice to provide evidence-based advice to inform policy [25,91]. In addition, careful forward planning will be pivotal to ensure a successful outcome.

A concerted cancer science policy in Europe is an unmet need [91]. Appointing a policy board with multiple competencies will be necessary to identify the best strategies to implement the comprehensive range of activities necessary to accomplish the mission goals.

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Conflict of interest

In the past 5 years, Dr. Baumann attended an advisory board meeting of MERCK KGaA (Darmstadt), for which the University of Dresden received a travel grant. He further received funding for his research projects and for educational grants to the University of Dresden by Teutopharma GmbH (2011–2015), IBA (2016), Bayer AG (2016–2018), Merck KGaA (2014–2030), Medipan GmbH (2014–2018). For the German Cancer Research Centre (DKFZ, Heidelberg), Dr. Baumann is on the supervisory boards of HI-STEM gGmbH (Heidelberg) and is also member of the supervisory body of the Charité University Hospital, Berlin. Dr. Baumann, as former chair of OncoRay (Dresden) and present CEO and Scientific Chair of the German Cancer Research Centre (DKFZ, Heidelberg), was or is responsible for collaborations with a multitude of companies and institutions, worldwide. In this capacity, he has signed/signs contracts for his institute(s) and for the staff for research funding and/or collaborations with industry and academia, worldwide, including but not limited to pharmaceutical corporations like Bayer, Boehringer Ingelheim, Bosch, Roche and other corporations like Siemens, IBA, Varian, Elekta, Bruker and others. In this role, he was/is further responsible for commercial technology transfer activities of his institute(s), including the DKFZ-PSMA617 related patent portfolio [WO2015055318 (A1), ANTIGEN (PSMA)] and similar IP portfolios. Dr. Baumann confirms that none of the above funding sources was involved in the preparation of this paper.

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Carolina Espina and Joachim Schüz state: where authors are identified as personnel of the International Agency for Research on Cancer/ World Health Organization, the authors alone are responsible for the views expressed in this article, and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/ World Health Organization.

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Author contributions

All authors contributed to the preparation of the manuscript.

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Theoretical and practical knowledge curriculum for European Breast Surgeons

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EXECUTIVE SUMMARY

The Breast Surgery theoretical and practical knowledge curriculum comprehensively describes the knowledge and skills expected of a fully trained breast surgeon practicing in the European Union and European Economic Area (EEA). It forms part of a range of factors that contribute to the delivery of high quality cancer care. It has been developed by a panel of experts from across Europe and has been validated by professional breast surgery societies in Europe. The curriculum maps closely to the syllabus of the Union of European Medical Specialists (UEMS) Breast Surgery Exam, the UK FRCS (breast specialist interest) curriculum and other professional standards across Europe and globally (USA Society of Surgical Oncology, SSO). It is envisioned that this will serve as the basis for breast surgery training, examination and accreditation across Europe to harmonise and raise standards as breast surgery develops as a separate discipline from its parent specialties (general surgery, gynaecology, surgical oncology and plastic surgery).

The curriculum is not static but will be revised and updated by the curriculum development group of the European Breast Surgical Oncology Certification group (BRESO) every 2 years.

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[1] See Appendix.

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1. BRESO mission statement

1.1. Training

Currently training across Europe in Breast Surgery is very heterogeneous with training hosted by general surgeons, gynaecologists and plastic surgeons. In general, training certification is achieved after 4–6 years of residency training, which is usually of mixed content, so for general surgery, residents will rotate through colorectal, upper GI, endocrine, breast and often vascular surgery with a substantial emergency surgery component. For gynaecology, rotation will include urogynaecology, breast, oncology, obstetrics etc as well as emergency work. Similarly for plastic surgery (rotations will include trauma, breast reconstruction, skin cancer, soft tissue sarcoma etc). Consequently at the time of certification, many surgeons will have spent very little time doing breast surgery. In some instances only a few months of residency training will be spent in breast surgery but the surgeon will be able to undertake breast surgery once certified.

Historically (40 years ago) breast surgery was quite simple, with all women treated with mastectomy and axillary clearance with no reconstruction and simple adjuvant therapy regimes. Modern breast surgery is now highly complex from both a surgical and oncological stand point and such limited training is not adequate for modern breast practice. Ideally, breast surgery training for those declaring a special interest during residency would be integrated at a high level into the 4–6 years of residency. Residency training programmes across Europe therefore need to recognise this need and move towards this model, as has happened in the UK already. However, this will take time and in the interim, BRESO proposes that all surgeons practicing breast surgery in Europe should be certified in breast surgery, by means of undertaking high level training either within their residency (if available) or by means of approved specialist fellowships. Certification will be based on the following (see Fig. 1):

1. Acquistion of knowledge as demonstrated by passing approved examinations.
2. Acquistion of practical skills as demonstrated by a certified period of training in an approved breast unit and by review of a signed log book.
3. Following completion of training and certification (as above) all breast surgeons should engage with on going continuous professional development (CPD) and apply for re-certification at

Fig. 1. Summary of measures to ensure high quality clinical practice for health care professionals.

intervals of 5 years by submission of proof of approved course attendance. Such courses should be evidence based, free from commercial bias and of high quality.

By these means BRESO will enhance and harmonise breast surgery training and practice across Europe, improving standards from the current very variable levels. Patients will also have a means by which to reassure themselves about the provenance and skills of their breast surgeon by using the BRESO searchable directory of certified breast surgeons.

To do so, it is proposed that breast surgeons should have undertaken a minimum of 2 years training in breast surgery (see Table 1 in the section below 'Proposed temporal patterns of breast training'). Twelve to 18 months of this may be in a breast unit practicing intermediate level care, exposing trainees to wide local excision (WLE), sentinel lymph node biopsy (SLNB), axillary clearance and mastectomy, with good MDT working (tier 1 training centres, basic training). This will enable trainees to develop basic skills and a broad understanding of the subject. This may either be during or after residency (certification) or a mixture of the 2. However in addition, a period of high quality training in a specialist breast center is required where higher level skills will be attained such as oncoplastics, reconstruction (although not necessarily practical expertise in all countries), research literacy, oncology and genetics. These latter centres (tier 2 training centres, advanced level skills) will need to be quality assured (for example EUSOMA certified). This training may be post-residency (certification) in most countries to allow full immersion in breast surgery without the distraction of emergency surgery and other specialist subject areas, unless such a specific post can be arranged during standard residency training (as in the UK where Oncoplastic training is a routine part of training for breast specialists). As a result, surgeons will be expected to have acquired a minimum number of procedures to the level required for post-residency practice, certified by a recognised trainer.

Tier 2 training centres should be nominated and approved as such by BRESO. Tier 2 will be similar in standard to EUSOMA certification but less proscriptive and we envisage that these will be large teaching hospitals with a minimum of 250 cancers per year, at least 3 specialist breast surgeons, a fully constituted MDT, access to training in genetics, pathology, imaging and reconstruction. Tier 1 centres will be smaller centres, with at least 150 cancers per year, access to MDT working but may not have access to all reconstruction options or genetics clinics. It is hoped that tier 2 centres will offer specific breast surgery fellowships to offer such training and the BRESO website will maintain a database of such fellowships, searchable by country and language.

The candidate will have to demonstrate their practical skills by means of a certified log book and evidence of ability to undertake key procedures to a good standard (axillary clearance (ANC), level 1 and 2 oncoplastic surgery (OCBS), wide local excision (WLE), mastectomy (Mx) and skin and nipple sparing mastectomy (SSM/NSM) for example). They will also be expected to demonstrate they have attained knowledge in breast cancer management and more in depth expertise in surgical management, as set out in the knowledge curriculum (which will be attested to by the passing of the UEMS European Board of Surgery Qualification (EBSQ) in Breast Surgery exam or holding an approved higher degree or certificate of competence, in addition to attendance at certified/approved courses and attendance at a minimum of 1 international breast congress).

There are 3 elements contributing to the acquisition of training. Theoretical knowledge acquisition, practical skills acquisition (and certification processes relating to the above) and accreditation of tier 2 centres/fellowships which provide training of adequate quality to meet the above needs. In the post-certification period, maintaining skills and knowledge is important and systems must be in place to mandate and certify that breast surgeons keep up to date in this rapidly progressing field.

1.2. Theoretical knowledge

The knowledge curriculum contained in this document has been developed to set out the required levels of theoretical knowledge a certified surgeon must possess. This will include both knowledge of facts, the ability to critically apply this knowledge in the clinical setting and the ability to assimilate and critically appraise new knowledge as it is produced by new trials. The knowledge curriculum will serve as the basis for courses, training programmes and examinations linked to certification and will be updated every 2 years.

The knowledge curriculum will be described in terms of 3 levels, a basic level, likely to be acquired during the tier 1 training period

(Basic level: B)/(Advanced level: A) which will be acquired during tier 2 training and optional specialist knowledge (Specialist: S) for example detailed knowledge of technical aspects of reconstruction).

All residents/fellows will be required to demonstrate detailed knowledge of the basic (B) and advanced (A) curriculum but the specialist knowledge (S) requirements may be used to tailor training to variations in national requirements where some countries do not require breast surgeons to be able to reconstruct, whereas others do. This will allow EU member states to engage fully with the programme with some ability to tailor requirements. Similarly the practical skills requirements may be tailored depending on national and speciality specific requirements (for example whilst all surgeons will be expected to be competent in axillary clearance, and level 1 and 2 oncoplastic surgery, whole breast reconstruction and pedicled, free and perforator flaps may only be appropriate for some countries or for plastic surgeons).

The knowledge curriculum will be provided within training and by attending courses and congresses and tested by examination. The curriculum is based on the UEMS EBSQ in Breast Surgery Exam syllabus and the passing of the UEMS exam will confirm adequate knowledge for the purpose of certification. Other breast examinations may also apply to serve a similar purpose, such as the University of East Anglia (UEA) MSc in Breast Surgery, the ESO CCB Certificate of Competence in Breast Cancer and the FRCS (Breast subspeciality interest) in the UK. Courses which provide the knowledge curriculum will include a requirement to attend at least 2 International evidence based congresses, focussed on breast diseases (such as San Antonio, St. Gallen, EBCC or similar).

There will also be a requirement to attend training courses, which may apply to be BRESO certified for this purpose, such as the ESSO Breast courses (advanced, oncoplastic), the ESO certificate course or masterclass, the University of East Anglia (UEA) Masters course and others. A small administration fee will be charged to course providers for approval ('approved by BRESO') after which they will be listed on the searchable BRESO website. Courses may be in English or other languages.

1.3. Practical skills

Acquisition of skills during training needs to be both numerically and qualitatively adequate for certification. It is envisaged that development of basic skills will be acquired during time spent in a tier 1 center (core biopsy, mammography interpretation, communication skills, diagnostic biopsy, simple mastectomy, level 1 oncoplastic WLE, SLNB and ALND).

Level 2 skills will include skin and nipple sparing mastectomy, level 2 oncoplastic skills, lipomodelling, implant management and reconstruction decision making, selection criteria and risks and benefits and complex oncological and genetic decision making and management. For those in National systems where reconstruction is not the role of the breast surgeon, but performed in conjunction with plastic surgery colleagues, observation of reconstruction of various types must be demonstrated but need not be performed personally.

All breast surgeons must have a theoretical understanding of breast reconstruction in order to be able to offer women appropriate treatment options. For those from national systems where reconstruction is a core role of the breast surgeon, operative numbers and quality assessments must be demonstrated. In this way the skills set may be tailored to national requirements/systems.

Training requirements will therefore be designated as Tier 1, Tier 2 or Specialised (determined by National agreement). Systems for certification of practical competencies will be developed by the BRESO skills working group and may involve designated trainers signing off cases or an on line system of log book validation.

1.4. Tier 2 centre/fellowship approval

An integral part of this process will be certification of centres as tier 2 training centres. Again, a small fee (varied according to the income of the host country to ensure it is affordable) will be charged to cover the cost of accreditation and centres will be listed in a searchable list on the website. In addition, formal tier 2 and specialist fellowships will be listed on the BRESO website if available.

1.5. Proposed temporal patterns of breast training

Table 1
Proposed temporal patterns of breast training.

Residency (usually 4–6 years in most European Countries)					Post residency	
Year 1	2	3	4	5	6	7
General training	General training	General training	General training	Br1	Br2	
General training	Br1	General training	General training	General training	Br2	
Br1	General training	General training	General training	Br2		
General training	General training	General training	General training	General training	Br1	Br2

Tier 1 breast training for 12 months could take place at any time during standard general training (from years 1–5) and may even be split into smaller blocks. If not present during standard training it must be part of a fellowship after completion of general training. It is shown as in years 1, 2 or 5 in the examples above but this is not exclusive and other permutations are possible.
Tier 2 breast training should take place towards the end of training, either as part of standard training in year 5 or as a fellowship after completion of general training.
General Training relates to standard residency in either general surgery, gynaecology or plastic surgery.
Br1: Basic Training in a Tier 1 unit.
Br2: Advanced (+/-specialist) fellowship training in a Tier 2 unit.

1.6. Continuing professional development

BRESO also proposes that for all practicing breast surgeons there should be some form of light touch re-certification at intervals of 5 years. This will include providing documentation that they have attended high quality oncology and oncoplastic courses that are free from commercial bias and have evidence based content.

2. Knowledge curriculum

The speciality of Breast Surgery requires different levels of knowledge at different stages during surgical training. Basic level knowledge (B) is appropriate for surgeons during their general training in general surgery, gynaecology or plastic surgery and is

the expected level of knowledge and skill for all surgeons within this discipline. Breast surgery is regarded as a specialist discipline within general surgery or gynaecology and all surgeons treating breast cancer should have advanced level skills and knowledge (A). It is recognised that some specialist-level knowledge and skills will only be provided by specialists in tertiary centres or by plastic surgeons (S). Throughout this curriculum knowledge is categorised into these 3 levels to guide training provision. Examinations approved by BRESO will test knowledge to advanced level with some specialist level knowledge. The knowledge curriculum is the responsibility of the BRESO theoretical knowledge working group and will be updated every 2 years.

3. Basic science

3.1. Physiology and development of the breast

- Development of the breast (A), proliferation during pregnancy (B), involution after lactation (B), involution during menopause and the hormonal stimuli that trigger these changes and how these may be affected by drugs, diseases, physiological variation (B).
- Abnormalities in breast development including hypoplasia (A) (including Poland's anomaly), hyperplasia, tubular breast, accessory breasts and nipples (A).
- The physiology of the male breast, its developmental stages, hormonal regulation and developmental variation (gynaecomastia) (A).
- Investigative work-up and management strategies for developmental and physiological abnormalities must be understood (A)

3.2. Surgical anatomy of the breast and axilla

- Muscles and fascia of the thoracic wall and axillary region (B)
- Blood supply to the breast, overlying skin and nipple-areola complex as well as the vascular anatomy of the axilla (B)
- Neural anatomy of the breast, thoracic wall, axillary area and upper arm (B)
- Lymphatic drainage patterns to the ipsilateral axilla, sub- and supraclavicular nodal basins, internal mammary nodal basin and contralateral axilla (B)
- Relevant surgical and vascular anatomy of common flaps used in breast reconstructive surgery (A,S)
- Anatomic variants and variants induced by treatments (such as the impact on vascular perfusion following radiotherapy, previous surgery and surgical scars) and how these may be managed clinically (A)

3.3. Pharmacology relevant to breast disease

- The endocrinology of the breast: influences of oestrogen (the oral contraceptive or menopausal hormone therapy (MHT)), progesterone, testosterone, oxytocin and prolactin (B)
- Impact of a range of drugs on breast function: drugs causing gynaecomastia, hypertrophy, secretion (A). Drugs causing breast development in gender reassignment (S).
- Drugs relevant to breast cancer: SERMS (B), aromatase inhibitors (B), fulvestrant (A), oestrogen (B), progestogens (B), GnRH agonists (A), chemotherapy agents (A) and GCSF (A), biological agents (trastuzumab, pertuzumab, lapatinib, neratinib TDM-1, CD4/6 inhibitors, PARP inhibitors, denosumab) (A), bisphosphonates (B), immune modulators (S).
- Drugs relevant to the treatment of breast pain: tamoxifen (A), danazol (B), GnRH agonists (A).
- Other: Analgesics for use in acute and chronic pain settings (B), antiemetics for the management of post-surgical nausea (B), antibiotics for use in the prophylactic setting in surgery and for the treatment of infections (B), low molecular weight heparins for DVT prevention in the perioperative period (B), local anaesthetic agents for use in the perioperative period for local and regional blocks (B).

3.4. Microbiology

- Common microorganisms causing breast pathology (B)
- Preferred antibiotics for common breast infections (B)
- Aetiology of breast sepsis (B)
- Management of breast sepsis (B)
- Signs and symptoms of severe sepsis (B)
- Management of severe sepsis including septic shock(B)

3.5. Epidemiology of breast pathologies

- Influence of age of menarche, pregnancies, lactation, menopause, hormonal treatments on disease risk (B)
- Family history (assess pedigrees, document and assess breast cancer risk factors and BRCA gene carrier risk status) (A)
- Genetics of breast cancer (high and moderate risk genes, single nucleotide polymorphisms SNPs) (A)
- Risk of previous breast conditions and procedures (B)
- Impacts of age, co-morbidities, medications, frailty on prognosis and risks of over and under treatment (B)
- Lifestyle risk factors for breast disease (e.g. smoking and risk of periductal mastitis; obesity, alcohol, exercise, oral contraceptives, menopausal hormone therapy (MHT), immunosuppressive therapy as risk factors for breast cancer) (B)

4. Diagnostic methods

4.1. Clinical examination

- Symptoms of benign or malignant breast diseases or conditions (B)
- Symptoms suggestive of nodal or distant metastases (B). Ability to perform an adequate examination of the breasts, axillary and other regional nodal basins (B)
- Understanding of the common signs and examination findings suggesting a range of breast pathologies and how these should be further investigated (B).
- Understanding the other clinical findings which may be linked to breast pathologies (evidence of metastatic disease, development of secondary sex characteristics (or lack thereof), physical signs that may link to gynaecomastia in the male (testicular abnormalities, hepatic dysfunction, obesity) (B)
- How to examine and assess a woman with breast augmentation, cosmetic or reconstructive breast surgery (A).

4.2. Breast (and related) imaging techniques

4.2.1. Mammography

- Age appropriate indications for mammography (B)
- Sensitivity and specificity and factors influencing these (A)

- ❖ Difference between analogue, digital, tomosynthesis and contrast enhanced mammographic techniques (A).
- ❖ Different views (craniocaudal and mediolateral oblique) and the role of compression views (A).
- ❖ Understanding of how to interpret standard mammographic abnormalities and the imaging features typical of benign or malignant pathology (B, A).
- ❖ Mammographic limitations in certain groups such as young females, females with dense breasts, lobular cancer and in the presence of implants (A)
- ❖ Eklund technique (Eklund GW et al. Improved imaging of the augmented breast. AJR Am J Roentgenol. 1988; 151 (3): 469–73) to optimise mammography in the presence of implants (A).
- ❖ Role of mammography in screening programmes (B)
- ❖ Role of mammography in stereotactic biopsies and different localization techniques (B)
- ❖ BI-RADS classification of malignancy (BI-RADS M1-5) and breast density (BI-RADS A-D) (A)
- ❖ Role of mammographic examination of operative specimens (A)

4.2.2. Breast ultrasound

- ❖ Age appropriate indications (B)
- ❖ Intraoperative localization techniques (B)
- ❖ Sensitivity and specificity, factors influencing sensitivity and specificity (A)
- ❖ Ultrasound guided breast biopsies, how performed, indications and contraindications (B)
- ❖ Understanding how to interpret standard ultrasound abnormalities and the imaging features typical of benign or malignant pathology (B, A)
- ❖ Role of Automated Breast Ultrasound (ABUS) (A)
- ❖ Stavros' criteria [Stavros AT et al. Radiology.1995 Jul; 196(1):123–34] for benign lesions (A)

4.2.3. MRI

- ❖ How performed, indications, limitations and contraindications, sensitivity and specificity, factors influencing sensitivity and specificity in invasive cancer and in DCIS (A,B)
- ❖ Role in surveillance of high risk women (A)
- ❖ Role when contradictory findings in triple assessment (A)
- ❖ Role in determining response in patients with neoadjuvant treatment (A)
- ❖ Role in detecting contralateral cancer (A)
- ❖ Role in the assessment of lobular cancer, multifocal cancer and dense breasts (A)
- ❖ Role when planning breast conserving surgery (B, A)
- ❖ The limited influence of pre-op. MRI on local recurrence rates (A)
- ❖ Management of lesions detected only on MRI (MRI localised biopsy) (A)
- ❖ Role in management of the occult breast primary (A)
- ❖ The benefits and risks of MRI: highly sensitive but risk of 'unnecessary' biopsies/mastectomies (A)
- ❖ Role in assessment of operability in locally advanced or recurrent disease of the breast and axilla (A)
- ❖ Use of MRI of areas outside the breast in the further evaluation of equivocal staging test results to diagnose liver, bone, CNS/spine metastases (A)
- ❖ Ability to interpret MRI imaging (obvious malignancy, obvious nodal disease, implant rupture (intra and extra capsular rupture) (A)

4.2.4. Staging CT

- ❖ Indications and contraindication for CT staging (B)
- ❖ Able to interpret simple CT abnormalities (liver, lung or obvious bone metastases) (A)
- ❖ Value of and indications and contraindications for the use of IV contrast (B)
- ❖ Use of CT angiography in planning free flaps (A)
- ❖ Indications for and value of PET CT (B)

4.2.5. Isotope bone scan

- ❖ Understanding how isotope bone scan works (B)
- ❖ Indications and contraindications for scanning (B)
- ❖ Able to interpret simple abnormalities (A)
- ❖ Follow on investigation in equivocal cases (e.g. CT scan or MRI of the bone when needed and rarely, use of bone biopsy) (A)

4.2.6. Dual emission X ray absorptiometry (DEXA) bone density scan

- ❖ Use in monitoring bone density in women on aromatase inhibitor (AI) therapy (B)
- ❖ Indications for DEXA scanning (B)
- ❖ Technical aspects of how this type of scan works and how it differs from an isotope bone scan (B)
- ❖ Understanding interpretation of bone density reports and scoring (B)
- ❖ Understanding of management of women with osteopenia and osteoporosis induced by ovarian function suppression, oophorectomy or in the presence of AI therapy (A)

4.2.7. PET_CT

- ❖ Use in staging in advanced breast cancer and in the investigation of axillary nodal disease of unknown primary (A)

4.2.8. Percutaneous needle biopsies

- ❖ Fine needle aspiration cytology – how performed, indications and contraindications, sensitivity and specificity, factors influencing sensitivity and specificity. Awareness that it is less sensitive and specific than core biopsy for the breast primary but has value in the assessment of lymph nodes (B)
- ❖ Core needle biopsy-how performed, indications and contraindications, sensitivity and specificity, factors influencing sensitivity and specificity (B)
- ❖ Vacuum assisted biopsy and vacuum assisted excision-how performed, indications and contraindications, sensitivity and specificity, factors influencing sensitivity and specificity (A)

4.3. Breast (and related) pathology

- ❖ The morphologic spectrum of normal breast tissue (juvenile/prepubertal breast, lactating breast, normal premenopausal breast, involution patterns, aberrations of normal development and involution (ANDIs), minimal changes, fibrocystic changes (B)
- ❖ Interpretation of preoperative diagnostic categories by fine-needle aspiration or discharge cytology (C1–C5) and core needle biopsy (B1–B5) (B)

- ❖ Radio-pathological correlations of major radiological features: circumscribed masses, spiculate masses, parenchymal asymmetry, microcalcification; Lack of correlation or correlations requiring further surgery (A)
- ❖ Subgross morphology of breast tumours, including the extent (measure of the tumour involved breast area/volume), the focality/distribution (unifocal, multifocal, diffuse), the size (invasive/prognostic tumour size) of the lesions (Tot T et al. The subgross morphology of breast carcinomas: a single-institution series of 2033 consecutive cases documented in large-format histology slides. Virchows Arch. 2019 Aug 13). (A)
- ❖ Specimen fixation, cold ischaemic time, pre-analytic conditions with influence on histopathological assessment prognostic and predictive markers; specimen of collection for tumour banking (A)
- ❖ Value of specimen mammography, both intraoperatively to ensure specimen identification and margin optimisation but also by the pathologist in disease localization and extent assessment (A)

5. Breast cancer epidemiology and natural history

5.1. Epidemiology

5.1.1. Incidence and mortality

- ❖ Rising incidence in the western world (B)
- ❖ Impact of aging populations (B)
- ❖ Impact of screening (B)
- ❖ Mortality trends and effect of earlier diagnosis, treatment impact (B)

5.1.2. Breast cancer risk factors: non-hereditary

- ❖ Age (B)
- ❖ Ethnic Group (B)
- ❖ Gender (B)
- ❖ Alcohol (B)
- ❖ Obesity (B)
- ❖ Dietary factors (B)
- ❖ Exogenous oestrogen use (menopausal hormone replacement therapy, oral contraceptive, IVF drugs, antioestrogens/SERMs and AIs) (B)
- ❖ Sedentary lifestyle (B)
- ❖ Mantle radiotherapy (B)
- ❖ Proliferative, non-high risk lesions of the breast (fibroadenoma, sclerosing adenosis, intaductal papilloma etc) (B)
- ❖ High risk lesions (lobular neoplasia in situ, radial scar (risk of concomitant cancer), atypical ductal hyperplasia, columnar cell hyperplasia) (B)

5.1.3. Genetic predisposition: breast cancer risk and risk of other malignancies

- ❖ High risk hereditary breast cancer risk syndromes: BRCA1 (B), BRCA 2 (B), tp53 mutation (Li-Fraumeni syndrome) (A), Cowden's syndrome (A), Peutz-Jegher's syndrome (A), Hereditary diffuse gastric cancer syndrome, (A), PALB2 (A).
- ❖ Risk counselling and risk management strategies for the unaffected (non-cancer) gene carrier and cancer management strategies for the gene carriers already diagnosed with cancer (A).
- ❖ Indications for gene testing and pre-test counselling (A).
- ❖ Moderate risk, germ line mutations: Ataxia-telangiectasia mutated (ATM) (A), CHEK-2 (A), PALB2 (A) and awareness of rapid rise in number of more recently identified clinically important mutations (A).
- ❖ Weaker hereditary factors such as low penetrance genes and single nucleotide polymorphisms (S).
- ❖ Genetic consortia programmes to accrue large cohorts globally to refine risk prediction for these newer genetic factors (A).
- ❖ The rise of commercial polygene arrays to risk assess and the potential risks and benefits of their use (A).
- ❖ Variants of unknown significance and how to manage these individuals (S)

5.1.4. Breast cancer risk estimation for healthy women with a family history

- ❖ Pedigree assessment (A, B)
- ❖ Tyrer-Cuzick (IBIS II) on line risk assessment tool (A)
- ❖ BOADICEA risk assessment tool (A, S)

5.1.5. Management of high and moderate familial breast cancer risk women

- ❖ Surveillance with breast imaging: age appropriate strategies and evidence of efficacy (MRI, MMG, US) (A)
- ❖ Risk reducing surgery: breast and ovary (A). Magnitude of risk reduction (A), impact on survival in bilateral non-cancer cases (A) and unilateral contralateral RRM in women with cancer (A), psychological impacts (A), techniques (skin or nipple sparing) (A), risk of occult malignancy (A).
- ❖ Chemoprevention (A): SERMS (tamoxifen, raloxifene), aromatase inhibitors (exemestane and anastrozole), trial evidence of benefit, indications for and contraindications to, age of use, duration of use. Adverse events.

5.2. Breast cancer screening

- ❖ Theoretical underpinnings of all screening programmes (WHO Principles, 1968, updated in 2008) (B)
- ❖ Quality requirements (EUSOMA), EU standards and own National specific quality measures and provision (B)
- ❖ Compliance rates for effective screening (A)
- ❖ Positive and negative influences of screening on breast cancer incidence, mortality, morbidity and survival rates (A)
- ❖ Factors influencing sensitivity and specificity (A)
- ❖ Validated screening tools (analogue and digital mammography, MRI) (B)
- ❖ Newer screening modalities (ABUS, tomosynthesis) (A)
- ❖ Targeted screening/surveillance in higher risk subgroups: familial risk, genomic risk, previous disease and treatment such as mantle radiotherapy (A)
- ❖ False positive findings and over diagnosis and their adverse impacts (B)
- ❖ Surgical and diagnostic techniques relevant to screening (vacuum assisted biopsy, localization techniques for surgery) (B, A)
- ❖ Management of screen detected borderline and premalignant lesions (radial scar, DCIS, atypias etc) (A)
- ❖ Screening age ranges and their justification (B)

5.3. Breast cancer: biology, natural history and prognosis

5.3.1. Basic concepts in cancer biology

- Cell kinetics, proliferation, apoptosis and the balance between cell death and cell proliferation (A)
- Angiogenesis and lymphangiogenesis (A)
- Knowledge of key molecular pathways in breast cancer of therapeutic significance (Her-2, ER) (A)
- Genome maintenance mechanisms to prevent cancer (A)
- Intercellular and intermolecular adhesion mechanisms and signalling pathways (A)
- Immunological mechanisms that either prevent or promote cancer growth and dissemination (A)
- Potential effects of surgery and surgery-related events on cancer biology (e.g. angiogenesis) (A)

5.3.2. Natural history, prognosis, prognostic and predictive factors

- Patterns and incidence rates of local, regional and distant dissemination (B)
- Differences in dissemination patterns due to biological tumour subtypes (A)
- Tumour and nodal stages (TNM Classification, version 8, January 2018) (B)
- Tumour grade (Elston and Ellis classification) (B)
- Ki-67 expression (A)
- Histological (morphological) subtypes of invasive cancer (B)
- Array based classification of Sorlie and Perou (luminal A, B, basal etc) (A)
- Oestrogen and progesterone receptor expression (Allred, H score) and clinical relevance (B)
- HER-2 (c-erb-b2) over-expression and clinical impact (B), Intermediate cases (2+) by IHC and HER-2 expression by FISH, CISH (A)
- The role of "conventional" breast pathology (tumour diagnosis, prognosis, specimen analysis, node analysis, neoadjuvant response assessment) (B)
- Intraoperative assessment techniques (frozen section, OSNA, imprint cytology for nodal staging, frozen section for margins) (A)
- The role of Multi-Gene Assays in both prognostic and predictive settings (costs, benefits and limitations) (A)
- Differences and similarities in tumour biology between sporadic and hereditary breast cancer (A)
- The influence of circulating tumour cells on prognosis and the new technique of 'liquid biopsy' (S)
- The risk of and risk factors for synchronous and metachronous breast cancer (A)
- Prognostic Tools: For example: Nottingham Prognostic Index, NHS PREDICT, MSKCC nomograms. Differences and applicability (A)
- The role of the immune system in tumour development, progression and regression; immune system related predictors of the response to treatment (adjuvant, neoadjuvant, immune-oncologic) – tumour infiltrating lymphocytes (A)

5.4. Breast cancer: staging

- Clinical staging of the primary tumour and the axilla and its accuracy (B)
- Preoperative axillary staging by ultrasound (sensitivity and specificity) (B)
- Surgical staging of the axilla - indications, methods, sensitivity, advantages, disadvantages (B)
- CT-scan: how performed, the indications, sensitivity and specificity (B)
- PET- CT scan: how performed, the indications, sensitivity and specificity (B)
- Isotope bone-scan: how performed, indications, sensitivity and specificity (B)
- Clinical and pathological TNM-classification (version 8) including post-neoadjuvant designation (B)
- Stage migration due to improved staging accuracy, (e.g. detecting micrometastases in sentinel lymph node biopsy) (A)
- Post neoadjuvant response categorisation systems such as residual cancer burden (A)

5.5. The role of the multidisciplinary team (MDT) in breast cancer

- Multimodality treatment of breast cancer (B)
- Ideal composition of the MDT (B)
- Responsibilities and tasks distribution among the MDT members
- Defining local protocols and workflows
- Understanding the role of the MDT in data flow
- Educational and training role of the MDT (B)
- Audit and governance role of the MDT (B)
- Costs of the MDT (A)
- EUSOMA guidelines regarding multidisciplinary teams and meetings (A)

6. Breast cancer surgery

6.1. Conservation surgery for breast Cancer/DCIS

6.1.1. Localization of impalpable lesions (benign, borderline or malignant)

- Guide wire (B)
- ROLL (radioguided occult lesion localization) (A)
- RSL (radioguided seed localization) (A)
- Magnetic seed or tracer localization (A)
- Guidance by intraoperative ultrasound (A)
- Advantages and disadvantages of various localization methods (A)
- The role of specimen radiography (B)
- Role and value of variety of margin assessment devices and techniques (A)

6.1.2. Conservative surgical treatment of (DCIS and invasive) disease within the breast

- Indications and contraindications for breast conservation (A, B)
- The location, size and the multifocality/multicentricity of the tumour (A)
- The size and the shape of the breast, including assessment of degree of ptosis (A)
- The predicted aesthetic outcome after breast conservation (A)
- The role of neoadjuvant systemic treatment in facilitating breast conservation, including indications and contraindications as well as predicting and evaluating the response (A)
- Patient preference (B)
- Medical contraindications for radiotherapy: previous RT, heavy smoker/COPD, dementia, confusion and agitation, positioning limitations (B)

6.1.3. Oncoplastic conservation surgery

- Volume displacement versus volume replacement: techniques and indications, risks (A)
- Level I and level II oncoplastic techniques in breast conservation. Aware of contraindication and indications for oncoplasty, different techniques by disease quadrant (atlas of technique by K Clough), risks of oncoplastic surgery (A)
- Management of cavity (marking with clips), pathological documentation and specimen marking (B)
- The need for contralateral surgery for symmetry: techniques, indications, contraindication, timing, impact of radiotherapy (A)

6.1.4. Breast conservation

- The influence of margin width on local recurrences (B)
- The role of cavity shavings to ensure sufficient margins (A)
- Risk of local recurrence and patient and tumour stage, margin assessment and biology related risk factors for local recurrence after breast conservation (A)
- The influence of breast radiotherapy on local recurrences (B)
- Role of boost radiotherapy and need to enable radiotherapy targeting including impact on local recurrence rates, indications, cosmetic impacts (A)
- The influence of adjuvant systemic treatment on local recurrences (A)
- Treatment of local recurrences after breast conservation including indications for re-do conservation surgery (A)
- The influence of local recurrences on survival (A)
- Nodal staging in patients with local recurrence after breast conservation and negative sentinel node biopsy (A)

6.1.5. Methods to correct poor aesthetic outcome after breast conservation

- Free fat grafting (S)
- Partial reconstruction (pedicle and perforator flaps) (S)
- The aesthetic outcomes after such procedures (S)
- Oncological safety of these techniques (S)

6.2. Mastectomy

6.2.1. Mastectomy indications and types

- Indications for mastectomy (absolute and relative) (B)
- Immediate and delayed reconstruction-indications and contraindications (A).
- Nipple-areola complex sparing mastectomy, indications, contraindications. Risk of and risk factors for complications (A)
- The risk of nipple involvement, the role of frozen section from central ducts (A)
- Evidence from trials comparing mastectomy and breast conservation (A)
- Psychological impacts of mastectomy (A, S)
- Bilateral risk reducing mastectomy (A)
- Contralateral risk reducing mastectomy (indications, outcomes) (A)
- Surgical complications of mastectomy and how to manage them (B).

6.2.2. Local recurrence after mastectomy

- The risk of and risk factors for local recurrences (A)
- The influence of radiotherapy on local recurrences (B)
- Presentations of local recurrence (B)
- The influence of adjuvant systemic treatment on local recurrences (A)
- Treatment of local recurrences after mastectomy including reconstructive methods in extensive recurrences (A)
- The influence of local recurrences on survival (A)

6.2.3. Breast reconstruction

- Implant reconstructions – indications, contraindications, complications, costs (A)
- Long-term sequelae of implant reconstruction: need for revision surgery (A), capsule formation (A), extrusion (B), infection (B), leakage (B), rupture (B), BIA-ALCL (A).
- Interactions and potential interactions of reconstructive surgery and oncology treatments (chemotherapy, radiotherapy, trastuzumab) (A)
- Acellular dermal matrices and synthetic meshes—biology, indications, contraindications, complications (A)
- Pedicle and perforator flap reconstructions (latissimus dorsi, LICAP, TDAP etc)—their indications, contraindications, complications, costs (S)
- Micro-vascular flaps – (DIEP, TRAM, SGAP, IGAP, TUG), their indications, contraindications, complications, costs (S).
- Factors influencing aesthetic outcome after breast reconstruction (S)
- Oncological safety of immediate and delayed reconstruction (A)
- Influence of reconstruction on quality of life (A)
- Surgical complications of reconstructive surgery (short, medium and long term), (A)

7. Axillary surgery

7.1. Sentinel node biopsy (SNB) in invasive cancer, DCIS and Paget's disease of the breast

- The sentinel node concept (B)
- The indications and contraindications for SNB (B)
- Sensitivity of SNB and factors influencing the sensitivity, (B)
- The role and outcome of SNB in patients with local recurrence and previous axillary surgery (A)
- The advantages, disadvantages and outcome of SNB before neoadjuvant systemic treatment (A)
- The advantages, disadvantages and outcome of SNB after neoadjuvant systemic treatment (A)
- The role of SNB outside the axilla, like in the internal mammary nodal basin (A)
- Radioisotope localization-advantages and disadvantages (B)
- Other localization methods (magnetic, indocyanine green) (A)
- Blue dye - advantages and disadvantages (B)
- The role of preoperative lymphoscintigraphy (conventional and SPECT) (A)
- The role of and methods for intraoperative assessment of sentinel node metastases (A)
- The histopathological methods in assessment of the sentinel node metastases (A)
- Other methods (such as OSNA) in assessment of the sentinel node metastases (A)
- Classification of tumour positive sentinel node findings (A)

- ❖ Management of patients with positive sentinel nodes (observation, axillary radiotherapy, axillary lymph node dissection) (B, A)
- ❖ The advantages and limitations of nomograms predicting further nodal involvement (B,A)
- ❖ Morbidity after sole SNB, and after further treatment of axilla with axillary radiotherapy and axillary lymph node dissection (B)
- ❖ Impact of isolated tumour cells, micro and macrometastases in prognosis and further axillary management (B)

7.2. Axillary lymph node dissection (ALND) in invasive cancer

- ❖ The indications and contraindications of ALND (B)
- ❖ Anatomy of the axilla (B)
- ❖ Advantages and morbidity of ALND in patients with axillary metastases (early, intermediate and late) (B)
- ❖ Alternative to ALND in low volume/low risk axillary disease (B)
- ❖ The role of preserving intercostobrachial nerves (A)
- ❖ Berg levels of the extent of ALND (B)
- ❖ Risk of lymphoedema, its classification and management (A)

7.3. Regional recurrences after axillary surgery (SNB, ALND)

- ❖ The risk of and risk factors for regional recurrences (B)
- ❖ The influence of radiotherapy on regional recurrences (B)
- ❖ The influence of adjuvant systemic treatment on regional recurrences (A)
- ❖ Treatment of regional recurrences after SNB and ALND (A)
- ❖ The influence of regional recurrences on survival (A)
- ❖ Assessment of operability (US/CT/MRI scan) and indicators for inoperability (A)

7.4. Axillary metastases with unknown primary

- ❖ Differential diagnosis and how to distinguish between axillary metastases from breast cancer and other malignancies (for example melanoma) (A)
- ❖ The role of imaging modalities, such as breast MRI (B)
- ❖ The role of pathology (A)
- ❖ The role of CT and PET-CT scans to rule out distant disease or other malignancy than breast cancer (B)
- ❖ Treatment (surgery, radiotherapy, systemic) (A)

7.5. Axillary management in the neoadjuvant setting

- ❖ Targeted axillary dissection (techniques, sensitivity, specificity, trials) (A)
- ❖ Use of different TAD markers (clips, iodine seeds, magnetic marker systems, ink marking) (A)
- ❖ Upfront SLND for the clinically negative axillary versus post NAC SLND (accuracy, sensitivity and specificity, trials) (A)

8. Adjuvant systemic therapies in breast cancer

8.1. Systemic chemotherapy

- ❖ Agents and regimens used in the adjuvant setting, including common side effects and contraindications (e.g. hair loss, myelosuppression, cardiac toxicity with some regimes) (A)
- ❖ Indications and contraindications (B)
- ❖ Internet based tools used to help in decision making (such as PREDICT), advantages, disadvantages of each (A)
- ❖ Multigene assays used to help for prognosis and decision-making (such as OncotypeDX, Mammaprint, PAM-50, Endopredict etc.) (A)
- ❖ Influence on local and regional recurrences and survival (B)
- ❖ Emerging data about adjuvant therapies after neoadjuvant therapy poor response (A)
- ❖ Cellular/molecular targets for chemotherapy, endocrine and targeted treatments, and their mechanisms (A)
- ❖ Common side effects and their management (A)
- ❖ Interaction with surgery, for example effect on wound healing, surgical delay before chemotherapy starts if surgical complications, risk of infections, risk of thrombosis (B)
- ❖ Local and regional recurrences and survival after adjuvant systemic chemotherapy (A)
- ❖ Agents in trials pipelines (S)

8.2. Systemic hormonal therapy

- ❖ Agents used (tamoxifen, aromatase inhibitors), duration of use (5 years, 10 years), strategies of AIs use (upfront, switching, late extended) (A)
- ❖ Indications and contraindications (B)
- ❖ Tools used to help in decision making (such as PREDICT), (A)
- ❖ Influence on local and regional recurrences and survival (B)
- ❖ Cellular/molecular targets for agents (the ER, aromatase enzymes) (A)
- ❖ Common side effects and their management (acute and long term) (A)
- ❖ Interaction with surgery, for example risk of thrombosis with tamoxifen (B)
- ❖ Bone density monitoring protocols and management in women on AIs (B)
- ❖ Use of ovarian suppression therapy to augment hormone blockage in certain subgroups: indications, evidence and adverse effects (e.g SOFT and TEXT trials). (A)

8.3. Adjuvant bisphosphonates

- ❖ Agents used, including route of administration and duration, indications and contraindications (A).
- ❖ Common and rare but significant (e.g. jaw necrosis) side effects (A)
- ❖ Evidence for benefit in the adjuvant setting (A)
- ❖ Impact on survival and rates of metastatic recurrence (A)

8.4. Adjuvant molecular targeted therapies

- ❖ Mechanism of action and receptor pathway and interactions (A)
- ❖ Agents: trastuzumab, pertuzumab, lapatinib, TDM-1, neratinib (A)
- ❖ Biology of Her-2 positive breast cancer (A)
- ❖ Regime, interval and duration of therapy and key supporting trials (A)
- ❖ Common adverse effects (A)
- ❖ Evidence of benefit on survival and local, regional and distant recurrence rates (B)
- ❖ CD4/6 inhibitors in adjuvant trials (A)
- ❖ mTOR inhibitors in adjuvant trials (S)
- ❖ PARP inhibitors in adjuvant trials (S)
- ❖ Immunotherapies in adjuvant trials (S)

- ❖ Denosumab in adjuvant trials (S)

9. Radiation therapy

9.1. Radiation therapy to the breast

- ❖ Indications and contraindications (B)
- ❖ Influence on local and regional recurrences on survival (B)
- ❖ Most common side effects and their management (early and late, including risk of second cancers including angiosarcoma) (B)
- ❖ Partial breast radiation therapy: techniques, indications, contraindications, advantages, disadvantages (A)
- ❖ Interaction with surgery including the effect on wound healing, breast fibrosis and shrinkage, breast lymphoedema (A)
- ❖ Radiation therapy and breast reconstruction (A)
- ❖ Indications for and impact of boost to the primary tumour bed (A)
- ❖ Use of marker clips to identify primary tumour bed for boost volume localization (B)
- ❖ Impact of Oncoplastic surgery on identification and size estimation for the target volume for radiotherapy boost (A)
- ❖ Modern fractionation regimes (B)
- ❖ Modern and alternative irradiation techniques to reduce the toxicity (IMRT, DIBH, IPRT, prone, lateral)
- ❖ Awareness of the current research interest in neoadjuvant radiotherapy in current trials (A)

9.2. Radiation therapy to the axilla

- ❖ Indications and contraindications (B)
- ❖ Adverse effects in the short and longer term including rates of lymphoedema (A)
- ❖ Interaction with surgery (pedicle fibrosis for subsequent axillary based pedicle reconstruction), fibrosis (A)
- ❖ Trial data comparing axillary RT with axillary surgery (A)
- ❖ Lymphoedema rates (B)

9.3. Radiation therapy to the chest wall

- ❖ Indications and contraindications (B)
- ❖ Adverse effects in the short and longer term (A)
- ❖ Interaction with reconstructive surgery (A)
- ❖ Trial data comparing RT with no RT in terms of local recurrence rates and survival (A)

9.4. Radiation therapy for palliation of locally advanced and metastatic disease

- ❖ Indications and contraindications for local and regional radiation therapy (B)
- ❖ Indications and contraindications for radiation therapy for distant metastases (B)
- ❖ Oligometastatic disease: definition; role of locoregional and metastases-directed radiation therapy (B)
- ❖ Role of primary radiotherapy in patients who are unfit for surgery (A)

10. Breast cancer in special groups

10.1. Breast cancer in young women

- ❖ Need for and indications for genetic counselling/testing (B)
- ❖ Imaging limitations in younger women (poor mammographic sensitivity) (B)
- ❖ Variation in tumour subtype, stage and biological behaviour (A)
- ❖ Local, regional and systemic treatment and how these may need to be modified in younger women (e.g. use of RT boost) (A)
- ❖ Local, regional and distant recurrence rates in younger women (A)
- ❖ Survival variance with age (A)
- ❖ Fertility, pregnancy and contraception during and after breast cancer (A)
- ❖ Breast cancer in pregnancy and how to manage disease in all 3 trimesters (A)
- ❖ Premature menopause due to breast cancer treatment and how to manage this, (B)
- ❖ BRCA associated cancers: presentation, type and management (A)
- ❖ Psychological impact (A)

10.2. Breast cancer in the elderly

- ❖ Tailoring local, regional and systemic treatments according to co-morbidities, frailty, cognitive impairment, polypharmacy and patient preference (A)
- ❖ Local, regional and distant recurrence rates in older women (A)
- ❖ Survival (overall and breast cancer specific) in older women (A)
- ❖ Treatment morbidity in older age groups (A)
- ❖ Adapted techniques and fractionation schemes to age and PS

10.3. Male breast cancer

- ❖ Risk factors for male breast cancer (A)
- ❖ Incidence, age specific incidence and prognosis (A)
- ❖ Need for genetic counselling/testing (A)
- ❖ Surgical treatment and how this may differ in males (B)
- ❖ Adjuvant treatment and how this may differ in males (B)
- ❖ Local, regional and distant recurrence rates (A)
- ❖ Survival (A)
- ❖ Psychological impact (A)

10.4. Other breast malignancies-incidence, diagnosis and treatment modalities

- ❖ Malignant and borderline phyllodes tumour (A)
- ❖ Sarcomas: primary and secondary (radiation induced) (A)
- ❖ Metastases from other malignancies (A)
- ❖ Lymphoma in the breast or axilla (A)
- ❖ Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) (A)

11. Atypias and in situ disease

11.1. Atypias (B3 lesions)

- ❖ Atypical ductal hyperplasia, atypical lobular hyperplasia, classical lobular neoplasia in situ (cLCIS), pleomorphic lobular neoplasia in situ (pLCIS), columnar cell hyperplasia, papilloma, radial scar: awareness of pathological appearance, diagnostic

criteria, mode of presentation and risk of malignant transformation (B)
- ❖ The prevalence of associated in situ or invasive cancer when risk lesions detected in core needle/vacuum assisted biopsy (B)
- ❖ Role of vacuum assisted excision (A)
- ❖ Appropriate indications for surgery in the management of atypias (B)
- ❖ Concomitant and later breast cancer risk of these lesions (B)
- ❖ Role of chemoprevention and enhanced screening in risk management (A)
- ❖ Risk reducing surgery indications (A)

11.2. DCIS

- ❖ Epidemiology: incidence, risk factors, prognosis (B)
- ❖ Classification of DCIS (encysted papillary, low, intermediate and high grade, Paget's) (B)
- ❖ Pathological criteria for the diagnosis of DCIS (B)
- ❖ Biological characteristics (ER positive, Her-2 positive, array based) (A)
- ❖ Incidence and role of screening. Screen detected versus symptomatic disease characteristics and prognosis (A)
- ❖ Treatment and prognosis of DCIS (see below in various treatment sections) including surgery, radiotherapy rates of recurrence and prognosis (B)
- ❖ Appropriate margins of resection (B)
- ❖ Rates of invasive and in situ recurrence and risk factors of recurrence (B)
- ❖ DCIS prognostic/risk scores (Van Nuy's, genetic arrays, on line algorithms) (A)
- ❖ Debate about over treatment and over-diagnosis in the screening setting and in the older women. Aware of ongoing trials (LORIS, LORD, COMET) (A)

12. Psychosocial issues and follow-up care. 'Survivorship' issues

- ❖ The need of psychological or social support in women with newly diagnosed breast cancer and during the entire course of disease (B)
- ❖ The role of follow-up care in breast cancer survivors: detecting recurrences, influence on survival, follow up protocols and methods (B)
- ❖ Methods of follow-up and the frequency of follow-up (B)
- ❖ Conservative and surgical management of lymphoedema (B, A)
- ❖ Chronic pain and sensory disorders after breast cancer treatment (A)
- ❖ Endocrine issues in breast cancer survivors, e.g. menopause symptoms and bone health, especially in the very young patient, including hot flushes, genitourinary syndrome of the menopause, premature osteoporosis (A). Role of menopausal hormone replacement therapy (systemic or topical vaginal creams) including risks and benefits (A). Role of menopausal hormone replacement therapy after risk reducing oophorectomy in BRCA gene carriers (A)
- ❖ Depression, anxiety and fear of recurrences (A)
- ❖ Cognitive disorders (A)
- ❖ Sexuality including psychosexual and physical issues such as early menopause/antioestrogen induced loss of libido, depression, anxiety, loss of confidence due to body image changes, genitourinary syndrome of the menopause. Awareness of the above, how to diagnose and manage (A)
- ❖ Fertility issues and how to manage them (A)

13. Benign breast diseases and conditions

13.1. Gynaecomastia

- ❖ Aetiology (pubertal, obesity, hormonal, alcohol and liver disease, therapeutic or recreational drug induced, genetic etc) (B)
- ❖ Assessment of diagnosis and severity (A)
- ❖ Management (reassurance, removal of underlying cause if possible, surgery for symmetry, surgery to reduce, liposuction, en bloc resection techniques, role of drug therapy) (A)

13.2. Nipple discharge

- ❖ Aetiology and presentation (B)
- ❖ Investigation and assessment (imaging and cytology – accuracy, sensitivity and specificity) (B)
- ❖ Role of microdochectomy or total duct excision (B)

13.3. Fibrocystic change

- ❖ Aetiology and presentation (B)
- ❖ Management (B)

13.4. Cyclical and non-cyclical mastalgia

- ❖ Aetiology and presentation (B)
- ❖ Management (B)

13.5. Breast hypertrophy

- ❖ Aetiology and incidence (A)
- ❖ Management strategies (A)

13.6. Puerperal and periductal mastitis

- ❖ Aetiology (B)
- ❖ Microbiology and antimicrobial therapy (B)
- ❖ Management (B)

13.7. Breast fistula

- ❖ Aetiology and incidence (B)
- ❖ Management strategies (B)

13.8. Other rare forms of mastitis

- ❖ Granulomatous mastitis role of clinical history, laboratory tests, cultures, microscopy in diagnosing the aetiology (B)
- ❖ Mondor's disease (A)
- ❖ Lymphocytic lobulitis (A)
- ❖ Tuberculosis (B)
- ❖ Plasma cell mastitis (A)
- ❖ Non-puerperal chronic periductal mastitis and fistula

13.9. Fibroadenoma

- Clinical and radiological features (e.g. Stavros' criteria), indications for biopsy (B)
- Natural history variant (tubular adenoma, juvenile fibroadenoma, lactating adenoma, myxoid fibroadenoma) and analogue (benign lesions with similar clinical and/or imaging features: nodular pseudoangiomatous hyperplasia, hamartoma) lesions; differences from (benign) phyllodes tumour (A)
- Management (A)

13.10. Benign phyllodes tumour

- Clinical, pathological and radiological features (B)
- Natural history (B)
- Management (B)

13.11. Macrocysts (simple, complicated, and complex)

- Aetiology, incidence and presentation (B)
- Management of simple cysts and risk factors for underlying malignant pathology (B)

13.12. Papilloma

- Multiple papilloma: association with nipple bleeding and discharge, increased risk of malignancy (A)
- Single papilloma: symptoms and signs, management (B)
- Papillary lesions (the morphologic spectrum and main differential diagnostic features: papillomas vs encapsulated papillary carcinoma, solid papillary carcinoma) (A)

14. Aesthetic breast surgery, breast implants and other medical implantable devices/materials

14.1. Breast implants

- Implant types: silicone, saline, polyurethane, surface (smooth or textured), round or anatomic shape, expandable or fixed volume (A)
- Capsule formation: presentation, rates with time, risk factors, classification (Baker), investigation, management (A)
- Rupture: presentation, rates with time, variation by implant type, causes, classification (intracapsular, extracapsular), adverse effects, investigation, management (A)
- Extrusion: presentation, rates with time, risk factors, management (A)
- Malposition: Assessment, management strategies. (A)
- Breast Implant Associated Anaplastic Large Cell Lymphoma (BIALCL): risk factors, incidence, presentation, diagnostic evaluation, management and prognosis (A)
- Implant surgery: indications, contraindications, preparatory work up, choice of incision, choice of implant type, choice of implant position. (A)
- Outcomes: short, medium and long term adverse events and patient satisfaction (A)
- Psychological issues related to breast aesthetics and augmentation (A)

14.2. Breast reduction and mammoplasty

- Indications, contraindications and risk factors for adverse outcomes (A)
- Techniques (pros and cons, specific indications for different techniques (A)
- Technical aspects of surgery and aftercare (A)
- Outcomes: short medium and long term complications and patient satisfaction (A)
- Impact on breast feeding and nipple sensation (A)

14.3. Acellular dermal matrices and implantable meshes

- Different types of material properties and handling characteristics: plastic mesh versus biological material (xenograpft, allograft) (A)
- Indications, contraindications (A)
- Safety and approvals. (A)
- Complications: rates and risk factors. Long term outcomes (A)
- Technical aspects of use: selection of technique, risks associated with individual techniques, risk factors for adverse outcomes (A)
- Placement (sub-pectoral sling versus pre-pectoral pocket). (A)
- Revision surgery techniques (A)
- Interaction with radiotherapy (A)

14.4. Autologous fat grafting

- Techniques and theoretical basis (A)
- Oncological and medical safety (A)
- Donor site and recipient site morbidity (A)
- Indications and contraindications (A)
- Pre-operative preparation and counselling (A)
- Aftercare (A)

15. Advanced breast cancer

15.1. Locally advanced

- The definition of locally advanced breast cancer (B)
- Primary systemic treatment in locally advanced breast cancer (endocrine, chemotherapy and targeted treatments) (A)
- Management of neoadjuvant (baseline scans and monitoring response, MRI), use of marker clips (A)
- Timing of axillary surgery (A)
- Inflammatory breast cancer (diagnosis, prognosis, management) (B)
- Surgery in patients with locally advanced breast cancer (A)
- The role of radiotherapy in locally advanced breast cancer (A)
- Response rates after primary chemotherapy (NAC) by tumour subtype (A)
- Extent of surgery after partial or complete pathological response (A)
- Pathological classification of response (A)
- Local recurrence rates after conservation surgery post NAC (A)
- Survival rates comparing primary chemotherapy (NAC) and adjuvant chemotherapy (A)

15.2. Treatment of disseminated (stage IV) breast cancer

- Palliative surgical procedures in disseminated (stage IV) cancer, for example palliative mastectomy, treatment and prevention of

pathological fractures, spinal cord stabilisation, recent research into liver resection in oligometastatic disease. (A)
- ❖ Removal of primary tumour in disseminated breast cancer-influence on survival (A)
- ❖ The oligometastatic disease – cure intent (A)
- ❖ Removal of liver or pulmonary metastases-influence on survival (A)
- ❖ The role palliative radiotherapy in disseminated breast cancer (B)
- ❖ Palliative treatments to relieve symptoms like pain and nausea (B)
- ❖ Social, psychological and spiritual support in patients with disseminated breast cancer (B)
- ❖ Management of cerebral metastatic disease: steroids, stereotactic radiosurgery, gamma knife, surgery, whole brain RT, systemic therapies (S).

15.3. Systemic agents used in the advanced setting

- ❖ Chemotherapy (A)
- ❖ Antioestrogens (A) (SERMs, aromatase inhibitors)
- ❖ CD4/6 inhibitors (A),
- ❖ Fulvestrant (A)
- ❖ Denosumab (A)
- ❖ GCSF (A)
- ❖ Immunotherapy (A)
- ❖ PARP inhibitors (A)
- ❖ mTOR inhibitors (A)
- ❖ Her-2 targeted agents (A)
- ❖ Analgesia, anti-emesis (B)

16. Research and evidence based medicine

- ❖ The p-value and the use of confidence intervals and their relation to the sample size; the importance of power analysis and sample size calculation in trials (B)
- ❖ The difference between statistical and clinical significance (B)
- ❖ Types of bias and how to avoid them (B)
- ❖ Prospective and retrospective study setting (B)
- ❖ Study settings (randomized, prospective non-randomized, case-control, retrospective etc) (B)
- ❖ Definitions of phase I, phase II, phase III and phase IV trials (B)
- ❖ Definitions of absolute and relative risk reduction or advantage (B)
- ❖ Levels of evidence and how these influence treatment recommendations (B)

17. Practical knowledge and skills curriculum

The following is a list of the practical skills that are required of a fully trained breast surgeon. Acquisition of these skills is estimated to take 2 years of full time training (for someone with basic general, gynaecological or plastic surgery competencies) and is divided into a number of discrete subject areas. Ideally candidates should spend time within multidisciplinary specialist disciplines (such as radiology, pathology, oncology) to achieve a full range of competencies but it is accepted that this may not be possible.

The candidates must keep a logbook, signed off by their trainer, of the operations they have attended as an assistant or operations they have carried out, supervised or unsupervised, and also of the clinics they have attended and the multidisciplinary meetings they have attended.

17.1. Radiology

Candidates should spend some time observing and learning about a range of procedures listed below:

- ❖ Breast imaging and percutaneous needle biopsies:
- ❖ Counsel patients regarding breast imaging methods and percutaneous needle biopsies: Indications, limitations and how these are performed
- ❖ Evaluate mammograms, ultrasound imaging and breast MRIs
- ❖ Perform core needle biopsy and punch biopsy (Fine needle biopsy is rarely used but may also be of value in some settings and centres)
- ❖ Knowledge regarding preoperative and postoperative staging by imaging:
- ❖ Indications, limitations and how these are performed
- ❖ Knowledge of axillary staging, US imaging of nodes and indications for biopsy
- ❖ Understand diagnostic staging: indications for CT imaging, bone scans, CT-PET in different breast cancer stages. Ability to interpret images at a basic level.

LOG BOOK:
Manage cases and review:
8 screening mammograms.
20 diagnostic/symptomatic mammograms.
10 breast MRIs.
Breast ultrasound: 15 (hands on) or 30 (observation only).
Percutaneous procedures: 30 including cyst aspiration, percutaneous core needle sampling, palpation or image guided, seroma aspiration with/without drain placement, percutaneous abscess drainage with/without drain placement.

17.2. Pathology

Candidates should follow specimens through pathology to understand specimen marking, cut up and processing to optimise their collaboration with pathology.

- ❖ Understand handling and different techniques for breast pathologic analysis (Frozen section, routine staining, immunohistochemistry)
- ❖ Knowledge about tumour margin assessment
- ❖ Nodal evaluation
- ❖ Sentinel lymph node
  - o Nodal dissection specimens
- ❖ Pathologic staging of tumours
- ❖ Intraoperative analysis

LOG BOOK: Observe or discuss with a pathologist.
8 cancer case sign outs.
(8 frozen or intraoperative evaluations, may not be applicable in all units).
8 benign and/or high risk lesions.

17.3. Clinical session types

- ❖ Participate in results clinics including 'breaking bad news' and initial therapy decision-making
- ❖ Participate in preoperative clinics including oncoplastic/reconstructive clinics
- ❖ Participate in breast cancer–specific operating lists
- ❖ Participate in diagnostic clinics for both benign and malignant diseases
- ❖ Participate in screening clinics

- ❖ Participate in breast oncoplastic and reconstructive clinics, ideally jointly with plastic surgeons or surgeons who undertake primary reconstruction
- ❖ Participate in familial risk assessment clinics
- ❖ Participate in postoperative clinics (assessing wound healing, primary aesthetic outcome and recovery from surgery, is further surgery required, or follow-up etc)
- ❖ Note: it is not expected that special clinics will exist for all of the above, but the clinics attended should offer the above as part of their remit (i.e. may be a generic breast clinic at which results are given or diagnostic tests performed etc).

17.4. Surgical management of the breast and axilla

- ❖ Diagnostic excisional biopsy, with/without wire/seed/ultrasound localization
- ❖ Central/Major/Terminal duct exploration and excision
- ❖ Breast conservative surgery with/without image-guided localization (wire/seed/ultrasound/magnetic)
- ❖ Oncoplastic breast conservative surgery-level I and II techniques
- ❖ Mastectomy:
  - Total mastectomy
  - Skin-sparing mastectomy
  - Nipple/areolar sparing mastectomy
    (Candidates should understand the techniques to ensure skin viability: careful plane dissection, careful tissue handling, high risk individuals where extra care is required such as smokers, diabetics and the obese, novel techniques for skin viability assessment, use of PICO/vac dressings in high risk cases)
- ❖ Lymph Node excision
- ❖ Axillary sentinel node biopsy using a recognised technique such as:
  - Blue dye
  - Radioisotope
  - Both
  - Other techniques for SLN (magnetic, iodine seed, US localization, indocyanine green)
- ❖ Axillary node dissection
- ❖ Breast asymmetry after breast conservation
- ❖ Awareness of the management techniques for repair of chest wall defects following resection of locally advanced breast cancer (it is accepted that these procedures are rare and direct experience may be difficult to obtain).
- ❖ Lymphoedema prevention and treatment

17.5. Surgical management after neoadjuvant treatments

- ❖ Indications for neoadjuvant systemic therapy, specifically with regards to optimisation of breast conserving therapy
- ❖ Breast conservative surgery with/without imaging guided support
- ❖ Targeted excision of axillary clipped node (guided by seed, wire, ultrasound, magnetic marker)

17.6. Surgical management/counselling for genetic syndromes

- ❖ Family history clinic attendance and skills in performing risk assessment (use of risk assessment tools such as IBIS II etc) and counselling
- ❖ Understanding of the surgical, screening and other risk management options for:
- ❖ BRCA 1
- ❖ BRCA 2
- ❖ P53 mutations (Li Fraumeni)
- ❖ Cowden's syndrome
- ❖ PALB2
- ❖ CHEK 2
- ❖ Knowledge of other panels

LOG BOOK

1. Must have attended at least 5 genetic/familial risk assessment clinics
2. Must have followed through at least 5 risk reduction cases as they undergo counselling and surgery (and be signed off as such by their trainer).

17.7. Reconstruction techniques

- ❖ Tissue expander placement
- ❖ Use of acellular dermal matrices or other biological or non biological meshes
- ❖ Permanent silicone implant placement
- ❖ Pedicle flaps for breast reconstruction:
  - Latissimus dorsi
  - TRAM
- ❖ Mastopexy for symmetry
- ❖ Therapeutic mammoplasty
- ❖ Fat grafting and lipofilling
- ❖ Nipple grafting
- ❖ Nipple reconstruction
- ❖ Autologous free flaps (observation only)
- ❖ Revision procedures following on from the above

LOG BOOK:

1. Attended at least 40 regular, at least weekly, pre- and post-surgical multidisciplinary case management meetings
2. Attended at least 70 outpatient clinics during a regular 1–2 year work on a surgical unit with at least 150 primary breast cancer cases a year, according to the local organization practise, including:
   A. Diagnostic, preoperative and postoperative clinics
   B. Clinics with the radiation/medical/clinical oncologist at which the decisions on adjuvant and neoadjuvant therapy are made.
   C. Follow-up clinics at which the side-effects of surgery and radiation can be assessed
   D. Clinics at which the management of women with advanced disease (both locally advanced and metastatic) takes place
   E. Genetic/family historic clinics, in which women at risk are advised
   F. Clinics at with oncoplastic and reconstructive counselling and planning are made
3. Personally performed or assisted as follows

Personally performed

- at least 40 operations on benign or borderline lesions
- at least 80 full axillary lymph node dissections or sentinel node biopsies, including
  - at least 30 full ALND
  - at least 30 SNB
- at least 100 breast cancer operations, including:

- at least 40 breast conserving surgeries, including at least 5 oncoplastic level I - II breast remodelling procedures
- at least 40 mastectomies, including at least 10 NAC- or skin-sparing mastectomies

Assisted or observed:

- at least 5 observed or assisted oncoplastic level II breast remodelling procedures
- observed or assisted at 10 immediate and delayed total breast reconstructions using both implants and autologous tissue.

17.8. Medical oncology

Candidates should attend some medical oncology clinics during their training to gain insight into the following:

- ❖ Management of common complications of chemotherapy administration
- ❖ Use of gene signatures to direct systemic treatment recommendations
- ❖ Management of hormone receptor positive breast cancers (early and late stage)
- ❖ Management of hormone receptor negative breast cancers
- ❖ Management of Her2 positive breast cancers
- ❖ Management of cancers by stage:
  - T stage
  - Node negative
  - Node positive
- ❖ Systemic treatment for the de novo stage 4 patient

LOG BOOK

Observe: 5 new adjuvant chemotherapy for early breast cancer consultations by oncologists.

Observe: 5 new adjuvant radiotherapy for early breast cancer consultations by oncologists.

Observe: 5 new recurrent or metastatic disease consultations by oncologists.

Observe: 5 Follow up visits during oncology treatment.

Observe: 2 new consultations relating to fertility preservation in women about to commence breast cancer therapy.

Manage secondary effects of breast cancer therapy including:

Lymphoedema, acute radiation dermatitis, genitourinary syndrome of the menopause, depression, hot flushes.

17.9. Radiation oncology

Candidates should attend some radiation oncology clinics and radiotherapy planning sessions to give them insight into the following:

- ❖ Radiation biology principles
- ❖ Radiotherapy indications and contraindications:
  - Breast conservation: Whole breast radiation (hypofractionated)
  - Post-mastectomy radiation
  - Regional radiotherapy
  - Primary radiotherapy
- ❖ Management of common radiation complications
  - Acute radiation dermatitis, including use of steroid creams and routine skin health measures
  - Lymphoedema
  - Chronic fibrosis
  - Interaction with implants
  - Secondary cancers (lung, angiosarcoma)
  - Poor wound healing
- ❖ Partial breast radiation techniques:
  - Interstitial brachytherapy
  - External beam partial breast
  - Intraoperative radiation therapy
- ❖ Radiation therapy for metastatic disease:
  - Distant Treatment
  - Palliation

LOG BOOK

15 new breast cancer consultations to discuss RT.

5 observations of radiotherapy administration and planning sessions.

15 f/u visits after radiotherapy treatment.

(10 partial breast irradiation (brachytherapy and or intra-operative RDT) if available).

18. Research

Candidates must have a basic ability to critically appraise evidence based research so they may incorporate new findings into clinical practice and keep up to date. BRESO is aware that undertaking primary research is not possible for all surgeons but a basic level of knowledge is required to keep skills and practices up to date. The following is a recommended knowledge and skills base:

- ❖ Protection of Human Subjects: understanding of the ethical and legislative framework relevant to the conduct of research
- ❖ Inclusion of diverse study populations
- ❖ Basic Statistical Analysis such as understanding means, medians, standard deviation, and simple comparative statistics.
- ❖ Institutional Review (Ethics committee) Board process and application
- ❖ Critical Evaluation of Study Design
- ❖ Assessment of Clinical Trial, Defining levels of Evidence/meta-analysis
- ❖ Defining study populations, sample size, power
- ❖ Basic Survival Analysis
- ❖ Assessment of Health Related QOL
- ❖ Fundamentals of Health Outcomes Studies

CV requirements: To have presented an audit or other piece or research or service evaluation at a local, national or international meeting as evidence of research engagement.

19. Communication skills

Good communication using lay terminology and expressed with empathy and sensitivity is key to good breast care. Candidates should understand the concept of shared decision making and have the skills to be able to support this in their practice.

Formal attendance at a communication skills workshop is best practice but may not be readily available.

- ❖ Communication with and education of the non-medical community (patients and patient groups, managers, students, other professional colleagues)
- ❖ Communication and interaction with patients, in particular breaking bad news, treatment counselling, risk counselling and skills in identification of anxiety and depression
- ❖ Communication and interaction with cancer support groups
- ❖ Communication with and education of non-oncologic physicians

- ❖ Understand and be able to explain the risks and benefits of screening, diagnostic tests, and treatments of cancer
- ❖ Able to identify patients who may benefit from formal psychological support and where this may be accessed locally

20. Optional module-autologous tissue transfer-aesthetic breast surgery

- ❖ Free or pedicled or perforator flaps for breast reconstruction:
  - o DIEP
  - o Gluteal
  - o TUG
  - o LD
  - o Perforator flaps or various types
- ❖ Cosmetic breast surgery
  - o Breast augmentation
  - o Cosmetic breast reduction (benign)
  - o Revision augmentation
  - o Counselling for cosmetic procedures

21. Additional training

Requirements include:

1. Attend two international breast cancer congress during training
2. Attend 2 international breast cancer educational courses
3. Work in a Unit with a properly constituted MDT

22. Approval criteria for tier 2 training centres

The training process for highly specialised breast cancer professionals, in particular breast cancer surgeons, equipped with the mandatory multidisciplinary knowledge and skills for modern breast cancer care, must be carried out in high quality, certified breast cancer centres.

Many hospitals claim to have specialist breast cancer services but it is known that only a few are well organized into Multidisciplinary Specialised Breast Cancer Units and the quality of each individual service remains often uncertain.

For this reasons training institutions to be in line with the BRESO project should fulfill the following minimal requirements in order to enable fellows to acquire advanced knowledge and skills in the surgical and multidisciplinary management of breast cancer:

1. Being accredited as a Certified Breast Center by an International **Quality Certification** process such as the EUSOMA or equivalent (e.g. German DKG/DGS); considering the inhomogeneous distribution of quality assurance initiatives across European territories, as an alternative some form of Quality Certification at national level can be accepted provided that is characterized by a process of accreditation based on fulfillments of mandatory requirements and continuing audit by third parties.
   Such National Certification systems, to be considered in line with the project, must include mandatory requirements in terms of:
   - Critical mass of at least 150 new cases/year per 250.000 inhabitants.
   - Core team, which should meet specific requirements in terms of composition and specialist training of its members
   - Clinical lead
   - Multidisciplinary case managements meetings
   - Protocols
   - Data management and quality assurance
   - Internal and external auditing
   - Facilities/services/clinics
   - Screening program
   - Associated services and personnel
   - Information to patients and waiting time
   - Collaboration with patient's representatives
   - Research activity
   - Continuing education program
   - Teaching

   Once a unified quality certification program, according to international standards for certification bodies, will be set in place across Europe, this will become the only mandatory certification required for an Institution to be accredited as Breast Surgery Training Center.
2. Being based on **multidisciplinary training and multidisciplinary care.**
   The role of the breast surgeon has changed and requires a clear understanding of the complex interactions among the different specialties involved in multidisciplinary approach to breast cancer management.
   The core team members of an accredited training centres for BC specialists, besides reaching the minimum standards in terms of number of treatments provided and time spent in the field of breast cancer, must also demonstrate to have gone through a dedicated specialist multidisciplinary training and multidisciplinary working experience.
   Multidisciplinary team working requires complex interactions and collaborations between specialists, who not only have to work with a common purpose but must have gone through specific training that goes beyond that of the specialty of origin, ensuring an overlap of knowledge. Each specialist must be aware of the working field of his/her colleagues and the most important aspects of the scientific evidence in those fields. Only this way he/she will be able to sit at the multidisciplinary table contributing with informed opinions to make aware therapeutic indications through a critical discussion.
   An accredited breast surgery training center must organize rotations for the trainees in all fields of breast cancer care, in order to allow the development of the necessary across-the-board knowledge and acquisition of all the management strategies to ensure optimal patient care.
3. Be **part of an international network** of referral clinical centres exclusively dedicated to the diagnosis and treatment of breast cancer (e.g. Breast Center Network).
   Such networking promotes interactions, collaborations and benchmarking activities improving breast cancer care and allowing connections among specialist working in the field.
   An accredited training center must offer the trainees opportunities for further international working experiences and collaborations.
   A directory of specialist breast units offers relevant information on centres with specific expertise in diagnosis, state-of-the-art treatment, and care of breast cancer in an attempt to broadcast international standards for multidisciplinary breast cancer care and to allow breast cancer patients to get easier access to fully equipped, quality assured, competent and comprehensive care.
4. **Academic endorsement:**
   Either as a University Hospital or through an academic affiliation the accredited training center must be recognised academically and issue a certificate at the end of the training module.

The working environment within the training institution should be such that students' rotations are in place, giving the breast surgery trainee the opportunity for practical and theoretical teaching activity.

5. Demonstrate to contribute to the continuous education of staff members through the implementation of **research and educational programs.**

   During the attendance of a practical module, the trainee must have the opportunity to participate in multiple teaching conferences internally organized throughout the year at the training Institution, some examples of which are listed here

   - Breast Education Conferences
   - Multidisciplinary Care Conferences
   - Breast Cancer Clinical Research Update/Journal Clubs
   - Yearly Institutional breast cancer meeting with national or international relevance

When we try to define the minimal requirements for standardized level of training, expertise and practice across Europe, we must keep in mind we are aiming at defining a program that can be undertaken all across Europe and must be suitable for different realities.

The course should be organized in **modules that can be completed over time,** not necessarily in one single center, but even in different accredited institution across Europe.

This should ease the attendance of those professionals who have been practicing for a long time and are caught up in everyday clinical practice (probably not capable to undergo a true fellowship program with the duration of 1 or 2 years) minimizing working leaves, expenditures and travelling.

We are not trying to develop the Breast-SUPER-surgeon, who is capable of everything and stands alone in the O.R., but the aim should rather be to obtain **solid basic knowledge** in all fields of breast cancer care and develop good practice in fundamental **surgical techniques** (conventional and oncoplastic). The breast surgeon should demonstrate an **"across the board" preparation** and capacity to sit at the MDM table, having the required **multidisciplinary** knowledge and skills.

23. Recommended further reading

Breast Cancer Management for Surgeons. A European Multidisciplinary Textbook

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St Gallen consensus statements for 2019, 2017 and 2015.

UK National Institute for Clinical Excellence (NICE) Guidelines relevant to Breast Practice.

Familial breast cancer
Pertuzumab
Herceptin
Early and locally advanced breast cancer
Bisphosphonates

National Comprehensive Cancer Network Guidelines (NCCN) for Breast Cancer, 2019. NCCN.Org.

Transforming Breast Cancer Together: European elections manifesto 2019 seizing the opportunities for breast cancer patients. Cardoso F, Bușoi CS, Cattaneo I, Decise D, Cardone A, Filicevas A, Gentile E, Wierinck L, Knox S, Sebastiani S, Terrasanta C, Ujupan S, Ventura R, Wilson B, Rubio IT. Breast. 2019 Dec; 48:54–57. https://doi.org/10.1016/j.breast.2019.09.003.

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Appendix

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Partner Societies

European Society for Radiotherapy and Oncology (**ESTRO**)

European Society for Medical Oncology (**ESMO**)

European Society of Breast Imaging (**EUSOBI**)

European Society of Pathology (**ESP**)

The European Working Group for Breast Screening Pathology (**EWGBSP**)