Meaning of the book cover

Identifying and improving excellence in translational research in Comprehensive Cancer Centers can be compared to the notion of the tree of life that has its branches downwards and roots upwards. Thorough reflection of the roots (core mission, vision and values) is necessary in order to focus improvement in all organizational processes. This ultimately leads to excellent outcomes.

Assessing translational research excellence in European Comprehensive Cancer Centres

Abinaya Rajan

Dear professors, colleagues, family and friends,

With great pleasure, I would like to invite you all to the public defense of my Ph.D. thesis entitled:

“Assessing Translational Research Excellence in European Comprehensive Cancer Centres”

The defense will take place on Friday, 11 September at 14.45 at the Prof. Dr. G. Berkhoff-zaal, Waaier building, University of Twente, Enschede, The Netherlands.

Looking forward to your presence!

Kind regards,

Abi

(Abinaya Rajan)
ASSESSING TRANSLATIONAL RESEARCH EXCELLENCE IN EUROPEAN COMPREHENSIVE CANCER CENTERS

DOCTORAL THESIS

by

Abinaya Rajan
ASSESSING TRANSLATIONAL RESEARCH EXCELLENCE IN EUROPEAN COMPREHENSIVE CANCER CENTERS

THESIS

to obtain
the degree of doctor at the University of Twente,
on the authority of the rector magnificus
Prof.dr. H. Brinksma,
on account of the decision of the graduation committee,
to be publically defended on
Friday 11 september 2015 at 14.45 hrs

by

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Introduction
INTRODUCTION

In 2012, an estimated 8.2 million deaths from cancer in the world (4.7 million in males and 3.5 million in females)\(^1\). In the same year, in Europe, there were approximately 3.45 million new cases of cancer (excluding non-melanoma skin cancer) and 1.75 million deaths from cancer\(^2\). The goal of cancer research (and innovation) is to ultimately reduce mortality and to improve population health. Translational research was created to transform research findings to be systematically and efficiently translated into clinical practice, thereby ultimately benefitting patient/population within a reasonable time frame.

Globally, there are many types of institutions offering cancer research and care such as general hospital structures, academic medical centers and Comprehensive Cancer Centers (CCCs)\(^3\). Although the general hospital structures remain to be the most common structure, in the last decade, CCCs have grown into prominence in both the US and the European contexts. These typically large centralised structures (covering research, education and patient care) are known to attract patients with all tumour types especially rare tumours. Usually, they tend to have a range of innovative clinical trials and rapid translational research, as well as for their exclusive cancer focus and excellent state of the art resources\(^4\).

The aim of this thesis is to contribute to the knowledge on how to identify and assess excellent performance of European Comprehensive Cancer Centers (CCCs) in translational research in order to improve their performance and to designate them as CCCs of Excellence (ExCCCs).

To answer the aim, the thesis takes a step-wise approach by addressing several research issues: (i) by making an inventory on the existing assessments for European CCCs is made so as to not reinvent the wheel with a new evaluation procedure. Existing assessments can be taken as a basis for this excellence assessment wherever possible; (ii) the possible added value of being a European CCC is explored so that specific characteristics of a CCC that add value can be taken into account while developing the evaluation framework; (iii) it is also important to understand the value of current European assessments for CCCs, i.e. do they bring any positive changes/benefits for CCCs?; (iv) identification of existing frameworks for assessing translational research in CCCs in order to develop an excellence framework based on prior evidence and best practices; (v) engagement of key stakeholders across Europe to give relevant input to the framework development process; (vi) piloting of the framework in a number of European CCCs to validate the emerging criteria of excellence.

This introductory chapter describes the research scope, the research questions, the research methods for each individual chapter and the overall outline of the thesis. To explain the purpose of this thesis, we provide two definitions upfront: (i) Comprehensive Cancer Centers (CCCs) and a description of how this concept was developed in Europe and (ii) definition of
and obstacles for translational research.

Because this thesis was conducted as part of a EU funded project (EurocanPlatform\textsuperscript{5}) the description of this project and its goals have also been presented.

**Development of the concept of Comprehensive Cancer Centers (CCCs) in Europe and a common European definition**

To improve the quality of research and care in European cancer centres, the Organization of European Cancer Institutes\textsuperscript{6} (OECI) (a voluntary network of over 70 cancer centres and organisations involved in Cancer field) launched an Accreditation and Designation (A&D) programme\textsuperscript{7} in 2008. This emerged from professional consensus among leading oncologists in Europe and taking into direct reference the national accreditation programmes of Canada, the Netherlands and France.

The programme is voluntary for cancer centres. It facilitates the collection of defined data and the assessment of cancer centre quality on research, education and care aspects. Designation enables centres to be categorized as one of the following based on quantitative standards: Cancer Unit, Clinical Cancer Centre, Cancer Research Centre and Comprehensive Cancer Centre.

Accreditation is about quality improvement and is based on qualitative standards. Centres first prepare themselves for the audit by checking which qualitative standards they meet and which they should implement. This phase (also known as self-assessment) generally takes a few months up to a year. After this period centres are audited by peer-reviewers (typically a team of 4 members audit every Centre). Team composition is usually: a researcher, a nurse, a manager and a clinician. The team is selected from a pool of experts from 75 European cancer institutions. Auditors give their final recommendations for improvement as well as a decision on accreditation. Centres must produce an improvement action plan detailing how they are going to follow the recommendations. The accreditation and designation status is valid for 4 years.

A report on the first series of 10 audited centers (activities and facilities) was published in the Journal of Oncology Practice (2014) by Mahasti et al\textsuperscript{8}. It describes the (anonymised) data that has been gathered by the OECI programme that can be used for benchmarking the performance of these centers (See for example, Figure 1 and 2 for the type of data being gathered).
Common European definition of Comprehensive Cancer Centers

The following features define a European Comprehensive Cancer Centre (CCC) based on the definition set by the Organization of European Cancer Institutes.\textsuperscript{6,7}

- A highly innovative character and multidisciplinary approach using the potential of basic, translational and clinical research and clinical facilities and activities, organized in a sufficiently identifiable entity,

- A direct provision of an extensive variety of cancer care tailored to the individual patient’s
needs and directed towards learning and improving the professional, organisational and relational quality of care,

- Broad activities in the area of prevention, education, and external dissemination of knowledge and innovation. In order to accentuate the differences with other cancer centres, a CCC separates itself in the following points: high level of infrastructure, expertise and innovation in the field of oncology research, maintenance of an extensive network including all aspects of oncology treatment and research, related to an academic/university centre or is an academic centre.

The OECI accreditation and designation programme has been taken the basis for the development of the excellence framework. That is only centers that have been designated, as a CCC by the OECI will initially be eligible for to be assessed and designated as EXCCC.

**Definition of translational research in oncology**

The role of translational research in ensuring rapid transfer of knowledge from basic science through to clinical studies and ultimately reaching patient benefit has been stressed for over the past two decades. It has rapidly evolved especially in the past decade\(^9\) and numerous definitions currently exist\(^{10,11}\). However, only few definitions cover the full continuum from bench to bedside and vice versa\(^12\). One definition\(^13\) that does, was put forward by the staff of the National Cancer Institute (NCI) while working with Dr. Richard Klausner, it’s former Director:

“Translational research uses knowledge of human biology to develop and test the feasibility of cancer-relevant interventions in humans OR determines the biological basis for observations made in individuals with cancer or in populations at risk for cancer. The term “interventions” is used in its broadest sense to include molecular assays, imaging techniques, drugs, biological agents, and/or other methodologies applicable to the prevention, early detection, diagnosis, prognosis, and/or treatment of cancer.”\(^{13}\)

**Obstacles for translational research**

To be able to understand the need of the research questions in this thesis, we must first know some of the current challenges for excellent translational research performance in CCCs. First and foremost is the issue of the time that it takes to translate research into practice. Evidence suggests that it takes several years (on average approximately 17 years) for research to be translated to practice\(^{14-20}\). Secondly, a number of issues have often been discussed both in the European as well as in the American context as bottlenecks to translational research\(^{21,22}\). These include: cultural differences between basic scientists and clinicians in the form of poor communication, differences in education and training, goals and reward mechanisms;
The need to identify and designate European CCCs as Excellent CCCs (ExCCCs) in translational research

The EurocanPlatform\(^5\) is an European Commission (EC) funded project that brings together 28 European Cancer Research Institutions and Organisations to work together with the aim of creating a platform for translational research to improve prevention, early detection and therapeutics. Lately, however, outcomes research and methodologies for evidence-based cancer medicine have become a very important component of translational research and consequently, the EurocanPlatform now includes four priorities that can be tackled using variable geometries. The long-term goal of the EurocanPlatform is the creation of a sustainable virtual European Cancer Institute\(^14\) (ECI) having the critical mass of expertise, resources, infrastructures, and number of patients that is needed to innovate and perform in all areas of cancer research.

As a result of the recent developments triggered by the creation of Cancer Core Europe\(^15\), quality assurance of cancer research centres has become a priority issue for the EurocanPlatform, which in collaboration with the European Academy of Cancer Sciences\(^16\) (EACS) has been working in a constructive way for the past few years to establish a designation methodology for Comprehensive Cancer Centres (CCCs) of Excellence (EXCCCs). The methodology will be helpful not only to organise CCCs for innovative research, but also to harmonise infrastructures, and contribute towards generating sustainability.

The aim of one of the work packages of this project was to develop criteria of excellence in translational cancer research (performed by The Netherlands Cancer Institute). The objectives were twofold: (i) to elaborate a system to identify and establish CCCs of outstanding performance that qualifies them to join translational research platforms and (ii) to use the methodology as a basis for assessing and designating ExCCCs for future platform initiatives.

There were four deliverables: drafting a designation set identifying excellent performing platform participants, containing a list of performance-based criteria, a data retrieval model, including a formal procedure; producing a quality assessment report on all participating platform members; reporting on the evaluation of the designation system as applied in the EurocanPlatform and; producing a proposal for assessing and designating EXCCCs for future platform initiatives based on the experience gained in this project.
Overall aim of the thesis, research questions and methods and how the different chapters are interlinked

This thesis aims to present an assessment framework to identify and designate excellent European CCCs in translational research. Linked to this aim are several sub-questions (see Figure 3). They include: checking the existing assessments in Europe and how this methodology contributes to new knowledge on assessing and improving translational research process (Chapter 2), to understand the benefits generated by an existing European accreditation & designation (Chapter 3), to understand the added value of being a CCC (Chapter 4), to identify existing assessments for translational research (Chapter 5), to develop the assessment framework with stakeholder consensus (Chapter 6). Finally, we piloted the framework with a number of CCCs (Chapter 7). This section presents the research questions, their rationale and the methods.

The rationale for checking existing assessments, added value of CCCs, added value of assessments for CCCs, existing assessments for translational research is to develop the current framework based on available best practices and evidence also in order to minimize bureaucracy.

Research question 1: What are the existing assessment frameworks for European CCCs?

Rationale European CCCs go through several assessments at regional, national and international levels. However, many things regarding these assessments remained unclear such as, the type of assessments being conducted, who conducts them and with what frequency, are these assessments focused on assessing research, patient care or both. Also it was unclear whether any existing assessments for CCCs in translational research already existed. This study helped us prevent the reinvention of wheel and to reduce unnecessary bureaucracy with a new (excellence) assessment framework if similar criteria were already

Figure 3. Summary of research questions
present in other assessments.

**Method** Data was collected on existing assessments through a survey with the quality managers from CCCs in 28 EU member states. Purposive sampling was employed. We contacted a leading CCC per member state that was member of the Organization of European Cancer Institute (OECI). This gave us an overview of existing assessments available for CCCs across Europe. Responses from all CCCs were analysed thematically and verified with the respondents for validity.

**Research question 2: What are the staff perceptions of change resulting from participation in the OECI European cancer accreditation program?**

**Rationale** This paper reports a qualitative evaluation of the OECI A&D programme by understanding the experiences of staff from the 8 Centers. This paper holds relevance to this thesis since it was necessary to understand whether an existing European assessment can bring positive changes/benefits for cancer centers (especially for CCCs). This paper is complementary to the study published by Mahasti et al, 2014 who did a quantitative analysis of the data gathered by the OECI A&D programme from 10 cancer centers. OECI A&D programme is the only European level assessment for CCCs, and so, it was important to learn from the experiences of cancer centers that had took part in it so that it can be taken into account while developing another European level (excellence) assessment.

**Method** Staff interviews were conducted from 8 cancer centers that had been through the OECI A&D Programme. 3 of the 8 Centers were in the initial stage of the process and 5 of them had undergone a peer-review. 24 interviews were conducted with clinicians (5), nurses (6), managers (8) and basic/translational researchers (5) on changes observed from participating in a European cancer accreditation program. Data was thematically analysed and verified with participants & checked against peer-reviewers’ feedback. Pawson et al’s change theory was applied to interpret the findings. According to this theory there are five types of changes that occur in healthcare organizations and dovetail each other: role change, administrative change, strategic change and organizational change and motivational change.

**Research question 3: What is the added value of being a CCC?**

**Rationale** Before developing and implementing an excellence framework for European CCCs in translational research, it was important to know the existing added value of being a European CCC so that the current excellence framework can be adapted to the specific needs and characteristics of a European CCC. The concept of a CCC was first coined in the National Cancer Institutes (NCI) in the US. So, we took the US definitions and NCI criteria as well as the European definition and criteria for CCCs set by the OECI A&D programme into account to understand the added value of being a European CCC. The findings from this
study helped inform the excellence assessment by showing the areas of a CCC that specific add value to cancer community when compared to other organizations involved in cancer research and patient care.

**Method** A systematic literature review (also including grey literature search) was conducted to identify criteria that can define the added value of a CCC. An initial set of criteria were drafted and placed in the European Foundation for Quality Management (EFQM) model. The draft criteria set was sent via a survey to all the OECI members (the lead contact person from 70 cancer institutions from all across Europe). The aim of the survey was to shortlist/prioritize the most important criteria. To validate the survey results, we conducted staff interviews with four disciplines: research, management, clinical and nursing from 6 CCCs. We employed a purposive sampling and invited one staff member per discipline per CCC (n=24, i.e. 4 from each center, one pertaining to each discipline). Data was thematically analysed using the criteria set. Both in the survey as well as in the interviews, before validating literature results, an open-ended question was posed to the participants on what they felt was the added value of the CCC. This was asked upfront in order to avoid any bias. After the interviews, respondents were also asked to select the criteria (from the same criteria set as used in the survey) that were most relevant for distinguishing the added value of CCCs. Respondents also suggested a list of indicators for each criteria that can be helpful to understand the added value of CCCs.

*Research question 4: What existing frameworks are suitable in assessing the performance of European CCCs in translational research?*

**Rationale** A systematic literature review was conducted to check whether there are any existing frameworks/models that can be used to assess the excellent performance of European CCCs in translational research. As mentioned in research question 1, the aim was to reduce bureaucracy and minimize the workload on CCCs with a new European excellence assessment. We checked for frameworks/models not just within oncology but also from other medical and non-medical fields since we wanted to include best practice examples from other fields as long as they were applicable to oncology.

**Method** To critically appraise existing frameworks/models, a set of questions/criteria was prepared from the literature review: Does the model present translational research as a continuum with bidirectional flow between research and practice? Was the purpose of the model performance assessment of translational research? Is translational research about generation of new knowledge? Does the model address systems integration? Does the model explain any strategies for performance assessment of translational research? Has the model reviewed other translational research models?
Research question 5: What are the results of a European consensus with stakeholders on the draft excellence framework?

**Rationale** To develop the excellence assessment framework, a draft criteria set was prepared and a consensus was achieved on key criteria using a stakeholder consensus building exercise across Europe. To develop a European assessment framework, consensus building was crucial since many regional, cultural and social barriers need to be taken into account to develop an inclusive framework. And this being a bottom-up development, including key actors such as clinicians, researchers, managers and patient representatives from across Europe became crucial.

**Method** A survey was conducted among different stakeholders (researchers, clinicians, managers and patient representatives) to cancer institutions (n=78) across Europe (including CCCs and Cancer Research Centers (CRCs), clinical cancer centers (CLCs) and cancer patient organizations). The survey identified and shortlisted important criteria. A focus group was conducted with a representative sample of the survey participants to validate the criteria from the survey that seemed to be the most relevant. Next, an expert team under the governance of European Academy of Cancer Sciences (EACS) was put together who checked these criteria and refined them. From this, we checked the reports of two CCCs to check for any other relevant criteria that were missing. The expert team from EACS once again checked the emergent criteria and approved them. This final set was disseminated to the cancer institutions (n=24) that are in the EurocanPlatform for an open comments round.

Research question 6: What are the pilot results of excellence framework with 3 CCCs?

**Rationale** A draft excellence assessment framework for CCCs in translational research was now ready. However, as part of the project and scientific requirement it had to be tested across Europe. Due to time and resource constraint, we decided to test it in a minimum of 3 CCCs. This would give us an idea whether the criteria that we have developed so far are sufficient to judge the excellent performance of CCCs in translational research or were additional criteria needed. The pilot was to rate the importance and reliability in terms of assessing excellence and also to check the feasibility of these criteria for implementation in CCCs across the EU. The pilot was thus to evaluate the excellence criteria themselves and so the aim here was not to designate the CCCs. Although, inevitably a pilot designation status was provided to the CCCs that were piloted.

**Method** 3 CCCs (The Netherlands Cancer Institute, Helsinki University Central Hospital Cancer Center and Cambridge Cancer Centre) volunteered to take part in the pilot of the excellence framework. They were asked to provide their existing reports of national/international evaluations (peer-review mechanisms). These reports were in English and not older than 5 years old. A review team of experts (n=4 from NCI, Canada and Europe) was put together by the EACS. They reviewed the reports against the set of draft excellence criteria.
and site-visited the 3 CCCs. Strengths and opportunities for each CCC was identified. After the pilot, the final draft set was shared with experts from the EACS\textsuperscript{16} (n=200) in an open comments round to vote whether the draft was adequate or whether it needed further amendments.

**Thesis outline**

**Chapter 1** summarizes the research questions, research methods and how these questions are covered in the chapters (see also Table 1). **Chapter 2** shows the need to use existing European assessment frameworks to minimize bureaucracy of assessments and by not reinventing the wheel with new assessments. **Chapter 3** summarizes the results of a qualitative study of the Cancer Centers that have been through the OECI A&D programme. **Chapter 4** identifies the added value of being a Comprehensive Cancer Center (CCC) and the ideal characteristics of a CCC from staff perspective and based on literature evidence. **Chapter 5** presents a systematic literature review of the existing translational research frameworks to identify the most suitable framework for performance assessment of Comprehensive Cancer Centers (CCCs). **Chapter 6** provides a draft framework that was developed through European consensus with stakeholders (researchers, clinicians, managers and patient representatives) from different cancer institutions. **Chapter 7** summarizes the results of piloting the draft framework with 3 European CCCs and getting the final approval of the framework with experts involved.

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**Annex – I** presents an additional paper (expert reflection piece) produced by an alliance of thirteen research institutes [as part of EU-LIFE (www.eulife.eu) translational research working group] with the common goal of promoting excellence in European life sciences.
It presents five ways to foster translational research: promote interdisciplinary research; collaborate to target unmet medical needs; nurture international collaborations; create and share the required resources; and encourage a cultural change. This paper has taken inspiration from number of criteria from the excellence framework that has been developed as part of EurocanPlatform. The Netherlands Cancer Institute has also contributed ideas and best practices input to the paper.
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Quality assessments for cancer centers in
the European Union

Anke Wind*
Abinaya Rajan*
Wim H. van Harten

Submitted
ABSTRACT

Objectives: Cancer centres are pressured to deliver high-quality services that can be measured and improved, which has led to an increase of assessments in many countries. A critical area of quality improvement is patient safety. An overview of existing assessments can help stakeholders (e.g. healthcare professionals, managers and policy makers) improve the quality of cancer research and care and lead to patient benefits. This paper presents key aspects of assessments undertaken by European cancer centers, such as: are assessments mandatory or voluntary? do they focus on evaluating research, care or both? And are they international or national?

Design, setting and participants: A survey was sent to 33 cancer centers in 28 EU member states. Participants were asked to score the specifics for each assessment that they listed.

Measures: An overview of the assessments per country with a differentiation of characteristics.

Results: Based on the responses from 19 cancer centers from 18 member states, we found 110 assessments. The numbers have steadily increased from 1990's till 2015. Although, a majority of assessments are on patient-care aspects (n=45), it is unclear how many of those include assessing patient outcomes. Only few assessments cover basic research. There is an increasing trend towards mixed assessments (i.e. combining research and patient-care aspects)

Conclusions: The need for assessments in cancer centers is increasing. To improve efforts in the quality of research and patient care and to prevent new assessments that “reinvent the wheel”, it is advised to start comparative research into the assessments that are likely to bring patient benefits. Do assessments provide consistent and reliable information that create added value for all key stakeholders?
INTRODUCTION

Cancer Centres (CCs) are located in complex organisational and regulatory environment and are increasingly faced with challenges to provide safe patient care [1]. More specifically, CCs in Europe as elsewhere are under intense pressure to deliver high-quality services and be transparent about it. In relation to this, there is an increasing emphasis on quality and safety improvement initiatives [2]. Patients and payees increasingly demand proof of guaranteed safety and quality of services. In addition, the financial claim that cancer research and care activities put on national and regional health systems at a time when fiscal austerity measures have led to deficits in public budgets and sustainability are putting an increasing demand on performance assessment [3,4]. This on-going impact on health budgets has led to additional demand for the already growing need for transparency [5].

Quality and safety of care is complex as it combines the perspectives of policy makers, purchasers, payers, healthcare professionals, researchers and patients [6]. Setting and applying clear performance standards through mechanisms, such as licensing, certification, and accreditation, is crucial to ensure patient safety [7]. CCs go through several assessments on their performance and quality, its nomenclature extending to accreditation, certification, and/or other types of evaluations; however so far an overview of these assessments on European level does not exist.

This article presents key findings from a survey that was conducted with CCs in the European Union. The goal was to obtain an overview of existing assessments in terms of whether they are: mandatory or voluntary; focused on evaluating research or patient care or both; regional, national and/or international. Unfortunately there is limited evidence on the added value of these (organisational) assessments for patient care or patient outcomes, primarily due to methodological issues related to limited insight into the mechanisms through which these exert their effects. However relevant, that is not the object of this overview.

The rationale for this study was originally to provide input for objective one of the BenchCan project [8]: To collect, compare and align, by consensus formation, the standards, recommendations and accreditation criteria of comprehensive cancer care adopted in selected European countries of different geographic areas. The BENCH-CAN project aims at linking 11 cancer centres in 10 EU Member States; the UK (N=1), Germany (N=1), Finland (N=1), the Netherlands (N=1), Portugal (N=1), Italy (N=2), Romania (N=1), Hungary (N=1), Poland (N=1), and Lithuania (N=1). The BENCH-CAN [8] objective is to benchmark comprehensive cancer centers and yield best practice example in order to contribute to improvement of multidisciplinary patient treatment. Because of the potential to inform decision makers about existing assessments so that they can take some steps towards regulating these as well as minimizing the related bureaucracy, an aspect that is especially relevant for clinicians [9] it was decided to expand the study. Organizations conducting these assessments and
(also non EU) CCs can gain better understanding of what type of assessments are currently undertaken in view of growing interest in cooperation in international research consortia [10,11]. A recent study among Canadian Oncologists by Lim et al [12] shows that one of the reasons for them not participating in this type of Quality Improvement initiatives is the lack of knowledge about various performance assessment initiatives.

The context of European cancer centres

Assessments are contextual, and so, first there is a need to understand the type of health system in which the CCs operate. Health systems in the EU can be described in different ways. For this article, the typology developed by Rothgang et al [13] and Wendt et al [14] was used, which presents four types of health systems: the National Health Service (NHS), National Health Insurance (NHI), Social Health Insurance (SHI) and the Etatist Social Health Insurance (ESHI). Three dimensions distinguish each of these systems: financing, service provision, and regulation [15]. Each dimension can be dominated by state, society (for example NGO’s, consultancy agencies or research institutes), or private actors. The US system has a mix of characteristics of those systems, however unique about the U.S. system in the world is the dominance of the private actors over the public actors (state and societal) [16]

Figure 1. Overview of typology of health systems in the EU

* Malta and Latvia have mixed public/private service provision
** Slovenia conflicts with the logic of the RW typology as societal actors are in charge of regulation and financing, but service provision lies predominantly in the hands of state actors. Slovenia is, however, gradually evolving into a SHI
METHODS

Survey
A survey was sent initially to the 11 BENCH-Can pilot sites. After the decision to expand the study, the survey was sent to one cancer center in each of the other EU member states with the exception of Belgium, Austria and the UK where 2 cancer centers were contacted. This was due to the lack of response within the given timeframe from the first contacted center. So, a second center was contacted in each of these countries. In total the survey was send to 33 cancer centers. For some member states, CCs could not be easily identified and so, other organizations dealing with cancer care and/or research were contacted. CCs were identified through the European Society for Medical Oncology (ESMO) [17] and Organisation of European Cancer institutes (OECI) [18]. The survey was addressed to the lead administrative person in each institute. Participants were asked to describe several topics for each assessment that were listed: (i) the name of the assessment body (ii) whether the body was public or private; (iii) if the assessment was mandatory or voluntary; (iv) the level (regional/national/international) at which the assessment was performed; (v) if the assessment focused on research, patient care aspects or a mix of standards (vi) the frequency of the assessment; (vii) if the assessment led to keeping/losing operating license and/or public funding and (viii) the year in which the assessment was first performed.

Data management and inclusion/exclusion criteria
Among the 28 EU member states that were asked to participate data were received from 18 member states i.e. one cancer institution per member state (64%), with the exception of Italy (two cancer institutions). Not all surveys were filled out correctly. So, a follow up was done by e-mail or phone with all respondents to clarify the answers. Two researchers (AW and AR) examined the data and excluded the listed assessments that did not fit the inclusion criteria. The inclusion criteria for the assessments were: the assessment had to assess cancer care, cancer research or a combination of both. All assessments that did not fit these criteria were excluded from the study. Eligible assessments were divided into three categories: clinical/patient care oriented assessments; research oriented assessments; and assessments that are oriented at a combination of care and research. The characteristics of the assessments were analysed with excel. The analysis of findings includes only centers that completed the survey. This full list of included assessments (see annex 1) was circulated amongst the respondents for final data validation.
## Table 1 Scope and nature of assessments

<table>
<thead>
<tr>
<th>EU member state</th>
<th>Pure research assessments</th>
<th>Patient care assessments</th>
<th>Research + Patient care assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mandatory Average frequency</td>
<td>Voluntary Average frequency</td>
<td>Mandatory Average frequency</td>
</tr>
<tr>
<td>Austria</td>
<td>1</td>
<td>2 years</td>
<td>0</td>
</tr>
<tr>
<td>Croatia</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Denmark</td>
<td>0</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Estonia</td>
<td>2</td>
<td>2 years</td>
<td>1</td>
</tr>
<tr>
<td>Finland</td>
<td>0</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>France</td>
<td>1</td>
<td>2 years</td>
<td>0</td>
</tr>
<tr>
<td>Germany</td>
<td>1</td>
<td>5 years</td>
<td>0</td>
</tr>
<tr>
<td>Hungary</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Ireland</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Italy</td>
<td>0</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Lithuania</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Poland</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Portugal</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Slovenia</td>
<td>3</td>
<td>1 year</td>
<td>2</td>
</tr>
<tr>
<td>Spain</td>
<td>1</td>
<td>MTOY²</td>
<td>1</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>5</td>
<td>4,25 years</td>
<td>0</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>16</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>TOTAL</td>
<td>28</td>
<td>45</td>
<td>37</td>
</tr>
</tbody>
</table>

¹ NC: Not Clear
² MTOY: More than Once a Year
³ OTE: One Time Event
RESULTS

Nature and scope of assessments

Based on the responses, we found 110 known cancer related quality assessments in total in 20 EU member states (See Table 1). The majority of the assessments focus on patient-care aspects (n=45), such as waiting and throughput times, patient participation and patient satisfaction followed by the mixed assessments that focus on patient care as well as some research aspects (n=37). In those mixed assessment especially organizational aspects of care and research such as multidisciplinary harmonization / integrated care and scientific interaction and integration receive emphasis, whereas pure research based assessments, which are the least (n=28), are directed towards research outcomes such as number of publications. The majority of patient care related assessments are reported to be mandatory. Mixed assessments are more voluntary.

The majority of assessments (n=63) is done at the national level, followed by thirty-eight assessments that are known to be operational at an international level. Some assessments are implemented at a national level, but are also operational at an international level, these have been counted as national. There are only a handful of regional assessments (n=9) such as in Estonia and in Finland (See Table 2). Almost all mandatory assessments are national and are mainly related to keeping license and/or receiving public funding. In contrast, most voluntary assessments are international, and rather aim at quality improvement and are seldom directly tied to licensing or funding.

Trend of assessments

Respondents were asked in which year the first assessment for the assessments began. For some this can be easily identified, but a majority it is difficult to date precisely. Similarly, first assessments may be considered as pilot testing rather than being operational. The graph in figure 2 shows a cumulative presentation of the trends in the number and types of assessments. It suggests that:

The numbers of assessments have steadily increased from the 1990's till 2015.

In over the past two decades, there has been most increase in patient care assessments, followed by the mixed assessments of patient care and research aspects. The rise in pure research assessments has been the least.
### Table 2 Level of assessments

<table>
<thead>
<tr>
<th>EU member state</th>
<th>International</th>
<th>National</th>
<th>Regional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>-</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Croatia*</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>2</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Denmark</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Estonia</td>
<td>-</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Finland</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>France</td>
<td>1</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Germany</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Hungary</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Ireland*</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Italy</td>
<td>6</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Lithuania</td>
<td>1</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Netherlands</td>
<td>3</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Poland</td>
<td>-</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Portugal</td>
<td>2</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Slovenia</td>
<td>12</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>Spain</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>2</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>38</strong></td>
<td><strong>63</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

Figure 2 Trends in the number and types of assessments
DISCUSSION

Continuous growth of assessments in Europe and how it compares to the US

The number of assessments in the EU has tripled since 2000. This shows that quality assessment in all its forms is a growing industry. It is particularly interesting to note a steady rise from 2000-2007, and especially following the economic crisis (2007/2008) more assessments seem to have cropped up. Whether this steep rise is related to the need for more accountability during and post financial crunch situations is hard to say. Although the emphasis on mandatory assessments will remain for the purpose of funding and licensing health services, voluntary assessments are equally gaining in popularity. In fact, most of the new assessments are voluntary, however, this does not exclude the pressure on CCs to participate in them. This shows that most assessments seem to be in a transition, moving from a friendly tool of self-assessment and development to a governing tool that agencies use for various purposes.

Regarding CC’s, in the US there are at least three main assessments: 1 The Joint Commission accreditation [19] for healthcare organizations and programs as a whole; 2. The Commission on Cancer (CoC) of the American College of Surgeons for the quality of cancer care delivery [20]; and 3 The National Cancer Institute (NCI) designation [21] for assessing excellent multidisciplinary translational cancer research programs, in which almost all leading CCs in the US participate. Europe is gradually moving towards common European assessment frameworks in order to benchmark and improve cancer research and patient care activities across the EU, but this has not been as developed as it is in the United States. It is with this intention that European Commission is allocating more budgets for research and innovation (e.g. through specific funding programs such as Horizon2020) [22] with the idea of improving EU competitiveness in excellent science [23]. However, the challenges that arise from health care being under national jurisdiction and individual responsibility of each EU member state has lead to only gradual steps towards harmonization towards EU assessments are seen so far. As healthcare is a major component of national economies (as a user of public funds but also as an investment that generates jobs, taxes and procurement opportunities for Small and Medium Enterprises) within a monetary union, increasing steps towards EU influence on these issues seems inevitable [24].

The link between a health system and nature and scope of assessments

A link between the type of health system and the nature of the assessments is visible only in some member states. For example, in the United Kingdom where a National Health Service is being used (regulation, financing and provision by the state, see figure 1) a lot of mandatory, national assessments seem to exist. The same goes for Spain. In other countries that have an NHS model, e.g. Finland and Portugal assessments seem to be more voluntary
than mandatory. Within the National Health Insurance system (regulation by the state) one would again expect a lot of mandatory and national assessments, but the opposite is the case in Italy, where a lot of international voluntary assessments are performed e.g. the Joint Accreditation Committee- International Society for Cellular Therapy and European Society for Blood and Marrow Transplantation (JACIE)[25] and International Organization for Standardization (ISO) [26] and the European accreditation by the Organization of European Cancer Institutes (OECI) [18] But these initially voluntary assessments are sometimes mandatory for either keeping license and/or are demanded by government to maintain Comprehensive Cancer Centre status, such as in Italy. So, the voluntary assessments end up being mandatory at some level.

In the Social Health Insurance (SHI) type, societal actors dominate healthcare regulation and financing, which is reflected in the assessments listed by the centres from Germany and Croatia e.g. in Germany accreditation of cancer care is performed by the German Cancer society [27] which is a societal actor dominated by physicians. In most Central and Eastern European countries that have an Etatist Social Health Insurance system, there is a tendency for more mandatory national assessments, while in the majority of Western Europe and Nordic countries there is tendency to participate in more voluntary international assessments. Only in few member states, did we notice regional level assessments e.g. Italy, Finland and Estonia. This can be partly explained by decentralization/devolution of powers to regions in some EU member states [28] Evidence suggests that mandated external quality assessments are less effective than voluntary assessments because the effectiveness of accreditation is dependent on its voluntary nature, non-threatening process, and interactive process with external reviewers as a means of effecting and speeding up quality improvements [29]

**Traditional view of assessments and shifting focus**

Assessments focused on research are still limited in Europe when compared to patient care assessments. One of the reasons is that, being an accredited centre in cancer care attracts patients or ensures a license to operate. Therefore, inevitably it is of more direct importance than assessing research. Another reason is that assessing impact of research on healthcare outcomes is more difficult than just assessing care outcomes [30] In research, metric-driven indicators such as impact factors are often criticized [31] and consensus on value-based indicators is still evolving e.g. how to define success in translational research (bench to bedside and back) in terms of practice-changing innovations [32] The awareness that alignment between research and clinical areas is essential in successful translational research [33] can explain why more mixed assessments are being introduced in the EU. This is comparable to the SPORE [34]— the Specialized Programs of Research Excellence — a cornerstone of National Cancer Institute's efforts dedicated to capitalize on research opportunities that have the potential to change the current paradigm in the prevention, detection, diagnosis, and/or treatment of human cancer. Given the amount of funding
that goes into research in the EU [35], evaluating research becomes indispensable. More specifically, comparative research assessments are needed to make evidence based decisions on most suitable therapies in clinical practice [36]

**Transparency**

The move towards statutory and governmental endorsement is associated with freer access by the public to the standards, processes and findings of assessments. Half of the assessments make their standards available at little or no cost; one-third also make full reports of individual assessments publicly available. However, many organizations are unwilling to share their standards and norm descriptions as this serves also as a source of income and intellectual property. For example, in many EU member states, the assessment reports as well as the program standards are in the local language and it takes time, money and effort to accurately translate the reports into English. This makes it hard to judge assessments in terms of how each assessment can bring added value to the different stakeholders. The first step in deciding the value of assessments is to make their outcomes publicly available and accessible. Next, public consultation must occur with key stakeholders to decide the parameters to evaluate the added value of assessments. A related issue is that whether the data, if made publicly available, are good enough for promoting real quality improvement and helping consumers make choices [6] Although most assessments focus on patient care aspects, it is unknown whether improving patient outcomes is a prominent feature of these assessments. Evidence shows that for example patient safety can be improved if a healthcare organization undergoes licensing, certification and accreditation [7] but this is unknown for patient outcomes. Hence, it is important to make this a mandatory part of assessments for cancer centres.

**Strengths and Limitations**

This study describes the type and number of assessments at 19 cancer centres in 18 out of 28 member states of the European Union. This is the first systematic European attempt to gather data on assessments for cancer centers. The results were validated with study participants by asking them not just to confirm the data for their own cancer center but also giving them an opportunity to comment on assessments that were listed by other cancer centers in Europe. This study gives sufficient evidence to start thinking about how to reduce the burden of assessments for cancer centers and how to make them more transparent and effective.

Content of these assessments (e.g. assessment reports, outcomes) were not easy to access due to language barriers (each cancer center has it in its local European language and is not always translated in English) and/or lack of publicly available information. The individuals from cancer centers who provided the data were quality managers (and/or research directors/senior executive managers) who are usually responsible for organizing
and implementing assessments in their center. However, many assessments are multi-disciplinary in nature, involving a wide range of staff, therefore future research should focus on validating the responses beyond quality managers. Our assumption is that non-responses may have been the result of not identifying or contacting the appropriate people, rather than reluctance to provide data and/or that formalized assessments do not exist in some member states. Another limitation related to the year in which the assessment started is the fact that, first assessments may be considered as pilot testing rather than becoming operational. It is therefore difficult in some cases to identify the year in which the actual assessment started.

CONCLUSION

There are 110 assessments that CC’s currently undergo in 20 EU states and the number keeps increasing. Although there are clear benefits of assessments, more robust research is needed to understand their value in terms of how they improve patient quality and safety. CCs go through frequent assessments, sometimes as often as more than once a year, this can be a very time consuming as well as expensive for those organizations. Rapid uptake of voluntary assessments is associated with direct financial incentives (such as linkage to core funding or reimbursement) and government encouragement. However, decision makers should regulate assessments to reduce unnecessary work for CCs that do not bring benefits or added value, that are bureaucratic, time-consuming and/or unaffordable by CC’s. This article shows that demand for assessments is increasing and changing rapidly in terms of international assessments as well as mixed assessments of cancer research and care. Assessments must be transparent to bring credibility and accountability among stakeholders. Given the importance of quality of care, patient safety and outcome improvement in cancer care, it would be desirable to evaluate the impact of assessments in these areas. We recommend future research to go deeper into understanding process and outcome related issues; how much time does each assessment take to prepare and implement, people and money consumed, who are the peer-reviewers and what are their backgrounds, how are standards developed and revised, sources of income for assessment bodies, and last but not least does the exercise meets its objectives?

Contributors: AW and AR designed and performed the survey, analysed and interpreted the data, and drafted the manuscript. WvH participated in the analysis and interpretation of the data, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Competing interest None declared.

Data sharing statement Additional data for reviewing purposes is available.
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Staff perceptions of change resulting from participation in a European cancer accreditation program: a snapshot from 8 cancer centers

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Anke Wind
Mahasti Saghatcian
Frederique Thonon
Femke Boomsma
Wim H. van Harten

eancer. 2015, 9; 547
ABSTRACT

Background Healthcare accreditation is considered an essential quality improvement tool. However, its effectiveness has been critiqued.

Methods 24 interviews were conducted with clinicians (5), nurses (6), managers (8) and basic/translational researchers (5) from 8 European cancer centers on changes observed from participating in a European cancer accreditation program. Data was thematically analysed and verified with participants & checked against auditor’s feedback.

Results Four change categories emerged: (i) growing importance of nursing and supportive care field (role change). Nurses gained more autonomy/clarity on their daily duties. Importance was given to hiring and training of supportive care personnel (ii) critical thinking on data integration (strategic change). Managers gained insight on how to integrate institutional level data (iii) improved processes within multi-disciplinary team meetings (procedural change). Clinical staff experienced improved communication between multidisciplinary teams (iv) building trust (organizational change). Accreditation improved center’s credibility with its own staff and externally with funders and patients. No motivational changes were perceived. Researchers perceived no changes. Auditor’s feedback included changes in 13 areas: translational research, biobanks, clinical trials, patient privacy and satisfaction, cancer registries, clinical practice guidelines, patient education, screening, primary prevention, role of nurses, multidisciplinary team, supportive care and data integration. However, our study revealed that staff perceived changes only in the last 4 areas.

Conclusion Staff perceived changes in data integration, nursing and supportive care and in certain clinical aspects. Accreditation programs must pay attention to the needs of different stakeholder groups, track changes and observe how/why change happens.

Keywords: Comprehensive Health Care; Quality Assurance, Health Care; Quality Improvement; Accreditation; Perception.
INTRODUCTION

Accreditation programs seem to have become an influential mechanism for improving the performance of many Healthcare organizations (HCOs). However, the value of accreditation for HCOs still remains unclear especially for clinical outcome improvement. One way of assessing the value of accreditation programs is to look into the changes that they bring in HCOs since continuous quality improvement is about culture change. Our study looks at staff perceptions on changes (from 8 European cancer centers) resulting from their participation in a European cancer accreditation & designation program developed by the Organization of European Cancer Institutes (OECI). Previously, we published an article on the quantitative data gathered by this program. Here, we present staff perceptions of perceived changes in their cancer centers brought by the implementation of the qualitative standards. The methods section has been summarised in Table 1.

Table 1: Research Methods presented in COREQ Guideline checklist

<table>
<thead>
<tr>
<th>Domain 1: Research team and reflexivity</th>
<th>Personal characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Which author(s) conducted the interview?</td>
<td>Interviews conducted by AR</td>
</tr>
<tr>
<td>2. What were the researcher’s credentials?</td>
<td>AR: PhD candidate in health policy/services research; AW: PhD candidate in health policy/services research; FB: MA; MS: MD; FT: PhD candidate in public health; WvH: MD-PhD</td>
</tr>
<tr>
<td>3. What was their occupation at the time of the study?</td>
<td>AR: PhD candidate; AW: PhD candidate FB: coordinator of the accreditation &amp; designation program; MS: medical oncologist; FT: PhD candidate; FB: accreditation and designation program coordinator; WvH: Professor of health services and technology assessment and member of board of directors, The Netherlands Cancer Institute</td>
</tr>
<tr>
<td>4. Was the researcher male or female?</td>
<td>5 females, 1 male</td>
</tr>
<tr>
<td>5. What experience or training did the researcher have</td>
<td>Experience in conducting qualitative research (AR, AW, FT), expertise in public health/health services research (all authors), expertise in translational cancer oncology (AR, MS, FT, WvH)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relationship with participants</th>
<th>The interviewer did not know the participants before the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Was a relationship established prior to study commencement</td>
<td>At the start of the study, the aim of the research project, as well as the objectives of the study was presented.</td>
</tr>
<tr>
<td>7. What did the participants know about the researcher?</td>
<td>Interviewer characteristics were not reported to participants</td>
</tr>
<tr>
<td>8. What characteristics were reported about the interviewer/facilitator?</td>
<td></td>
</tr>
</tbody>
</table>


Domain 2: Study design

Theoretical framework

9. What methodological orientation was stated to underpin the study?

We used thematic analysis. We used an existing framework developed by Pawson et al that captures the typologies of changes in healthcare programs. We applied Pawson et al. theory that deals with “different aspects of change in complex organizations by taking a theory-driven review underpinned by an understanding of dynamics of social change in complex organizations”. This would suit the complex nature of cancer centers that include research and patient care. This approach argues “healthcare interventions are often evaluated by simply presenting (sub-typing) their outcomes but rarely do they provide lessons on how to improve organizations by understanding the types of change that occur”. Pawson et al, suggest “the need for a ‘theory-driven review’ reinforced by multi-layered types of changes: Strategic change - the key change mechanism lies in the better coordination of practices and process by rethinking the entire pathway; Role change - this element proposes a dramatic change in which systems and organizational structures remain intact but within which roles and responsibilities are shifted; Procedural change - this type of change is at the level of individual practice by increasing the efficiency and effectiveness of procedures. Motivational change - includes the practice of offering incentives to encourage key actors to reshape their behaviour. The intended change is behavioral and driven by personal interest rather than peer learning. Organizational change - improvements include new produces; a better division of labor, better-cost containment, better information flow, better training. In this approach, lasting system transformation depends on the dovetailing of these types of changes that are interconnected with each other.”

We selected this theory to see if these proposed typologies of changes appear in cancer centers and whether the ideology of dovetailing of typologies of changes is relevant to cancer centers.

Participant selection

10. How were the participants selected?

We did purposive sampling and invited 32 participants (a researcher, a clinician, a nurse and a manager from each center) from 8 cancer centers across Europe. These individuals were responsible for gathering data for the audit as well as participating in the audit. This strategy ensured that a diverse group of staff was interviewed from a variety of contexts. 5 of these centers had been audited. These were located in Finland, Lithuania, Portugal, Spain and the UK. The remaining 3 centers were preparing themselves for the audit. They were located in Norway, the UK and Italy. The centers were either freestanding Comprehensive Cancer Centers (independent entities, not located within a university or a general hospital structure) or they were part of a general university hospital. In the latter case, key facilities e.g. radiology are then not just dedicated to cancer but also to other diseases and specialties. The participating centers agreed that ethical consent was not necessary for this study.

11. How were the participants approached?

Originally by email

12. How many participants were in the study?

24: clinicians (5), nurses (6), managers (8) and basic/translational researchers (5)

13. How many participants refused to participate or dropped out? Why?

8 (due to time constraint). However, managers from 3 centers also gave feedback on behalf of a few clinicians and/or researchers from their Centre (who had handed them their answers as they couldn't participate in the interview themselves due to lack of time). This indirect feedback from 4 participants (2 researchers and 2 clinicians) was also taken into account while coding.

Setting

14. Where was the data collected?

Telephone interviews were conducted from AR's office

15. Was anyone else present besides the participants and researcher?

No.
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>16. What are the important characteristics of the sample?</td>
<td>Diversity of backgrounds and occupation. There were basic/translational researchers, clinicians, nurses and managers.</td>
</tr>
<tr>
<td>17. Were questions, prompts, guides provided by the author? Was it pilot tested?</td>
<td>The topic guide was to the participants in advance. The interview guide was prepared based on the chapters/topics of the OECI accreditation and designation program standards. No repeat interviews.</td>
</tr>
<tr>
<td>18. Were repeat interviews carried out? Details</td>
<td>Yes</td>
</tr>
<tr>
<td>19. Did the researcher use audio or visual recording to collect the data?</td>
<td>Field notes taken during all interviews. Memo made immediately after the interview.</td>
</tr>
<tr>
<td>20. Were field notes made during and/or after the interview or focus group?</td>
<td>30-45 minutes.</td>
</tr>
<tr>
<td>21. What was the duration of interviews or focus groups?</td>
<td>No</td>
</tr>
<tr>
<td>22. Was data saturation discussed?</td>
<td>No</td>
</tr>
<tr>
<td>23. Were transcripts returned to participants for comments and/or correction?</td>
<td>No</td>
</tr>
<tr>
<td>24. How many data coders coded the data?</td>
<td>Two authors (AR, AW) created the initial coding tree using 5 sample interview transcripts.</td>
</tr>
<tr>
<td>25. Did authors provide a description of the coding tree?</td>
<td>No but we show the themes/categories that emerged and the peer-reviewers findings from the cancer centers based on the on-site visit.</td>
</tr>
<tr>
<td>26. Were themes identified in advance or derived from the data?</td>
<td>The themes were derived deductively using Pawson et al framework. Our triangulation technique involved two strategies. First, we sent the emergent themes and a brief explanation to all participants. They confirmed that they were able to relate to our findings. As a next step, we analysed auditor’s recommendations for improvement to the 5 centers. We checked whether these themes related to the themes emerging from staff interviews.</td>
</tr>
<tr>
<td>27. What software, if applicable, was used to manage the data?</td>
<td>NA</td>
</tr>
<tr>
<td>28. Did participants provide feedback on the findings?</td>
<td>Yes</td>
</tr>
<tr>
<td>29. Were participant quotations presented to illustrate the themes/findings? Was each quotation identified?</td>
<td>We present some quotations to illustrate findings.</td>
</tr>
<tr>
<td>30. Was there consistency between the data presented and the findings?</td>
<td>The data presented and the findings are consistent</td>
</tr>
<tr>
<td>31. Were major themes clearly presented in the findings?</td>
<td>We present the most important themes related to the study objectives in the findings</td>
</tr>
<tr>
<td>32. Is there a description of diverse cases or discussion of minor themes?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
RESULTS

The thematic analysis of the interview data led to four categories (also see Figure 1).

![Figure 1. Perceptions of change by staff from cancer centers from participation in a European accreditation program](image)

**Growing importance of nursing and supportive care field (role change)**

In most centers, psychosocial counselling referrals are initiated by a physician based on his/her knowledge, experience and attitude to psychosocial counselling. The referral was a solo activity of the doctor and not so was not based on a structural multi-disciplinary approach. The nurses available per patient was found to be insufficient. Auditors found that some supportive care disciplines only had one representative staff member e.g. one psychiatrist and one social worker. In some cases patients were transferred to other general hospitals to provide supportive palliative care. Workers knew about the palliative and terminal care services outside the center but the availability of those services was not clearly communicated to patients and was therefore unknown to patients. A job description with specific roles and responsibilities of the functions of supportive care staff was not structurally implemented.

Based on the interviews with nurses, their autonomy seems to have changed quite a lot with regards to their role especially in pain management and palliative care. The clinicians and managers from the majority of centers said that they were expanding their supportive care team. The information flow to those patients on external palliative care seems to have been improved. Staff perceived that allocating more responsibilities to nurses and/or supportive care team improved due to data integration including access to patient data and improved communication within the multi-disciplinary team of which nursing and supportive care members are also a part.
“We have managed to merge certain tasks of physicians and nurses to give additional responsibilities to nurses.” (Clinician, Center 6, audited)

“Nurses now also report on problems of different processes, programs for audit of nurses have improved. Now we nurses think critically, now we propose solutions to problems proposed by our unit.” (Nurse, Center 4, audited)

“Before starting the accreditation process you couldn’t see how accreditation could impact on Nurse’s work, but since the start of the process you are saying it’s good to know how you can perform better, self-reflection of nurses has improved.” (Nurse, Center 2, unaudited)

“There are differences in pain management of patients across Europe. This needs to be addressed and has started to be addressed.” (Nurse, Center 6, audited)

“We are looking for more social workers, staff for psychological and supportive care.” (Clinician, Center 4, after audit and Manager Center 7, audited)

**Critical thinking on data integration (strategic change)**

In all cancer centers except one that underwent the audit, reviewers felt that it was unclear whether and how an annual report from different departments of the oncology center was being integrated and how it helped formulate future improvements for the institute and for specific departments. It was also unclear how scientific programs (colloquia, seminars, conferences) disseminate research results between clinicians and researchers. Managers reported that other centers across Europe were starting to contact them about ideas for data integration. Data integration was seen crucial to improve communication between staff and also from staff to patients.

“Our information is more accessible and integrated now across research, education and care.” (Manager, Center 5 audited)

“What information do we have now? What are we missing? How do we obtain it? Ensuring all information that we have is available as a Central intelligence to information, how to fit it under one roof? How can we benchmark ourselves against other Centers and identify new ways of data collection” (Manager, Center 1 unaudited)

**Improved processes within multi-disciplinary team (MDT) meetings (procedural change)**

The reviewers found that in almost every center that was peer-reviewed there were differences in the multi-disciplinary team (MDT) meetings for admitted patients and outpatients. Although meetings were held every 1-2 weeks depending on the tumour type, it
was unclear if every new patient was being discussed. A general description of the selection criteria to decide which patients were being discussed was not written. However, MDT members knew the criteria. For MDT organization (outpatient), the specific responsibilities of the physicians in the follow-up period of the patients was not clear, such as who will announce the treatment plan and will take care of the patient during his/her follow up. There were also differences in the procedures of each MDT e.g. urology and melanoma. For the weekly breast cancer meetings, a list of all patients that will be discussed was sent in advance to all team members. It also contained information on pathology results and the staging. But for other tumours such a list was not used. Who is responsible for evaluating the execution of the conclusions and advice from the MDT meetings was not clearly described and could not be made clear during the review visit. The procedures describing how the conclusions and advice from the MDT was evaluated and by whom was unclear. But all final decisions of MDT meetings were registered in the patient’s health record.

Staff interviews suggest that the number of meetings between the MDTs has increased and the role of nurses and supportive care personnel in MDTs was clarified. The reviewer’s recommendations brought more uniformity in MDTs for all tumour types (including in setting up of selection criteria and discussing new research proposals). This led to formally approved rules and guidelines in 3 of the 5 centers. Finally, the contact person for each individual patient in each tumour group became more visible. Staff believed that the changes in MDT processes were enabled mainly by the data integration, that in turn facilitated communication and interaction especially between clinicians and researchers. Staff also felt that the improvements in MDT processes were indirectly also related to better training and autonomy of nurses and supportive care personnel.

“Integrated data in our center has been a main reason for improved communication between the multidisciplinary teams especially between researchers and clinicians. Patient care has become more fluid as a result of better communication.” (Manager, Center 6, audited)

“There has been critical thinking on-going about how to improve palliative care especially the communication to informal carers. How they can be involved in the care process.” (Clinician, Center 2, unaudited)

**Building trust with staff and with public (organizational change)**

Building internal trust with staff is connected to data-integration, creation of a quality improvement unit and/or identifying specific staff responsible for total quality improvement of the organization was strongly recommended by the reviewers to almost all centers. Based on the interviews, this was a perceived change among staff from almost all centers.
“People now internally listen to quality advice from quality managers after the external experts came and gave their recommendations. Before there was a lot of skepticism about ideas for quality improvement.” (Manager, Center 4, audited)

Accreditation also helped improve the centers credibility with funders (in three audited centers) and made the Center more reliable with patients. Managers said that other centers had started viewing their centers as role model especially in terms of how they integrate their data and how they are improving the multi-disciplinary processes.

Centers use accreditation as a tool for benchmarking the performance of their centers against other centers of similar standing in Europe. This perception was shared among all respondents. The nurses mentioned that they would like the performance of nurses of their Center to be benchmarked with that of other centers.

“There are differences in the education and autonomy of nurses across Europe. We would like to compare our performance with other centers to improve our performance and learn from each other” (Nurse, Center 2, unaudited)

“We couldn’t believe that accreditation can have so much power. Before accreditation, we found it difficult to convince decision-makers to make the case for funding. We got more negotiating power since having our audit” (Manager, Center 5, audited)

“Other centers now want to come and see our data integration processes and learn from us” (Manager, Center 7, audited)

**Unique view of basic/translational researchers**

In centers that had undergone a peer-review, reviewers found that translational research was not structurally and visibly embedded in the center’s strategy and planning. Some departments have their own strategic plan and it is not clear how this fits in with the institutional level plan. The procedures for allocating resources and funding available for translational research were not clearly defined. The board of directors gave an estimated budget for translational research. The systematic transfer of research results into daily practice though a scientific program was missing in many of these centers. Based on staff feedback, the centers that had been through the peer-review process have developed and/or refined a five-year plan with clear objectives and actions for translating research into practice. However, it is unclear whether those objectives/actions have yet been put into practice. In addition, indicators for evaluating the actions are largely missing. Budget allocated to research and translational research was unclear in three out of five centers.

During the interviews, almost all researchers reported that they had not experience any changes from taking part in the accreditation process. They felt that clinical areas gain far more from accreditation than research.
“I don’t know if accreditation has brought any visible impact on research teams, the impact is noted more on the clinical side. But certainly communication between research and clinical teams has improved and this has led to more thinking about translational research.” (Basic/Translational Researcher, Center 8, audited)

“We need more cooperation between researchers and clinicians not only in our Center but also externally, this can advance translational research. Maybe such collaborations will appear in the near future, the next steps should be applying for joint proposals with other centers to visit other labs and clinics and learn from them.” (Basic/Translational Researcher Center 7, audited)

**Data verification with peer-reviewers suggestions to audited centers**

We accessed the accreditation reports of the audited centers to see what recommendations auditors had given them. The grey boxes in Figure 2 are derived from the recommendations based on the accreditation standards topics as listed in the reports. In Figure 2, part a) summarizes 13 areas (presented in grey boxes) where auditors identified the need for changes in audited centers. In the same figure, part b) highlights the 4 areas (in green boxes) where the interview respondents perceived changes from taking part in the accreditation program. The remaining 9 areas are discussed below:

*Prioritizing translational research:* The reviewers emphasized a clear strategic vision for embedding translational research into the mainstream organizational culture. As a next step, it was necessary to identify resources (staff, budget etc.) to make this vision happen. Connected to translational research is the issue of biobanks that is crucial for research.

*Bio-specimen banks:* Reviewers pointed out several issues regarding the policy for bio-banking and standard operating procedures (SOPs) and concerning collection; storage, registration, quality and use of biological samples that were not fully implemented at many of the centers across all tumour types.

*Managing clinical trials:* In a few centers, the reviewers found that no full-time staff is available with clear roles to initiate, conduct and manage academic clinical trials. Industry sponsored trials were selected and initiated after a review by a separate committee also using good clinical and laboratory practices and the number of patients was also significantly higher in industry-sponsored trials than in academic trials.

*Patient privacy and satisfaction:* In a few centers, reviewers found that facilities for safeguarding patient privacy while sharing information with the patient’s family during treatment, especially at the end of life and the immediate bereavement period could be much improved. In some cases, relatives could stay overnight with patients but in uncomfortable conditions.
Cancer registries: In many centers, the registry is not always used to facilitate future improvement actions in some centers. Waiting times are available but a structural continuous improvement process of monitoring and evaluation by pathology and care pathway leading to define improvement actions of planning and/or organizing the care and treatment of departments or the complete hospital was missing.

Clinical practice guidelines: Deviations from guidelines are documented in patient’s paper files, which are accessible for the core team. Guidelines were available and accessible on the intranet. The coordination on how guidelines are produced, managed, used, updated were not standardized in each department or within each multi-disciplinary team.

Patient education: The reviewers found that in centers, patients and relatives receive oral information about pain management. Written information is only accessible after consultation with a physician since information brochures are stored in the electronic system. Patients are referred to palliative care through the institutional process of requesting internal consultation. In two centers, a written procedure on referring patients to any
discipline was not available.

**Screening:** All centers were performing and were responsible for some screening programs. But in some cases, those programs only covered small percentage of the total population. Centers organise, plan, participate and follow-up on these programs and report to the funding body on how the money was spent. Centers offer consultation to patients but no full support program.

**Primary prevention:** The reviewers found that the interaction with General Practitioners is not formally structured in some Centers. Lack of written/formal agreements with other institutions e.g. community home care teams or with palliative care/hospice organizations/genetic lab testing were lacking.

**DISCUSSION**

The aim of our study was to capture the perceived changes by staff from cancer centers taking part in an accreditation program. Pawson et al’s approach seems to be a useful guide for our categorization of changes taking place in cancer centers as a result of their participation in an accreditation program. The statement that dovetailing of types of changes is responsible for ever-lasting changes is justified. Different types of changes in cancer centers are interlinked. For example, according to staff perceptions, critical thinking about data-integration (strategic change) is a major source for better communication and alignment of processes within multi-disciplinary teams (procedural change). The strategic change also has an impact on the organizational change e.g. data integration improved trust with other cancer centers. We did not find any evidence of motivational change in our data. The transtheoretical model of behavioral change suggests that motivational change is a “process” that takes places in different phases, rather than a single event might explain this. Motivation is needed to move through all these phases of change and seems to form an underlying basis of all change typologies (strategic, administrative, role or procedural).

Our study confirms that accreditation programs act as an indispensable tool for quality improvements in HCOs. For example, we found that the role and autonomy of nurses improved through this accreditation program. Also, more supportive care personnel were deemed necessary in centers. In a study of acute care hospitals, the number of infection control nurses increased after the accreditation of medical care services. The nurses that we interviewed suggested that pain management was an important aspect to be improved as well as where they perceive improvements. Previous studies suggest that accreditation has positive impact on several clinical outcomes including pain management. Nurses saw the role of accreditation in the improvement of quality care for patients and had an overall positive attitude regarding accreditation. Nurses and Managers were the most positive
Clinicians saw the relevance but were largely skeptical about accreditation. They perceive it to be cumbersome and bureaucratic. Basic/translational research group stood out as they did not feel motivated. They felt that accreditation has more potential to improve patient care than research areas of cancer centers. Motivation of organizational members to implement change depends on how they value change. Despite high levels of research resources few centers have a clear mechanism for integrating research and care e.g. clearer policies/processes for basic/translational research. A key reason accreditation was preferred by European cancer centers was for benchmarking. This is similar to evidence from a previous Canadian study.

By applying Deming’s Plan-Do-Study-Act cycle (PDSA cycle), we can say that the plan and do phases tend to occur before the audit however, the majority of do phase and the study and act phases are more likely to occur after the audit. Each PDSA cycle takes time, however, the landscape of Oncology research and care is rapidly changing. Unless, change management is part of the organizational culture, planned changes will be prone to external elements that can delay or revoke the implementation of necessary changes.

CONCLUSION

We recommend future research to test multiple change theories that capture not just change typologies but also explain how and why change occurs. Accreditation programs have the potential to bring changes but it is important that they take the differing needs/expectations of stakeholder groups into account while developing and/or revise their standards. Staff perceptions are one way of interpreting changes. Accreditation agencies as well as participating organizations should invest in tools that more effectively and objectively help track ongoing changes in centers. This will help strengthen the international evidence base on the effectiveness of accreditation.

CONFLICT OF INTEREST

Authors’ institutions are members of the Organization of European Cancer Institute (OECI) and some authors (MS, FB, WvH) are involved in the development of the OECI Accreditation and Designation program.
REFERENCES

Understanding the added value of a comprehensive cancer center

Abinaya Rajan
Joachim Nagel
Joeri Both
Wim H. van Harten

Submitted
ABSTRACT

Introduction
Cancer care is developing rapidly and structures are needed that can provide excellent care and which have the ability to translate research findings and innovation into clinical practice. An organisational concept initially established in the US and that in recent years has been adopted in Europe is ‘Comprehensive Cancer Centres’ (CCCs) combining basic-, translational-, clinical research and patient care. This study aims to find out the added value of being CCC and how this value can be demonstrated.

Methods
A (systematic) literature review was conducted to identify existing evidence on this topic. To aid clarity, the findings were organized in the European Foundation for Quality Management (EFQM) model. A survey with members of the Organization of European Cancer Institutes (a lead contact person from 70 cancer institutions) and a series of 24 interviews, with a researcher, clinician, nurse and a manager from 6 CCCs, were followed to validate these findings.

Results
The literature review yielded few articles (n= 28). A number of indicators were identified that can help understand the added value of being CCC. Findings suggest that CCCs provide an added value in a number of areas including: availability of state of the art resources, excellent interdisciplinary collaboration between researchers and clinicians, high patient satisfaction. Other areas that seem to distinguish a CCC’s performance are: contributions to guideline development, improved patient outcomes (within and outside of the CCC’s), better career development possibilities especially for nurses, speed of research and clinical processes, high patient accrual in clinical trials.

Conclusion
Based on a literature review and surveys among a European audience, we conclude that CCCs can add value and outperform other providers in a range of areas spread across the entire organizational pathway. To evaluate how far a CCC performs differently from other organisations involved in cancer research and/or patient care, the findings should be piloted to validate the terminologies for use in benchmarking different types of cancer provider organisations. Consensus is needed on terminologies related to “Added value” and organisational concepts, such as “CCC” for these to be added to the MESH terms in search databases so that evidence can be more easily tracked.
INTRODUCTION

Cancer services represent up to one third of medical specialist care and in many countries there is debate on how to optimally organize this important resource. Quality criteria on multidisciplinarity, diagnostic- and therapeutic infrastructure and on continuous education of oncologists contribute to a tendency to cooperate between providers and to concentrate services. Data on volume-outcome relations reinforce this trend. Most cancer patients are treated within the general hospital- or general oncology practice setting and a minority are cared for in dedicated cancer centres (freestanding or within the hospital setting). In some countries experiments are taking place in which networks of hospitals align or allocate services to match growing external demands and quality criteria. Some state that focused services or integrated practice units are likely to improve performance in providing affordable and high-quality care\(^1\) but so far little evidence is available on the relative performance of different forms of care provision. This also relates to developments such as “value based health care” for which Porter initiated the International Consortium for Health Outcomes Measurement (ICHOM) model\(^2\). Although not directly focusing on organisational performance, the value-based health care approach claims to contribute to improving long-term patient outcomes and reduce costs. This underlines the relevance of establishing the (added) value, or relative performance, of different health care providers.

The US has National Cancer Institute (NCI) designated Comprehensive Cancer Centres. They have to comply with a set of criteria and demonstrate a certain level of excellence in cancer care and especially translational research is funded for this research program by the NCI (NCI, 2012). In Europe, the Organisation of European Cancer Institutes (OECI) started a program in 2008 in which both Clinical Cancer Centres and Comprehensive Cancer Centres can be designated (OECI, 2013a). This program focuses on both care and research and is a bottom up development because currently no central EU funding system for CCC programs exists. The exact definition of a CCC in both European and American context is provided in Box -1.

CCC’s are considered by many to be the top of the cancer care pyramid. Focusing on specific diseases is believed to increase efficiency and possibly improve outcome.\(^5,6\) The claim of CCC’s outperforming other cancer providers is so far not supported by evidence or reviews. We decided to explore the issue of the possible added value of CCC’s from a European perspective. This is rather a challenge as comparing organisational performance is rather complicated due to many influencing factors and the black box character of decisive internal mechanisms.
Box-1 Definition of Comprehensive Cancer Center

**Definition by the National Cancer Institute, USA**

In the first place, the National Cancer Institute (NCI) in the US designated (Comprehensive) Cancer Centres in 1973. Since that time the designation has developed constantly, resulting in the definition of two types of NCI-designated cancer centres:

"1) An NCI-designated cancer centre must demonstrate scientific leadership, resources, and capabilities in laboratory, clinical, or population science, or some combination of these three components. It must also demonstrate reasonable depth and breadth of research in the scientific areas it chooses and transdisciplinary research across these areas.

2) An NCI-designated Comprehensive Cancer Centre must demonstrate reasonable depth and breadth of research in each of three major areas: laboratory, clinical, and population-based research, as well as substantial transdisciplinary research that bridges these scientific areas. In addition, a comprehensive centre must also demonstrate professional and public education and outreach capabilities, including the dissemination of clinical and public health advances in the communities it serves."^{3}

**Definition by the Organization of European Cancer Institutes**

The OECI uses similar definitions as the NCI, although it has developed its own accreditation and designation program adjusted to the context of European organisations. In the designation of the OECI, the comprehensiveness of the professional infrastructure and performance is the central aspect.

The designation types which are handled by the OECI are: Cancer Units, Clinical Cancer Centre, Cancer Research Centre and Comprehensive Cancer Centre (OECI, 2013b).

“Cancer Units are defined as a clinical facilities or hospital departments covering at least radiotherapy and medical or surgical oncology. Additionally they have a formalized collaboration with other hospital specialties.

A Clinical Cancer Centre is characterized by the clinical capacity covering a sufficient degree of all-medical, surgical and radiotherapy services and occasionally a limited degree of clinical research.

A Cancer Research Centre is characterized by the capacity in cancer research focusing on one or more areas in the field of fundamental and translational oncology.

Comprehensive Cancer Centre (CCC) is probably the hardest category to define as many different interpretations on a CCC already exist. Based on available information and many definitions on the concept of a CCC, the following features are considered to be essential for this particular category:

- A highly innovative character and multidisciplinary approach using the potential of basic, translational and clinical research and clinical facilities and activities, organized in a sufficiently identifiable entity,
- A direct provision of an extensive variety of cancer care tailored to the individual patient’s needs and directed towards learning and improving the professional, organisational and relational quality of care,
- Broad activities in the area of prevention, education, and external dissemination of knowledge and innovation. In order to accentuate the differences with other cancer centres, a CCC separates itself in the following points:
  - High level of infrastructure, expertise and innovation in the field of oncology research,
  - Maintenance of an extensive network including all aspects of oncology treatment and research,
  - Related to an academic/university centre or is an academic centre."^{4}
The aim of the study was to explore the added value of being a CCC by reviewing the literature, identifying the relevant criteria through a survey and through interviews with stakeholders from the centres. The combination of these different methods can help generate an evidence-based criteria set for assessing the added value of CCCs. The result of this exercise should be used in research to assess performance of a CCC that adds value.

**METHODS**

First we performed a systematic literature review in Pubmed, Embase and Scopus to identify existing criteria/indicators of added value of a CCC (see search strategy in box 2). Literature obtained through snowballing and grey literature were also included if deemed relevant.

Our inclusion criteria were:

1. The study focuses on the added value of being a Comprehensive Cancer Centre (CCC) in performance areas such as research, education, patient care and their integration.

2. The study is conducted in Europe or the US, since other definitions throughout the world differ widely from the definitions, which are used, by the NCI and the OECI.

3. We did not use a time limit for our search.

A total of 1113 articles came up but only 1 met our inclusion criteria (see box 3). All other articles mainly described the value of a specific clinical intervention/therapy for patients. These indicated that those articles play a significant role in the field but were not relevant for our study based on our inclusion criteria.

Because the first attempt at a systematic review did not give us sufficient papers, we attempted a more unstructured literature review second round with different search key words as depicted below. We kept the same inclusion criteria here also. JA and AR selected the abstracts and the selection of papers of both parts I of the systematic review and part II of general literature review.

The resulting criteria covered many organisational areas and were structured according to the European Foundation for Quality Management (EFQM) model (see table 2). The EFQM Excellence model is an organizational management tool comparable to the Baldrige award system in the US and its format can help organizations to measure where they are on the path to excellence.

A survey and staff interviews were conducted with the identified criteria to prioritize the
Box 2 Search Strategy

Scopus search:

( (TITLE-ABS-KEY (cancer care facilit*) OR TITLE-ABS-KEY (comprehensive cancer cent*) OR TITLE-ABS-KEY (tumor facilit*) OR TITLE-ABS-KEY (tumor hospital*) OR TITLE-ABS-KEY (tumor cent*) OR TITLE-ABS-KEY (tumour facilit*) OR TITLE-ABS-KEY (tumour hospital*) OR TITLE-ABS-KEY (tumour cent*) OR TITLE-ABS-KEY (cancer facilit*) OR TITLE-ABS-KEY (cancer hospital*) OR TITLE-ABS-KEY (cancer cent*) OR TITLE-ABS-KEY (institut*) OR TITLE-ABS-KEY (academ*)) ) AND ( (TITLE-ABS-KEY (added value) OR TITLE-ABS-KEY (additional value) OR TITLE-ABS-KEY (increased value) OR TITLE-ABS-KEY (added efficiency) OR TITLE-ABS-KEY (additional efficiency) OR TITLE-ABS-KEY (increased efficiency) OR TITLE-ABS-KEY (added qualit*) OR TITLE-ABS-KEY (additional qualit*) OR TITLE-ABS-KEY (increased qualit*) OR TITLE-ABS-KEY (added satisfaction*) OR TITLE-ABS-KEY (additional satisfaction*) OR TITLE-ABS-KEY (increased satisfaction*)) ) AND ( (TITLE-ABS-KEY (accreditat*) OR TITLE-ABS-KEY (licensur*) OR TITLE-ABS-KEY (certificat*) OR TITLE-ABS-KEY (permit*)) ) ) AND (LIMIT-TO (SUBJAREA, "MEDI") OR LIMIT-TO (SUBJAREA, "BIOC") )

PubMed Search (which is the same as the Embase search)


Box 3 Article from first search result
Towards quality, comprehensiveness and excellence. The accreditation project of the Organisation of European Cancer Institutes (OECI) (2008). From this article, we understood that the OECI standards cover research, education and care standards and so we made use of some of them in our criteria list (See Table 2). For example, indicators such as: internal collaboration between research and clinical departments, career opportunities for staff are taken from the OECI standards.

Table 1. Literature study: Added value of (Comprehensive) Cancer Centres- search terms and results

<table>
<thead>
<tr>
<th>Item</th>
<th>Search Terms</th>
<th>PubMed Results</th>
<th>Web of Science Results</th>
<th>Scopus Results</th>
<th>Cochrane Results</th>
<th>All Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cancer AND centre</td>
<td>206625</td>
<td>32952</td>
<td>42977</td>
<td>29</td>
<td>282583</td>
</tr>
<tr>
<td>2</td>
<td>Value AND cancer AND centre</td>
<td>11652</td>
<td>3263</td>
<td>5028</td>
<td>4</td>
<td>19947</td>
</tr>
<tr>
<td>3</td>
<td>NCI AND designated</td>
<td>851</td>
<td>80</td>
<td>89</td>
<td>2</td>
<td>1022</td>
</tr>
<tr>
<td>4</td>
<td>OECI AND cancer AND centre</td>
<td>2</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>Quality</td>
<td>393976</td>
<td>832799</td>
<td>1301516</td>
<td>4154</td>
<td>2532445</td>
</tr>
<tr>
<td>6</td>
<td>1 AND 3</td>
<td>271</td>
<td>56</td>
<td>59</td>
<td>2</td>
<td>388</td>
</tr>
<tr>
<td>7</td>
<td>4 OR 7</td>
<td>271</td>
<td>64</td>
<td>67</td>
<td>2</td>
<td>404</td>
</tr>
<tr>
<td>8</td>
<td>7 AND 5</td>
<td>20</td>
<td>19</td>
<td>25</td>
<td>2</td>
<td>66</td>
</tr>
</tbody>
</table>
most important in distinguishing the added value of CCCs. The survey was sent to all OECI members (this included the Eurocan Platform members) via their main contact persons. The survey was sent to a lead contact person from 70 cancer institutions (see Annex for the full survey questionnaire).

Respondents were asked to score how important an identified criterion is to determine the added value of a Comprehensive Cancer Centre. A 5-point Likert scale was used for this scoring ranging from most to least important (See Annex- I A for full questionnaire). There was space to suggest additional criteria.

At the end of the survey, respondents were asked if they would be willing to give an in-depth interview on this topic (see Annex I B for interview questions). Based on this 6 CCCs responded: Netherlands Cancer Institute, Christie Cancer Center Manchester, Institute Curie, Hungarian National Cancer Center, IPO Porto and Cambridge Cancer Center. The interviews were conducted between June-July 2013. In each cancer centre, a senior clinician, a researcher, a leading person from the management department and a nurse were interviewed. The aim of the interview was to get a deeper insight into the views of different stakeholders from these centres about the criteria that can help understand the added value of a CCC. AR and JN thematically coded the interviews for each stakeholder group using the survey themes.
RESULTS

The results of the (systematic) literature review are summarized below in Table 2 along with the relevant sources for each criterion that we used in our survey.

Table 2. Selected criteria from the 28 articles listed according to the EFQM model headings

<table>
<thead>
<tr>
<th>Leadership</th>
<th>People</th>
<th>Strategy</th>
<th>Partnerships &amp; Resources</th>
<th>Processes, Products &amp; Services</th>
<th>People Results</th>
<th>Customer Results</th>
<th>Society Results</th>
<th>Business Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Representation of health professionals and researchers in the general direction of the organization</td>
<td>Well-defined job roles for staff</td>
<td>Specialization in specific cancer type(s)</td>
<td>Availability of state of the art resources (staff skills, equipment)</td>
<td>Speed of translation of research results from bench to bedside (clinical research, technology)</td>
<td>Staff satisfaction</td>
<td>Patient satisfaction</td>
<td>Making information accessible for society (e.g. for prevention)</td>
<td>Impact of specialization on cancer types on average cost per patient</td>
</tr>
<tr>
<td></td>
<td>Career advancement opportunities</td>
<td>Focus on specific cancer types within the centre</td>
<td>Internal collaboration between research and clinical departments</td>
<td>Speed of implementation of new clinical practice guidelines</td>
<td></td>
<td></td>
<td></td>
<td>Impact of specialization on cancer types on average cost per patient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patient volume per tumour type</td>
<td>On-going collaboration with providers (material, technology, pharmaceutics)</td>
<td>Adherence to clinical practice guidelines</td>
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<td>Financial efficiency (proving that services are cost beneficial and cost effective)</td>
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<td>Internal collaboration between research and clinical departments</td>
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<td>Ability to receive funding or charitable gifts (e.g. in the US by the NIH)</td>
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<td>On-going collaboration with other cancer centres</td>
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<td>On-going collaboration with patient organizations</td>
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<td>Speed of processes within the centre - related to type of tumour</td>
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<td>(Defined by: Average access time; Average waiting time (1: First appointment =&gt; Diagnosis; 2: Diagnosis =&gt; Treatment plan; 3: Treatment plan =&gt; Treatment); Average length of stay)</td>
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<td>Accrual percentage of patients in clinical trials</td>
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<td>Number of publications (considering quantity and quality)</td>
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Survey
The response rate was 47%; we received reactions from 34 persons from 33 centers out of 70 that were approached. 20 of the 34 respondents stated that they were primarily managers, but also had a role clinician and/or researcher. Seven were clinicians and seven were researchers. In the survey that was based on the review, (of Table 2), almost all criteria were scored as important at least. A mean and SD was calculated based on the responses. The highest scoring criteria were the ‘internal collaboration between research and clinical departments’, the ‘availability of state of the art resources (staff skills, equipment)’ and ‘patient satisfaction’.

Internal collaboration between research and clinical departments ($\mu=4.88; SD=0.33$): This criterion is described as defining for a Comprehensive Cancer Centre in the interviews. Although others, e.g. university hospitals can have the same mechanism, this is considered to be distinguishing a Comprehensive Cancer Centre from most of the other organisations in cancer care.

Availability of state of the art resources (staff skills, equipment) ($\mu=4.77; SD=0.5$): This finding is in line with the results of the interviews, which identified this as a distinguishing characteristic of a Comprehensive Cancer Centre. One interviewee explained: “what is distinguishing, is that, if you want to be really innovative, you always need to have the state of the art equipment. So the equipment and staff and the skills of employees is very important for our organisation.” It is also related to providing services throughout the whole continuum of cancer care and the link to research, which allows the organisation a great variety of equipment.

Patient satisfaction ($\mu=4.77; SD=0.5$): Although this is considered to be a very important criterion in showing the added value of Comprehensive Cancer Centres in general, the sub-group analysis shows that there are mixed opinions about this. This observation can also be made in the responses to the interviews, where respondent’s answers vary from “patients are satisfied with everything, but patients cannot really define their treatment” to “Absolutely. This is why patients want to be treated here.”

The relatively low scoring criteria were: representation of health professionals and researchers in the general direction of the organization ($\mu=4.34; SD=0.97$); specialization in specific cancer type(s) ($\mu=4.12; SD=0.88$); focus on specific cancer types within the centre ($\mu=4.06; SD=0.85$); On-going collaboration with patient organizations ($\mu=4.27; SD=0.83$).

Staff interviews
We present views of the different professional groups (clinicians, managers, nurses and researchers) reflecting the results of the criteria from the literature review. We described especially what each group felt is important to assess the added value of CCCs.
Clinicians’ view on added value of CCC

*Patient satisfaction:* It is important that patient satisfaction scores are very high, but that it is not unique for a Comprehensive Cancer Centre. There may be high patient satisfaction also in general hospitals. Patient satisfaction and outcome are not always connected. *Outcomes:* Clinicians answered that they presume that this is distinguishing, especially when looking at the clinical outcomes in general and not just related to clinical trials. However, it is difficult to evaluate this criterion, since there are many confounding factors in the measurement. *Impact on guideline development:* The clinicians were critical about this criterion although they considered it distinguishing. The reason was that some of the interviewed could not participate in guideline development due to conflict of interest such as the relationship between industry and clinicians.

Nurses’ view on added value of CCC

*Career advancement opportunities:* Most of the nurses said that this is special for a Comprehensive Cancer Centre, especially in relation to the multidisciplinary training, which they receive, specialisation in oncology and the possibility to participate in research activities. Therefore it can be regarded as differentiating especially for this profession. *Specialization in specific cancer types:* All of the nurses agreed that this is a distinguishing characteristic of a Comprehensive Cancer Centre. Other disciplines had mixed opinions about this. Looking at the answers of the nurses, it appears that it is not the specialisation itself that is considered to be special, but the coverage of a broad range of tumour types as well as providing treatment of complex and rare pathologies.

Senior executives’ view on added value of CCC

*Adherence to guidelines, increased provision of second opinion, speed of processes, and patient accrual in clinical trials:* Managers said more often than other disciplines that they do not know if a criterion is distinguishing. However, they did emphasise that a CCC has the ability to perform better in clinical trials when compared to other types of organizations due to the multidisciplinary environment, speed and efficiency of translational research processes, and state of the art facilities. Adherence to guidelines and provision of second opinion was also seen as a distinguishing feature of CCCs. *Business results- impact on average cost per patient, financial efficiency:* Managers talked far more about these criteria than staff from other disciplines. From their answers it can be concluded that these criteria are very difficult to analyse and that no clear statement can be made regarding how it differentiates a CCC, since a lot of confounding influences are included in this, ranging from case-mix to the background of the health and funding systems of the different countries.
Researchers’ view on added value of CCC

**Speed of implementation guidelines, provision of second opinion:** Researchers often explained that criteria, which are more related to the clinical department, are distinguishing. They find the research and the care processes both to be adding equal value to a CCCs existence. **High agreement on scientific aspects- clinical trial participation, publications:** There is a high consensus between researchers on these criteria, which are related to their own field of work. Participation in clinical trials and high impact publications are regarded as distinguishing characteristics of a CCC from the perspective of researchers. **Ability to receive funding:** researchers explained that the ability to receive funding is not distinguishing. They feel that it is not the mere ability to receive funding, but the prestige and competition of funded programs that is distinct and that it is a good indicator for quality, but they added that there is no difference between a CCC and other academic research institutions in this respect.

The results from the survey and interviews helped us in three ways: (i) to refine each criterion for clarity by providing a clear description (see table 3); (ii) to prioritise the criteria into three sets- likely to be tested in CCCs, likely to rejected for testing in CCCs and criteria that need to be researched further before testing in CCCs; and (iii) a number of qualitative and quantitative indicators were identified for each criterion that can help in the testing of the criteria set in CCCs.

**DISCUSSION AND CONCLUSION**

Our aim was to identify the added value of CCCs in terms of how this value can be demonstrated and with which indicators. The systematic literature review on this subject yielded few results in the first attempt. So, we used a different set of search terms in a second attempt that enabled a more general literature review. This gave better results, however, there is an issue with the search in relating key words to “added value” and “Cancer Centres”. Specific well-defined MESH terms for this subject are as yet unavailable. Many articles discussed added value in terms of specific clinical treatments whereas our aim was to find articles that discussed the added value of integrating research, education and care in one entity: the added value of being a CCC. So, the multidisciplinary aspect was missing in the description of many articles as they only focused on describing the value of a specific clinical treatment or intervention for patients.
Translating the criteria into measurable qualitative information and/or exact defined quantitative indicators

In the survey, almost all criteria were scored as important and 3 were really scored as most important: ‘Internal collaboration between research and clinical departments’, the ‘availability of state of the art resources (staff skills, equipment)’ and ‘Patient satisfaction’. These findings reflect the importance of these criteria for the excellent performance of a CCC and lead to an adaptation of the draft set of criteria (from earlier Table 2). Based on the survey and interview data (mainly from the open-ended questions at the beginning of the survey and interviews), we also arrived at measurable qualitative and quantitative indicators (see Table 3 adapted draft criteria and indicator set to identify and assess the added value of CCCs). There are 3 types of criteria: 1. Criteria that are likely to be tested in CCCs 2. Criteria that are likely to be rejected for testing in CCCs; and 3. Criteria whose relevance is debatable and should be carefully included for testing.

Table 3. Draft criteria set and qualitative and quantitative indicators identified from the study that can be piloted in the CCCs

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Career advancement opportunities</td>
<td>- Junior medical staff: funded clinician scientists (academic)</td>
</tr>
<tr>
<td>Description: Do staff get access to internal and external job postings and get to discuss job advancement, promotion and career pathways, are their educational and training needs being met?</td>
<td>- Nursing staff going on to have senior roles</td>
</tr>
<tr>
<td></td>
<td>- Amount of protected time of clinicians for research</td>
</tr>
<tr>
<td></td>
<td>- Number of MD-PhDs</td>
</tr>
<tr>
<td></td>
<td>- Number/quality of MDT training</td>
</tr>
<tr>
<td></td>
<td>- Number of moves from research to clinic to research department</td>
</tr>
<tr>
<td></td>
<td>- Is there a strategy for education?</td>
</tr>
<tr>
<td></td>
<td>- 5-year strategy for education</td>
</tr>
<tr>
<td></td>
<td>- People getting involved in translational research</td>
</tr>
<tr>
<td></td>
<td>- Workshops, conferences, etc.</td>
</tr>
<tr>
<td></td>
<td>- Research supporting staff</td>
</tr>
<tr>
<td></td>
<td>- Researchers trained in clinical aspects</td>
</tr>
<tr>
<td></td>
<td>- Internal training</td>
</tr>
<tr>
<td>Availability of state of the art resources (staff skills, equipment)</td>
<td>- Specialisation in certain procedures</td>
</tr>
<tr>
<td>Description: Are excellent core and shared resources available for conducting research and patient care?</td>
<td>- Capital budget, spent on equipment</td>
</tr>
<tr>
<td></td>
<td>- Training records</td>
</tr>
<tr>
<td></td>
<td>- Skill mix (staff at different grades per patient)</td>
</tr>
<tr>
<td></td>
<td>- Research portfolios</td>
</tr>
<tr>
<td></td>
<td>- Number of new equipment and number of cases treated with it</td>
</tr>
<tr>
<td></td>
<td>- Availability of relevant equipment</td>
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<tr>
<td></td>
<td>- Number of investigator initiated clinical trials</td>
</tr>
</tbody>
</table>
### Internal collaboration between research and clinical departments

**Description:** Does the structure of CCC facilitate the internal collaboration between researchers and clinicians?

- Number of multidisciplinary team meetings
- Joint research publications
- Joint grants (applications)
- Number of academics practicing in clinics
- Research outputs with clinical endpoints
- Collaboration in studies
- Number of boards mixing researchers and clinicians per year
- Shared education programmes
- Phase I,II trials
- Money devoted to translational research (and development over time)
- Reports about basic, translational, clinical excellence
- Time from first description to clinical use.
- Look at different phases of development of a new research finding and time between the phases
- Number of clinicians doing basic or translational research
- Number of MDs with PhD-title

### Speed of translation of research results from bench to bedside (clinical research, technology)

**Description:** Does the structure of the CCC facilitate rapid translation of research to practice and vice versa?

- Number of patients having biopsies for research
- Throughput/collection rate in biobank
- The fact of delivering genomic sequence testing
- Patents granted
- Licenses granted for new technologies/new treatment
- Time from first description to clinical use. (You have to define start/end point, e.g. licensing, first use in men)
- Look at different phases and time between the phases (Development of the process and dynamics)
- Publications on translational research
- x day setup time/target for translational studies
- New investigator initiated clinical trials
- Number of basic research projects carried out

### Adherence to clinical practice guidelines

**Description:** How much do staff in CCC adhere to clinical practice guidelines?

- Are the decisions made according to standard?
- Are the guidelines peer-reviewed?
- Is adherence and deviations being monitored?

### Provision of second opinion by the Comprehensive Cancer Centre (percentage of changed treatment plans after second opinion through Comprehensive Cancer Centre)

**Description:** Does the CCC provide active second opinion to patients and what are the consequences?

- Number of second opinions
- Number of patients coming on own initiative
- Percentage of changed treatment plans after second opinion through Comprehensive Cancer Centre to benchmark quality

### Speed of processes within the centre - related to type of tumour

**Definition:** Average access time; Average waiting time (1: First appointment => Diagnosis; 2: Diagnosis => Treatment plan; 3: Treatment plan => Treatment); Average length of stay

**Description:** Are the organisational processes within the CCC efficient?

- Time from referral to diagnosis to treatment
- Existing protocols/records/standards
| **Accrual percentage of patients in clinical trials** | - Sufficient percentage of patients in clinical trials  
- Records (be careful with measure, which patients actually could have been included in clinical trials?)  
- Split per phase: Phase I, II, III clinical trials and cancer site, also register interventional and academic trials |
| **Description:** Is there sufficient patient recruitment in clinical trials? |
| **Number of publications (considering quantity and quality)** | - Impact factors  
- H-index |
| **Description:** Is the number and quality of publications of the CCC excellent? |
| **Patient satisfaction** | - Patient satisfaction survey  
- Survey in public to hear about reputation of the organisation |
| **Description:** Is there high patient satisfaction of the services offered by the CCC? |
| **Outcomes of traditional epidemiological measures related to taking part in clinical trials (5-/10- year mortality rate; Quality of Life)** | - Cancer registries  
- (Disease free) survival rate  
- Quality of life  
- Mortality rate |
| **Description:** Are the outcome measurements of the CCC excellent/promising? |
| **Impact on guideline development (developing own guidelines, being cited in guidelines developed by others)** | - Consumer satisfaction on participation in patient-centered guideline development  
- Consumer satisfaction on guideline implementation and use.  
- Recognition by international guideline bodies |
| **Description:** Does the CCC have a high impact on guideline development both nationally and internationally? |
| **Impact of specialization on cancer types on average cost per patient** | - Evidence from Health Technology Assessment |
| **Description:** What is the impact of specialization on cancer types taking into account the average cost per patient? |
| **Financial efficiency (proving that services are cost beneficial and cost effective)** | - Evidence from Health Technology Assessment |
| **Description:** Are the services of the CCC financially efficient? |
| **Likely to be rejected for testing in CCCs** | - Representation of academics on the board of the hospital throughout the hospital hierarchy (e.g. divisional directors)  
- Number of of researchers, clinicians, senior management and nurses in board of direction and organisational management  
- Clear chart to show the hierarchical structure of the organisation  
- Description of multidisciplinary background of board members |
| **Representation of health professionals and researchers in the general direction of the organization** |
| **Description:** How does the representation of staff members from different discipline in the general direction of CCCs add value? |
| **On-going collaboration with patient organizations** | - Patient organisations involved  
- Joint projects and other initiatives  
- Patient surveys |
<p>| <strong>Description:</strong> Does the collaboration of CCCs with patient organisations add value? |</p>
<table>
<thead>
<tr>
<th>Specialization in specific cancer type(s)</th>
<th>Presence of multidisciplinary teams for specific cancer types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description: Does the specialization of CCC in specific cancer types add value?</td>
<td>Skill mix of staff</td>
</tr>
<tr>
<td>- Presence of multidisciplinary teams for specific cancer types</td>
<td>Number of second opinion</td>
</tr>
<tr>
<td>- Skill mix of staff</td>
<td>Minimum range of tumors covered</td>
</tr>
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<thead>
<tr>
<th>Focus on specific cancer types within the centre</th>
<th>Number of operations by surgeon per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description: Does the focus of CCCs on specific cancer types add value?</td>
<td>Skill mix of staff</td>
</tr>
<tr>
<td>- Presence of multidisciplinary teams for specific cancer types</td>
<td>Number of operations by surgeon per year</td>
</tr>
<tr>
<td>- Skill mix of staff</td>
<td>Skill mix of staff</td>
</tr>
</tbody>
</table>

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<tr>
<th>Should be further researched before testing with CCCs</th>
<th>Qualitative catalogue with activities of the centre; modes of communication/sort of programs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Making information accessible for society (e.g. for prevention)</td>
<td>Website, quality and quantity of information</td>
</tr>
<tr>
<td>Description: Does the CCC have added value through knowledge dissemination to the society?</td>
<td>Conferences for public</td>
</tr>
<tr>
<td>- Number of operations by surgeon per year</td>
<td>Interviews</td>
</tr>
<tr>
<td>- Skill mix of staff</td>
<td>Number and volume of initiatives</td>
</tr>
<tr>
<td>- Minimum range of tumors covered</td>
<td>Initiatives for different target groups</td>
</tr>
<tr>
<td>- Qualitative catalogue with activities of the centre; modes of communication/sort of programs:</td>
<td>Epidemiology department publications</td>
</tr>
<tr>
<td>- Number of operations by surgeon per year</td>
<td>National media prevention campaigns</td>
</tr>
<tr>
<td>- Skill mix of staff</td>
<td>Having a department of public relations</td>
</tr>
<tr>
<td>- Minimum range of tumors covered</td>
<td>Formal/informal publications</td>
</tr>
<tr>
<td>- Qualitative catalogue with activities of the centre; modes of communication/sort of programs:</td>
<td>Lobbying, political/public</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ability to receive funding or charitable gifts (e.g. in the US by the NIH)</th>
<th>Amount of external grant funding</th>
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<tbody>
<tr>
<td>Description: Does the CCC’s ability to receive charitable gifts and funds add value?</td>
<td>Number of grants received</td>
</tr>
<tr>
<td>- Presence of multidisciplinary teams for specific cancer types</td>
<td>Number of grants received</td>
</tr>
<tr>
<td>- Skill mix of staff</td>
<td>Number of grants received</td>
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<tr>
<th>Provision of on-going support for surviving patients</th>
<th>Number of survivorship programs</th>
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<tr>
<td>Description: Does the provision of on-going support for cancer survivors by CCC add value?</td>
<td>Participants in survivorship programs</td>
</tr>
<tr>
<td>- Number of operations by surgeon per year</td>
<td>Number of patients seen for follow-up (per year)</td>
</tr>
<tr>
<td>- Skill mix of staff</td>
<td>Department for follow up/communication</td>
</tr>
<tr>
<td>- Minimum range of tumors covered</td>
<td>Mediums for support</td>
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<th>Staff satisfaction</th>
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<tr>
<td>On-going collaboration with providers (material, technology, pharmaceutics)</td>
<td>Evidence of interaction: Publications, meetings, (number of) contracts etc.</td>
</tr>
<tr>
<td>Description: Is there added value due to the on-going collaboration with providers (material, technology, pharmaceutics)?</td>
<td>Being a pilot training centre</td>
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<tr>
<td>- Number of operations by surgeon per year</td>
<td>Number of clinical trials with industrial promotion</td>
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<tr>
<th>On-going collaboration with other cancer centres</th>
<th>Joint publications</th>
</tr>
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<tbody>
<tr>
<td>Description: Is there added value due to the on-going collaboration with other cancer centers?</td>
<td>Joint projects/studies</td>
</tr>
<tr>
<td>- Joint publications</td>
<td>Joint grants (application)</td>
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<tr>
<th>Patient volume per tumour type</th>
<th>Number of registration in a given time period</th>
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<tbody>
<tr>
<td>Description: How does the patient volume per tumor type affect the added value of a CCC?</td>
<td>Number of registration in a given time period</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Well-defined job roles for staff</th>
<th>Organisational protocols for staff where job roles are written and used to explain to staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description: Is there added value in terms of the well-defined job roles for staff in a CCC?</td>
<td>Organisational protocols for staff where job roles are written and used to explain to staff</td>
</tr>
</tbody>
</table>
Similar to the findings from another study (Rajan et al, 2015), both researchers and clinicians agree that clinical aspects of a CCC add the same or more value than research aspects. Nurses spoke of a clinical area in terms of the specialization of a CCC in different tumour types. Nurses feel that a CCC gives better career advancement opportunities than other types of institutions. Managers feel that added value of a CCC is not just in terms of clinical aspects but also in terms of the efficiency and effectiveness of the processes that takes place within the institution. This gives an impression that an active consensus on added value and a universal definition of CCCs is necessary, as there seems to be variances in staff perception (from different staff groups) even within a CCC.

The final draft set emerging from this study (table 3) shows that a number of criteria can help identify the added value of CCCs. Such as, career advancement opportunities, availability of state of the art resources (staff skills, equipment), internal collaboration between research and clinical departments, speed of translation of research results from bench to bedside (clinical research, technology), patient satisfaction. However, not all criteria can easily help identify and assess the added value of CCCs. There is consensus that criteria such as the ability to achieve charitable gifts and staff satisfaction were seen as not that important to assess the added value. Some criteria clearly distinguish the added value of CCCs (e.g. efficiency related to research and clinical processes, patient satisfaction, career development opportunities). Some criteria do not seem to be relevant to distinguish the added value of CCCs (e.g. staff satisfaction, focus and specialization on tumors). Some criteria although important were seen by staff as difficult to be implemented e.g. financial efficiency (proving that services are cost effective and cost beneficial). This could be because gathering data regarding efficiency and effectiveness take time especially in the case of some early stages health technologies that lack evidence.

Participants identified a number of qualitative and quantitative indicators for each criterion (see table 3). The quantitative criteria are straightforward and relatively easy to measure (e.g. publications, guidelines, protocols) than the qualitative criteria that are more difficult to measure e.g. in the criterion “internal collaboration between the research and clinical departments”, the indicators that were mentioned were: time from first description to clinical use; identification and measurement of different phases of development of a new research finding and time between the phases. In a recent systematic review conducted by Thonon et al., they found that indicators for measuring internal/external research collaboration are not identified in existing studies. Our study contributes to this knowledge by identifying measurable indicators for this criterion that can be tested in CCCs.

The strengths of this study are: (i) it is the first explorative study that tries to understand the added value of CCCs using a European audience, (ii) a mixed method approach (systematic review, survey and focus group) was used to answer our research question. There are obviously some limitations: (i) due to the novelty of the topic, evidence has only started...
emerging and this was reflected in a low number of papers and conference abstracts. Since we finalised our study by the end of 2013, we have observed an increase in articles in this field. Some articles talk about the added value of NCI designated CCCs mainly in terms of the improved survival and effect of care at these centers\textsuperscript{32-35} (ii) we encountered a moderate response rate (47\%) in the survey. This study reveals how to identify and assess the potential added value of CCCs in a number of areas including: contributions (from clinicians) to guideline development, better patient outcomes, career development possibilities in oncology, speed of focused processes in research as well as patient care, a higher percentage of patient accrual in clinical trials, etc. The study participants unanimously agree that CCCs add value in several areas. To evaluate how far a CCC performs differently from other organisations involved in cancer research and/or patient care (e.g. general hospitals and academic medical centres), the findings should now be piloted to validate the terminologies for use in benchmarking different types of cancer organisations.

A step-wise approach to validation is advised. First data collection and –verification in order to identify which of the criteria are available preferably from existing assessment reports of-and data registries related to CCCs. Further these should also be applied to other oncology service providers and –research organisations in order to establish a basis for comparative research.

This research could benefit from the body of knowledge that is built using data from patient registries and the tier-based approach as suggested by Porter\textsuperscript{2}. So far consensus around the meaning of ‘value’ is still lacking and absent at the organisational level. As CCC’s commonly claim to be a special category in cancer research and -service provision and sometime receive considerable funding, research using this framework can be helpful in actually proving the basis for this claim and better justify the investments in these organisations.
REFERENCES


32. J.A. Wolfson et al. Impact of care at NCI Comprehensive Cancer Centers (NCICCC) and payor status on outcomes in osteosarcoma (OS), Ewing sarcoma (ES) and rhabdomyosarcoma (RMS) (2015).


34. J.A. Wolfson. Evaluation of the effect of care at NCI comprehensive cancer centers (NCICCCs) on disparities in outcome within adolescents and young adults (AYAs) with cancer (2014).

ANNEX A: SURVEY QUESTIONNAIRE (CHAPTER 4)

**Q1. Do you think there is any added value of being a comprehensive cancer center?**

- Yes
- No

*Please explain your reasons for selecting 'Yes' or 'No' in the comment box below. Are there any indicators that you think can help identify and measure the added value of being a Comprehensive Cancer Center?*
The added value of being a Comprehensive Cancer Center - An

Q2. We have identified a number of indicators through literature review that may help identify and measure added value in Comprehensive Cancer Centers. We would appreciate if you could rate them. This will help us prioritise indicators that are most suitable for this study.

**Leadership**

- Representation of health professionals and researchers in the general direction of the organization

  - Not at all important
  - Somewhat important
  - Moderately important
  - Important
  - Very important
  - Do not understand the indicator

**People**

- Well-defined job roles for staff
- Career advancement opportunities

  - Not at all important
  - Somewhat important
  - Moderately important
  - Important
  - Very important
  - Do not understand the indicator

**Strategy**

- Specialization in specific cancer type(s)
- Focus on specific cancer type(s) within the center
- Patient volume per tumor type

  - Not at all important
  - Somewhat important
  - Moderately important
  - Important
  - Very important
  - Do not understand the indicator

**Partnerships & Resources**

- Availability of state of the art resources (staff skills, equipment)
- Internal collaboration between research and clinical departments
- Ongoing collaboration with providers (materials, technology, pharmaeuticals)
- Ongoing collaboration with other cancer centers
- Ongoing collaboration with patient organizations

  - Not at all important
  - Somewhat important
  - Moderately important
  - Important
  - Very important
  - Do not understand the indicator
### The added value of being a Comprehensive Cancer Center - An

#### Processes, Products & Services

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Not at all Important</th>
<th>Somewhat Important</th>
<th>Moderately Important</th>
<th>Important</th>
<th>Very Important</th>
<th>Do not understand the indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed of translation of research results from bench to bedside (clinical research, technology)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Speed of implementation of new clinical practice guidelines</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Adherence to clinical practice guidelines</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Provision of second opinion by the comprehensive cancer center (percentage of changed treatment plans after second opinion through comprehensive cancer center)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Speed of processes within the center - related to type of tumour (Defined by: Average access time; Average waiting time (1): First appointment ↔ Diagnosis; 2: Diagnosis ↔ Treatment plan; 3: Treatment plan ↔ Treatment; Average length of stay)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Accrual percentage of patients in clinical trials</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Number of publications (considering quantity and quality)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

#### People Results

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Not at all Important</th>
<th>Somewhat Important</th>
<th>Moderately Important</th>
<th>Important</th>
<th>Very Important</th>
<th>Do not understand the indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff satisfaction</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

#### Customer (Patient) Results

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Not at all Important</th>
<th>Somewhat Important</th>
<th>Moderately Important</th>
<th>Important</th>
<th>Very Important</th>
<th>Do not understand the indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient satisfaction</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Provision of on-going support for surviving patients</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Outcomes of traditional epidemiological measures related to taking part in clinical trials (5-10-year mortality rate, Quality of Life)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
### The added value of being a Comprehensive Cancer Center - An

#### Society Results

<table>
<thead>
<tr>
<th>Making information accessible for society (e.g., for prevention)</th>
<th>Not at all Important</th>
<th>Somewhat Important</th>
<th>Moderately Important</th>
<th>Important</th>
<th>Very Important</th>
<th>Do not understand the indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact on guideline development (developing own guidelines, being cited in guidelines developed by others)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Business Results

<table>
<thead>
<tr>
<th>Impact of specialization on cancer types on average cost per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial efficiency (proving that services are cost beneficial and cost effective)</td>
</tr>
<tr>
<td>Ability to receive funding or charitable gifts (e.g., in the US by the NIH)</td>
</tr>
</tbody>
</table>

#### Q3. After having rated the indicators above, do you have any suggestions for other indicators that might be useful to identify and measure the added value of Comprehensive Cancer Centers?  
- Yes
- No

Please write your comments below:

---
The added value of being a Comprehensive Cancer Center - An

* We would like to do in-depth face-to-face interviews with at least one representative from your center for each of these stakeholder groups: basic researchers, clinicians, nurses and senior executives. The interviews will be conducted from June until mid July 2013. Would your center be willing to participate in these interviews? Anonymity of participants and Centers will be strictly maintained with respect to any information/data provided.

[ ] Yes
[ ] No

Thank you for participating in this survey. We will prepare a detailed report based on the results of this survey and the interviews. This report will be shared with all of you.
ANNEX B: INTERVIEW QUESTIONS

1. Introduction on project and researchers

2. Ask interviewee to introduce himself, especially:
   
   Job Title:
   
   Years of experience in the current job:
   
   Background:

3. Do you think there is any added value of being a CCC?

4. Please explain your reasons why you think there is/is not an added value.

5. Which method(s) do you consider to be most suitable to show the added value of being a Comprehensive Cancer Centre?

6. Are there any indicators (in general/from your own job) that you think can help identify and measure the added value of being a Comprehensive Cancer Centre? (In which way is that different from other centres that are not comprehensive?)

7. Through a literature review a number of indicators were found that might help us to prove the added value of CCCs. Based on this literature search we did a survey (table below) with the OECI members to identify the importance of these indicators. Most of the indicators scored high. However, there are two points which we would like to discuss:

   a) Can these indicators distinguish CCCs against other institutes that are not comprehensive?

   b) Are these indicators measurable?

8. Are there any other indicators that you would like to add on this level of the organization?

9. Do you know of any projects, studies or (unpublished) literature from your centre/other centres concerning the added value of Comprehensive Cancer Centres?
Critical appraisal of translational research models for suitability in performance assessment of cancer centers

Abinaya Rajan
Richard Sullivan
Suzanne Bakker
Wim H. van Harten

Oncologist. 2012; 17(12): e48-57
ABSTRACT

**Background** The aim of the study is to critically appraise translational research models for suitability in performance assessment of cancer centers. Translational research is a complex cumulative process that takes time. However, the operating environment for cancer centers engaged in it is now financially insecure. Challenges are to improve results and reduce time from discovery to practice innovations. Performance assessment can identify improvement areas that will help reduce translational delays. Currently, there is no standard method to identify models for use in performance assessment. **Methods** We conducted a systematic review to identify models and developed a set of criteria based on: scientometrics, complex adaptive systems, R&D processes and strategic evaluation. Models were assessed for: linkage between research & care components; new knowledge; systems integration; performance assessment; review of other models. **Results** Twelve models were identified; six described phases/components for translational research in different blocks (‘T’ models) and six described the process of translational research (‘process models’). The similarity between the two types of models is that they view translational research as an accumulation of new knowledge. Where they differ is that process models more clearly: address systems integration; link research and care components; were developed for evaluating and improving the performance of translational research. However, T models are more likely to review other models. **Conclusion** Process models seem to be more suitable for performance assessment of cancer centers than ‘T’ models. The two most suitable process models (the Process Marker Model and Lean & Six Sigma applications) must be thoroughly tested in practice.
INTRODUCTION

Translational research is a complex, cumulative and often unpredictable process focused on moving a single or combination of basic research findings into clinical practice. The recent identification of and attention to this field is not just meant to raise awareness and to consider it as manageable, but also to improve performance in terms of efficiency and effectiveness. A particular challenge to translational research in oncology, as in other clinical fields, are perceptions about unnecessary delays in- or complete blockage of translation.

In the fiscal year 2004/2005 the global spend on cancer research was approximately 14 billion Euros (c. 17.64 billion US Dollars). The USA (dominated by the National Cancer Institute) accounted for the largest absolute spend, that was almost three times the level of per capita spend compared to Europe. Yet in terms of publications and an increasing trend towards more applied clinical outputs, relative research productivity was better in Europe [1]. Apart from effectiveness issues, translation of research into practice still takes a lot of time. There are claims that translation of only 14% of new health-related scientific discoveries to clinical practice [2] takes an average of 17 years [3]. A study by Ioannidis et al found that from 101 promising claims of new discoveries with clear clinical potential that were reported in major basic science journals between 1979 and 1983, only five resulted in interventions with licensed clinical use by 2003 and only one had extensive clinical use [4].

Imatinib is an example of successful translation from oncology. It shows the time it took for an intervention to reach licensed clinical use based on knowledge that emerged slowly over many decades. The drug focuses on disrupting one specific protein that seems to fuel the cancer while sparing other enzymes. The initial knowledge appeared in the 1960’s when scientists first noticed chromosomal abnormalities in the blood of CML patients. But, it wasn’t until the 1980’s, that genetic mapping helped determine that chromosomal abnormality produces a cancer-causing kinase enzyme. It took two years to create and test 400 molecules, to find one that would target this enzyme without disrupting any of the hundreds of other similar enzymes in a healthy cell. Another eight years of safety testing and development was needed before the drug could be tested with patients, finally giving remarkable results. While clinical trials were being expanded, FDA put the drug on fast track for approval in 2001 [5].

Translational research is cumulative. To improve its performance and reduce unnecessary delays, acquiring insight into the process and performance assessment can add value. This means assessing performance in cancer centers against a set of predetermined criteria of the economy, efficiency and effectiveness of that organization in conducting translational research (adapted from the OECD definition) [6] with the purpose of supporting continuous improvement and transparent accountability at multiple organizational levels. This would help address delays by identifying areas for improvement including: innovation transfer
management; organizational administration of research projects; incentive mechanisms to motivate researchers; and communication strategies between researchers and other key stakeholder groups. These areas can promote multidisciplinary collaboration that in turn can speed the rate at which basic research discoveries eventually become clinically viable health technologies.

For performance assessment it is essential to know ‘what’ is being translated and ‘how’ it is being translated. Initially, models need to be systematically identified and critically appraised before they can be tested in practice. To a large extent, the process of translational research seems to be generic and it is not clear if a specific model should be preferred for oncology. At present it is unknown how many models exist and which of those are suitable for performance assessment. Most recent references are based on two studies. Trochim et al. reviewed and synthesized four models to illuminate important issues to evaluate translational research [7]. Morris Wooding and Grant looked at quantification of translational time lags and in that context offered a tentative model based on synthesis of a few models [8]. However, the studies do not specify if they conducted a systematic identification of models nor did they use systematic criteria to appraise the identified models. Moreover, in Morris Wooding and Grant’s study it is not clear how many models were used to synthesize their model.

The current study aims to identify models of translational research using a systematic literature review and critically appraise them by using common criteria that were specifically developed for this purpose. The rationale is to identify the model(s) that are most suitable in assessing the performance of cancer centers in translational research.

METHODS

Identification of models

A systematic literature review was carried out to identify translational research models using a combination of search terms in four databases: PubMed, Embase, Trip Database and Scopus (supplemental online). The first search included scientific terms & common expressions for translational research and terms associated with models & performance assessment, while the second search included scientific terms & common expressions for translational research and different phases of translation denoted by ‘T’s (Figure 1). In addition, we tracked the references and citations for a few papers that were identified through the previous search method. They either proposed a model and/or identified other models. We did not limit our search to models specific in oncology nor to the year of their publication.
Criteria development to appraise models

At present, there is no standard methodology to assess the suitability of translational research models for performance assessment purposes. We developed a set of criteria (CR), Table 1 CR.1-CR.6. The models were awarded a “Yes” or “No” for each question where “Yes” meant that the model seemed suitable for performance assessment. Our focus on appraising the models looked at how they present translational research in terms of: its main purpose; component(s) that can be evaluated; strategies to evaluate the identified components and testing of the chosen strategies in practical settings. To validate our focus we referred to a range of literature from both medical and non-medical disciplines e.g. organizational management. With reference to the scientometric analysis conducted by Jones, Cambrioso and Mogoutov we deduced that translational research emerged to link the research and care components (CR.1) [9]. Cancer research is a complex adaptive system in which the components must be regularly assessed to improve their performance (CR.2 & CR.3) [10]; Fifth generation R&D suggests that performance assessment strategies should integrate organizational systems to link the process of translation that occurs through cross-boundary learning and knowledge flow (CR.4) [11]. Using the theory of the evaluation of strategic options by Johnson & Scholes we framed criteria for evaluating the strategies of the models; they need to be evaluated for suitability and feasibility (CR.5 & CR.6) [12]. A seventh criterion based on acceptibility (CR.7) was meant to check if models have been tested or applied in practice. This last criteria has not been presented in Table 1 as we were able to assess only one model.
RESULTS

Translational research models identified

A total of 2397 studies were identified after removing the duplicates (Figure 2). Title screening showed that the majority were related to specific biomedical discoveries focusing on basic & translational issues. Many studies referred to animal models and not to the conceptual models we were searching for. Only 385 papers contained a description of translational research. Abstract screening led to 182 papers which contained bench to bedside issues; 89 used descriptive statements to define translational research. Only 12 papers that contained and described a model were included in the resulting appraisal. Of these, six papers described the main phases/components for translational research within different translational blocks (‘T’ models). The remaining six papers mapped the steps/processes for translational research (process models). Both type of models start at basic discovery and the following phases extend to clinical trials or even beyond these to widespread diffusion or population impact (Figure 3).

Overview of ‘T’ models

The terminologies and position of the types of translations or T’s are inconsistent in all ‘T’ models. Overall, the ‘T’ blocks identify the specific translational areas that are at the same time barriers for translation but steps to overcome these barriers and improve performance are not clearly addressed.

Type 1 translation or T1: In the six models, descriptions of Type 1 translation (or T1) have similar starting points but are phrased differently. T1 encompasses: “basic research to patient based research” [13], “basic science research to human clinical research” [2], “basic science research (phase 0) to early human trials (phase 1)- early clinical trials (phase 2)” [14], “basic biomedical science to clinical efficacy knowledge” [15] “basic biomedical to clinical science knowledge” [16] and “gene discovery to health applications” [17]. Because of these variations it is hard to establish where T1 ends.

Type 2 translation or T2: The description of T2 is also inconsistent over all models. T2 encompasses: “patient oriented to population oriented research” [13], “human clinical research to practice based research” [2], “early clinical trials (phase 2) to late clinical trials (phase 3)” [14], “clinical efficacy knowledge to clinical effectiveness knowledge” [15], “clinical science knowledge to improved health” [16] and “health applications to evidence based guidelines” [17].

Type 3 translation or T3: The location and extent of T3 also varies in all models. T3 encompasses: “population based research to basic research” [13], “practice based research to clinical practice” [2], “late clinical trials (phase 3) to implementation phase (phase 4)” [14], “clinical effectiveness knowledge to improved population health” [15], In Sung et al’s
model there is no T3 [16] and in Khoury et al’s model T3 is the translation of guidelines to health practice [17].

Type 4 translation or T4: Only Khoury et al’s model contains a T4, which is the translation of practice to population health impact [17].

Overview of process models

Three process models use ‘T’ terminologies. The early translational pathways by Ernest, Matrisian and Nelson et al [Translational Research Working Group (TRWG, National Cancer Institute)], uses the T1-T2 model but the pathways are mapped only for ‘T1’. They were developed to aid the transformation of scientific discoveries into new clinical modalities for oncology. Specifically: risk assessment modalities (bio specimen based risk assessment devices and image-based risk assessment) and interventive modalities (agents, immune response modifiers, interventive devices, lifestyle alterations) [18]. The biomedical research continuum by Drolet and Lorenzi consists of a zone of translation with three translational
chasms (T1-T3): T1 is laboratory to clinical research between basic science discovery to proposed human application; T2 is safety and efficacy research between proposed human application and proven clinical application; T3 is implementation and adoption research between proven clinical application and clinical practice. A pathway, inquiry & action for each chasm has been given [19]. The Lean & Six Sigma applications to clinical and translational research by Schweikhart and Dembe uses the T1-T4 phases by Khoury et al to improve the efficiency of translational research. Each phase consists of business management strategies for process assessment [20]. The Process Marker Model by Trochim et al identifies key steps of translational research that is not represented by ‘T’s but described as three integrated systems: basic research system, clinical trials system and practice-based system. The model aims to evaluate the process of translational research in order to reduce the time lag [7]. Lane and Flagg’s Need to Knowledge model identifies unmet needs that lead to the generation of knowledge through the outputs of three activities: research

Figure 3 An overview of ‘T’ models and process models of translational research
discovery, prototype intervention and product innovation. It recognizes that knowledge implementation and beneficial societal impacts involves effective communication of each successive knowledge state to the relevant stakeholders [21]. Finally, Ogilvie et al’s model is a framework to advance translational research that identifies a pivotal role for evidence synthesis that translates knowledge of non-linear & intersectoral interfaces to the public realm [22].

**Oncology specific models**

It was hard to confirm which of the appraised models are currently being used to inform translational research in cancer centers in Europe and/or in the USA. However, only one model was specifically developed for oncology: the early stage translational pathways by Ernest, Matrisian and Nelson et al. (TRWG, NCI) [18]. They use the T1-T2 model proposed by the President’s Cancer Panel [23]. This was one of the first models in translational research to emerge and is also known as bench-to-bedside-to-practice. The pathways were developed in T1 phase to facilitate the process of basic discoveries in cancer to be developed into clinical modalities, but they have not been adopted in practice.

**Evidence from appraisal of ‘T’ models and process models**

The process models were more favorable when appraised against our criteria than ‘T’ models (Table 1) suggesting that they may be better suited for performance assessment in cancer centers. There is only one similarity between the two types of models that they view translational research as accumulation of new knowledge. The differences are that process models more clearly: address systems integration; link research and care components; were developed for evaluating and improving the performance of translational research. In contrast, ‘T’ models tend to review other models and their purpose is to present the phases of translational research but not to assess and improve its performance. Three process models (Lean & Six Sigma applications; Process Maker Model and the Need to Knowledge Model) seem to have been developed to evaluate translational research. In particular, the first two models scored highest in the appraisal (See Figure 4 & 5). They track the time between various steps of the different translational phases in order to improve translational process efficiency. The Lean & Six Sigma applications is the only model that clearly gave evidence that it had been tested in practice in a process improvement project focused on redesign of the scheduling system at the clinical trials unit of Ohio State University [20].

**Possible implementation of Lean and Six Sigma techniques in translational research**

A recent process improvement project involving redesign of the scheduling system in the Clinical Trials unit of the Ohio State University (see Figure 5) seems to show a five-stage intervention: a practical example of Lean and Six Sigma techniques in translational research. Within the clinical trials unit, the aim was to improve the efficiency of the patient scheduling
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Rubio et al (T1-T3)</th>
<th>Sung et al (T1-T2)</th>
<th>Thornicroft, Lemp &amp; Tansella (T1-T3)</th>
<th>Dougherty &amp; Conway (T1-T3)</th>
<th>Khoury et al (T1-T4)</th>
<th>Westfall, Mold &amp; Fagnan (T1-T3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR 1. Does the model present translational research as a continuum with bidirectional flow between research and practice?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Bidirectional arrows between T1 T2 &amp; T3.</td>
<td>Unidirectional arrows between T1 &amp; T2.</td>
<td>Unidirectional arrows between 5 phases and 3 blocks.</td>
<td>Bidirectional arrows between T1, T2 &amp; T3.</td>
<td>It connects the four phases T1-T4 although no bidirectional arrows are shown.</td>
<td>Bidirectional arrows between T1 T2 and T3.</td>
</tr>
<tr>
<td>CR 2. Was the purpose of the model performance assessment of translational research?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Defines translational research as a basis for developing appropriate training programs.</td>
<td>Describes the major phases of translational research.</td>
<td>Describes the major phases of translational research.</td>
<td>No</td>
<td>No</td>
<td>Describes the major phases of translational research.</td>
</tr>
<tr>
<td>CR 3. Is translational research about generation of new knowledge?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Recognizes the integration of basic, patient-oriented &amp; population-based research to move multidisciplinary knowledge from discovery to the implementation phase.</td>
<td>Need to look at the factors that promote or delay knowledge flow across the three communication blocks that they identified (T1-T3)</td>
<td>Clinical efficacy knowledge between T1 and T2 and clinical effectiveness knowledge between T2 and T3.</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>CR 4. Does the model address systems integration?</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Focused on training programs in translational research. Although it suggests collaboration among scientists from multiple disciplines.</td>
<td>Translation is seen from a systems perspective that addresses: incompatible databases, fragmented infrastructure, practice limitations for knowledge to flow better.</td>
<td>It is primarily focused on points where communication blocks can occur. However, it does not focus on how to overcome these with better systems integration.</td>
<td>Translation is seen from a systems perspective that addresses: incompatible databases, fragmented infrastructure, practice limitations for knowledge to flow better.</td>
<td>It refers to multiple disciplines being involved in but it does not refer to systems integration directly.</td>
<td>Rethinks the interface between basic science &amp; clinical practice. Practice based research is the common pathway on which different stakeholders &amp; interest can be engaged to improve patient care &amp; outcomes.</td>
</tr>
<tr>
<td>CR 5. Does the model explain any strategies for performance assessment of translational research?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Does not explain how translational research continuum can be assessed. It only provides a logic model for performance assessment training &amp; education programs for translational research.</td>
<td>It does not give any strategies for performance assessment. It does not give any strategies to assess them.</td>
<td>It is looking at factors that promote or delay knowledge flow but it does not give any strategies to assess them.</td>
<td>Identifies key facilitators of translation: shared leadership, transdisciplinary teams, tools that help improve quality &amp; value and better financial resources but does not give any strategies for performance assessment</td>
<td>Presents a framework with questions related to performance assessment of genomics. It is unclear if these strategies that can be used to assess the performance along the entire continuum of translational research.</td>
<td>Advocates for practice based research as a crucial scientific step in the continuum. But it does not give any strategies to assess translational research performance.</td>
</tr>
<tr>
<td>Criteria</td>
<td>Rubio et al (T1-T3)</td>
<td>Sung et al (T1-T2)</td>
<td>Thomicroft, Lemp &amp; Tansella (T1-T3)</td>
<td>Dougherty &amp; Conway (T1-T3)</td>
<td>Khoury et al (T1-T4)</td>
<td>Westfall, Mold &amp; Fagnan (T1-T3)</td>
</tr>
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<td>-----------------------------</td>
</tr>
<tr>
<td>CR 6. Has the model reviewed other translational research models?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>NIH roadmap; IOM roundtable; Westfall, Mold &amp; Fagnan; Sung et al; Dougherty and Conway.</td>
<td>IOM roundtable</td>
<td>MRC framework; Craig et al; Sung et al; Crowley et al; NIH roadmap; Presidents' Cancer Panel; Westfall, Mold &amp; Fagnan.</td>
<td>NIH roadmap</td>
<td>NIH roadmap; Human Genome Epidemiology Network (HuGE); US task force report on genetic testing (ACCE framework).</td>
<td>NIH roadmap</td>
</tr>
<tr>
<td>Process models</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Criteria</td>
<td>Trochim et al (Process Marker Model)</td>
<td>Drolet &amp; Lorenzi (Biomedical Research Translation continuum)</td>
<td>Ernest Matrisian &amp; Nelson et al. (early stage developmental pathways)</td>
<td>Schweikhart &amp; Dembe (Lean &amp; Six Sigma applications to clinical &amp; translational research)</td>
<td>Lane &amp; Flagg (Need to Knowledge Model)</td>
<td>Ogilvie et al (Translational Framework for Public Health Research)</td>
</tr>
<tr>
<td>CR 1. Does the model present translational research as a continuum with bidirectional flow between research and clinical practice?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Views translational research as bidirectional. It shows that translational research can be evaluated at any level by assessing length of any segment or sub-segment of processes along the continuum.</td>
<td>Describes the zone of translation with three translational chasms. Findings at any stage in the continuum feed back to previous research stages for more examination &amp; action.</td>
<td>It views translational research as bench to bedside and vice versa. But the pathways themselves are confined to the early translational research phase.</td>
<td>The continuum of translational research is the context in which the techniques are being applied across the continuum.</td>
<td>It represents the complete continuum of activities from problem statement to solution delivery. These need collective actions by stakeholders and those may be recursive or iterative. So basically it looks at the flows of knowledge.</td>
<td>It reviews the critical pathway for translation of health research in the UK, which is bidirectional. It refers to the Cooksey report that describes a translation pathway for health research into healthcare development.</td>
</tr>
<tr>
<td>CR 2. Was the purpose of the model performance assessment of translational research?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>It is about assessing translational efforts that seek to reduce the time it takes to move research into practice and health impacts.</td>
<td>It reviews, synthesize and clarify current models and terminology and proposes a new model called the biomedical translational continuum. But, it does not propose strategies for performance assessment.</td>
<td>The pathways are engineering flowcharts that schematize the process of early translational research. However, the direct purpose was not to evaluate the performance of translational research.</td>
<td>It is about improving the processes involved in clinical and translational research through performance assessment using the principles, practices and methods from Lean &amp; Six Sigma strategies.</td>
<td>It gives an operational framework where an application needs knowledge transformations to reach the marketplace as a device or service. The action cycle for each phase shows the performance assessment focus.</td>
<td>It poses a research agenda to advance translational research. It does not provide clear strategies to assess translational research performance.</td>
</tr>
<tr>
<td>CR 3. Is translational research about generation of new knowledge?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>It provides a common framework that can link many studies and types of knowledge together to give a shared basis for assessing and reducing translational time.</td>
<td>Translational research occurs along the entire continuum as knowledge progresses to public health gains.</td>
<td>Knowledge transfer needs stakeholders to work outside organizational boundaries in interdisciplinary teams and this shapes the type of knowledge produced.</td>
<td>Based on discovery, intervention &amp; innovation there is a need to ensure that product knowledge is effectively communicated to the relevant stakeholder groups.</td>
<td>It acknowledges that knowledge flows along the elements of the pathway and that many types of research contribute to shaping policy practice and new research.</td>
<td></td>
</tr>
<tr>
<td>Criteria</td>
<td>Rubio et al (T1-T3)</td>
<td>Sung et al (T1-T2)</td>
<td>Dougherty &amp; Conway (T1-T3)</td>
<td>Khoury et al (T1-T4)</td>
<td>Westfall, Mold &amp; Fagnan (T1-T3)</td>
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<tr>
<td>CR 4. Does the model address systems integration?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>It shows that processes can be tracked across three systems- basic research, clinical trials and practice research.</td>
<td>It tries to map the zone of translation and particularly translational chasms where activities remain vague. It does not address systems integration.</td>
<td>It addresses systems integration only for the early translational phase. It recognizes that pathways are idealized representations that don’t capture real world complexity.</td>
<td>Business strategies are applied to all phases of translational research to show how to make the process more efficient &amp; cost effective thus improving the research quality and translation.</td>
<td>Integrates three phases: discovery creation, intervention creation &amp; innovation creation. Looks at how to accommodate the commercialization aspect of new knowledge.</td>
<td>Translation should move from institutionalizing effective interventions to improving population health by influencing the individual and collective determinants of health.</td>
<td></td>
</tr>
<tr>
<td>CR 5. Does the model explain any strategies for performance assessment of translational research?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Identifies process &amp; subprocess markers that can track performance at different points in translational research continuum.</td>
<td>Presents translational research in a way that makes sense to physicians. However, it does look at performance assessment.</td>
<td>The pathways identify opportunities for collaboration across research disciplines. But they were not directly developed for performance assessment.</td>
<td>Details management strategies associated with Lean &amp; Six Sigma. It shows how application of the two approaches is relevant to all translational research phases.</td>
<td>A seven stage model: discovery creation stages 1-3 &gt; discovery output. Intervention: stages 4-6 &gt; invention output. Innovation stage 7 &gt; innovation output.</td>
<td>It only outlines a translational framework for public health research but it does not give any specific strategies for performance assessment.</td>
<td></td>
</tr>
<tr>
<td>CR 6. Has the model reviewed other translational research models?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Sung et al; Westfall, Mold &amp; Fagnan; Dougherty and Conway; Khoury et al.</td>
<td>NIH roadmap, IOM roundtable, Sung et al, Westfall, Mold &amp; Fagnan, Dougherty and Conway</td>
<td>It recognizes T1-T2 by the President’s Cancer Panel but did not review any models.</td>
<td>It adapts the Knowledge to Action model but did not review any models.</td>
<td>It looks at translational pathway presented in Cooksey report but it does not review other models.</td>
<td></td>
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</tbody>
</table>

NIH Roadmap- National Institutes of Health roadmap for Clinical and Translational Science Awards [24]

2) IOM roundtable- Institute of Medicine clinical research roundtable [25]

3) MRC framework – Medical research council framework for translational research, NIHR UK- National Institute for Health Research, UK [26]

4) Presidents' cancer panel 2004-2005, USA Translating research into cancer care: delivering on the promise [23]

5) Human Genome Epidemiology Network (HuGE Net) is for a systematic inquiry on applications of epidemiologic methods and approaches in population-based studies of the impact of human genetic variation of health and disease [27]

6) ACCE framework for genetic test evaluation, ACCE stands for Analytical validity, Clinical validity, Clinical utility, Ethical, legal and social implications of genetic testing [28]

7) Cooksey report- A review of UK health research funding [29]

8) Knowledge to Action model- Canadian Institutes for Health Research [30]
process by replacing paper-based calendar system with a more coherent data-driven computerized scheduling system based on multiple factors.

There five-stage intervention in how Lean and Six Sigma techniques were applied: Stage 1- an environmental scan was undertaken by a process improvement team to understand the various activities that are involved in the patient scheduling process. This included several key steps such as: determining customer needs; systematically evaluating each process step in detail; identifying sources of inefficiency and waste per step and; assessing organizational structure, culture and management. Stage 2- the team considered different scheduling approaches that incorporated the salient activities identified as important for an efficient schedule based on stage 1. Stage 3- repeated improvement cycles and field-testing for evaluating the various scheduling algorithms were conducted. Stage 4- an acuity table was developed that assigns an acuity estimate (in minutes per activity) for each specific activity identified as crucial in the previous stages. For example the activity of “simple specimen collection” was given an acuity score of 5. A scheduling algorithm matched the scores with key internal and external factors (e.g. availability of a specific number of nurses per shift, room availability and protocol related requirements etc.) to optimize patient and
staff scheduling on a given day. **Stage 5** ensured that staff was trained to use this new scheduling model. Their concerns and suggestions regarding the practical use of the model were addressed during the training. These stages finally led to the adoption of the model in daily practice [20].

Drawing from the above example in more generic terms, the five-stage intervention for applying performance assessment models in translational research in cancer centers would be: (i) environmental scanning to understand key activities within the whole continuum or specific phases of translational research; (ii) elaborating different algorithms (approaches) in which the identified key activities will be efficient; (iii) evaluation of these algorithms by performing continuous improvement cycles to check which algorithm is most suitable; (iv) using estimates (such as frequency or duration where possible) to map the key activities identified and correlating that to key internal and external factors that may affect those estimates; (v) training the staff on the new algorithm and ensuring that its implementation within the cancer center is acceptable to key stakeholders.

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**Figure 5** Example of a process improvement project at a clinical trial unit using Lean techniques (borrowed from Schweikhart SA, Dembe AE. The applicability of Lean and Six Sigma techniques to clinical and translational research. J Investig Med. 2009 Oct; 57(7): 748-755, with permission from Wolters Kluwer Health obtained through Copyright Clearance Center)
DISCUSSION

This paper aimed to identify models of translational research and appraise their suitability for performance assessment of cancer centers. We managed to identify twelve models of translational research: six ‘T’ models and six process models.

‘T’ models contribute to our understanding of translational research by mapping its key components but these components vary from model to model, confirming the statement of Australia’s chief scientist, “If you were to ask ten people what translational research means, you’re likely to get ten different answers” [31]. It is not clear whether the variations in ‘T’ models reflect actual variations in practice or are related to specific objectives or circumstances of various stakeholders. These variations may also reflect models being developed for specific research and/or clinical domains. In contrast, process models identify methods to facilitate, track and assess knowledge flows and interfaces along the continuum that include: multiple starting points for innovation; pathway mapping; process markers; using strategies and tools from business management and; inclusive evidence synthesis.

Based on our appraisal, two process models seem to be most suitable for performance assessment of cancer centers: the Process Marker Model and Lean & Six Sigma applications. Process markers can help cancer centers assess the performance of translational research by tracking the time taken between markers such as: pre-piloting of studies; submission of research proposals; funding of studies; the start and end of data collection for studies; inclusion of the study in research synthesis (e.g. publications or mainstreaming of research activities) that leads to subsequent stages of translational research. Process markers can include both process steps as well as reflect the transfer process per step (known as sub-process markers). This can be defined for phases such as clinical trials for: proposal submission, Institutional Review Board approval, funding of proposal, accrual of first subject; closed to accrual; presentation and publishing of results etc [7]. Process markers might help to identify and possibly reduce the time between different phases of clinical trials in cancer. Lean & Six Sigma are complementary to the Process Marker Model and might help cancer centers define markers more clearly. For example, in basic research, process makers could include: turnaround time of toxicology results, transfer of samples in laboratory and responding to regulatory requests. In clinical trials, cancer centers could track the unnecessary time waste and/or added value per process step for: bio-statistical consultations; minimizing protocol amendments; checking if placebos are needed; patient recruitment campaigns; patient monitoring process and eliminating early phase design errors [20].

However, the models still have some limitations. Lean & Six Sigma applications are from a non-medical field. Although, their pilot results are positive, they need to be tested in other phases of translational research to fully validate their use along the continuum. The Process Marker Model lacks precisely stated operational definitions of markers and an inferential statistical analysis framework [7]. And although, markers primarily measure time lags,
qualitative value related criteria are still lacking.

The five-stage intervention for the possible implementation of Lean & Six Sigma techniques can be adapted to different areas of the translational research continuum to improve its performance, starting from basic science to population impact. However, defining activities or markers for the earlier phases of the continuum is relatively easier than for the later phases such as population impact, which may even go beyond the primary scope of some Comprehensive Cancer Centers. Hence, more integrated research is needed to especially understand the later phases from a broader public health and societal perspective [22] before Lean and Six Sigma or any other performance assessment models can be implemented.

Translational research is not a simple linear process and some may argue that its complex and unpredictable nature prevents us from the use of models for performance assessment. The fear regarding such assessments among some stakeholder groups is that it might: jeopardize serendipity that is characteristic for many research processes; fail to capture research excellence that might exist partially or completely outside the scope of assessment criteria and; enable bureaucrats to take control of fields they do not really comprehend. A cautious and stepwise approach is therefore advisable if cancer centers are to use these models for performance assessment. As a first step acquiring structured insight into the various aspects of the translational process and comparing these between cancer centers might help centers identify improvement opportunities. For that purpose more precise operating definitions are needed at three levels: performance dimensions, performance indicators and sufficiently detailed metrics [32]. It is hard to say whether the cancer field has specific needs but we should be open to the idea that models from other medical and/or non-medical fields can also be used to assess cancer centers. They should be thoroughly tested in practice to know their potential for actual performance assessment.

The strengths of the study are that, to our knowledge, this is the first time that a systematic review has been undertaken to identify models of translational research that were appraised using a set of criteria. These were based on a range of issues for translational research identified from relevant literature. Undoubtedly, the criteria that we used can be critiqued. However it is necessary for cancer centers to carefully select models for performance assessment and our framework provides a basis for that. The criteria can be refined with views from key stakeholder groups (e.g. basic researchers, clinical researchers, clinicians, funding agencies, senior executives and patients).

There are two possible limitations to our study. The first limitation is that we could not check if all the models had been tested and implemented in practice. One could argue that the elements of these models are supported by “findings” or evidence from academic or experiential literature. The second limitation is that due to a lack of consensus on terminologies in translational research it was hard to identify models. So, there could be models that we did not consider in this appraisal. To increase the possibility of identifying
models in future, the title, abstract and key words in papers should clearly use a common term and/or commonly associated terms of translational research. Substitutions such as bench to bedside, implementation science, biomedical research should be restricted to the main content of the papers with clear explanation of these terms that can help the reader understand the model. Addition of a specific MeSH term for models in databases (e.g. conceptual models of translational research) may be useful to ensure that models are easily listed and identified.

CONCLUSION

Performance assessment can help improve the process of translational research by identifying areas for improvement in its management, knowledge exchange and engagement of multidisciplinary teams to deliver efficient and effective translational research. This would help reduce unnecessary time lag. Two models of translational research appear to be more suitable for performance assessment: the Process Marker model and the Lean & Six Sigma applications to clinical and translational science. It will be necessary to thoroughly test them in practice. Finally, cancer centers need to have consensus on terminologies in translational research. This will help identify and select models for performance assessment that can improve the performance of translational research for the benefit of patients.
REFERENCES


8. Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. JRSM 2011; 104 (12): 510-520.


### SUPPLEMENTARY MATERIAL

**Search terms used to identify models of translational research in databases**

<table>
<thead>
<tr>
<th>PubMed</th>
<th>Embase</th>
<th>Scopus</th>
<th>Trip Database</th>
</tr>
</thead>
<tbody>
<tr>
<td>(biomedical research [mesh] OR &quot;Translational Medical Research&quot; [mesh] OR research [majr]) AND (translation*[all fields] OR &quot;bench to bedside&quot; OR &quot;bench to practice&quot; OR &quot;bedside to practice&quot;) AND (model OR models OR pathway OR continuum OR framework OR strategy OR strategies OR definition OR process OR processes) AND (evaluation OR assessment OR added value OR relevance)</td>
<td>biomedical AND 'research'/exp OR 'translational medical research' OR 'research'/exp AND (translation OR 'bench to bedside' OR 'bench to practice' OR 'bedside to practice') AND ('model'/exp OR models OR pathway OR continuum OR framework OR strategy OR strategies OR definition OR process OR processes) AND ('evaluation'/exp OR assessment OR added value OR relevance) AND [embase]/lim</td>
<td>(biomedical research OR &quot;Translational Research&quot;) AND (&quot;bench to bedside&quot; OR &quot;bench to practice&quot; OR &quot;bedside to practice&quot;) AND (model OR models OR pathway OR continuum OR framework OR strategy OR strategies OR definition OR process OR processes) AND (evaluation OR assessment OR added value OR relevance)</td>
<td>(&quot;Translational Medical Research&quot; [mesh] OR research [majr] OR biomedical research [mesh]) AND (translation*[all fields] OR &quot;bench to bedside&quot; OR &quot;bench to practice&quot; OR &quot;bedside to practice&quot;) AND (1 AND type AND 2 OR (1 AND 2 AND type AND 3) OR (1 AND 2 AND 3 AND type AND 4) OR (1 AND 2 AND 3 AND 4 AND type AND 0) OR (T1 AND T2) OR (T1 AND T2 AND T3) OR (T1 AND T2 AND T3 AND T4) OR (T1 AND T2 AND T3 AND T4 AND T0)) AND [embase]/lim</td>
</tr>
<tr>
<td>(&quot;Translational Medical Research&quot; [mesh] OR research [majr] OR biomedical research [mesh]) AND (translation*[all fields] OR &quot;bench to bedside&quot; OR &quot;bench to practice&quot; OR &quot;bedside to practice&quot;) AND (1 AND type AND 2 OR (1 AND 2 AND type AND 3) OR (1 AND 2 AND 3 AND type AND 4) OR (1 AND 2 AND 3 AND 4 AND type AND 0) OR (T1 AND T2) OR (T1 AND T2 AND T3) OR (T1 AND T2 AND T3 AND T4) OR (T1 AND T2 AND T3 AND T4 AND T0))</td>
<td>'translational medical research' OR 'research'/exp OR biomedical AND 'research'/exp AND (translation OR 'bench to bedside' OR 'bench to practice' OR 'bedside to practice') AND (1 AND type AND 2 OR (1 AND 2 AND type AND 3) OR (1 AND 2 AND 3 AND type AND 4) OR (1 AND 2 AND 3 AND 4 AND type AND 0) OR (T1 AND T2) OR (T1 AND T2 AND T3) OR (T1 AND T2 AND T3 AND T4) OR (T1 AND T2 AND T3 AND T4 AND T0))</td>
<td>'translational medical research' OR 'research'/exp OR biomedical AND 'research'/exp AND (translation OR 'bench to bedside' OR 'bench to practice' OR 'bedside to practice') AND (1 AND type AND 2 OR (1 AND 2 AND type AND 3) OR (1 AND 2 AND 3 AND type AND 4) OR (1 AND 2 AND 3 AND 4 AND type AND 0) OR (T1 AND T2) OR (T1 AND T2 AND T3) OR (T1 AND T2 AND T3 AND T4) OR (T1 AND T2 AND T3 AND T4 AND T0))</td>
<td>(&quot;Translational Medical Research&quot; [mesh] OR research [majr] OR biomedical research [mesh]) AND (translation*[all fields] OR &quot;bench to bedside&quot; OR &quot;bench to practice&quot; OR &quot;bedside to practice&quot;) AND (1 AND type AND 2 OR (1 AND 2 AND type AND 3) OR (1 AND 2 AND 3 AND type AND 4) OR (1 AND 2 AND 3 AND 4 AND type AND 0) OR (T1 AND T2) OR (T1 AND T2 AND T3) OR (T1 AND T2 AND T3 AND T4) OR (T1 AND T2 AND T3 AND T4 AND T0))</td>
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Assessing excellence in translational cancer research: a consensus based framework

Abinaya Rajan
Carlos Caldas
Henri van Luenen
Mahasti Saghatchian
Wim H. van Harten

Transl Med. 2013 Oct 29; 11: 274
ABSTRACT

It takes several years on average to translate basic research findings into clinical research and eventually deliver patient benefits. An expert-based excellence assessment can help improve this process by: identifying high performers; best practice; improving the quality and efficiency of the translational research process. This can help build networks of excellent Centres by aiding focused partnerships. In this paper we report on a consensus building exercise that was undertaken to construct an excellence assessment framework for translational cancer research in Europe. We used mixed methods to reach consensus: a systematic review of existing translational research models critically appraised for suitability in performance assessment of Cancer Centres; a survey among European stakeholders (researchers, clinicians, patient representatives and managers) to score a list of potential excellence criteria, a focus group with selected representatives of survey participants to review and rescore the excellence criteria; an expert group meeting to refine the list; an open validation round with stakeholders and a critical review of the emerging framework by an independent body: a committee formed by the European Academy of Cancer Sciences. The resulting excellence assessment framework has 18 criteria categorized in 6 themes. Each criterion has a number of questions/sub-criteria. Stakeholders favoured using qualitative excellence criteria to evaluate the translational research “process” rather than quantitative criteria or judging only the outputs. Examples of criteria include checking if the Centre has mechanisms that can be rated as excellent for: involvement of basic researchers and clinicians in translational research (quality of supervision and incentives provided to clinicians to do a PhD in translational research) and well designed clinical trials based on ground-breaking concepts (innovative patient stratification, substantial fraction of phase I/II trials, investigator-initiated trials). Critically, the framework supports reduced bureaucracy by building on existing European evaluation systems. The excellence framework is the product of an intense stakeholder consensus building exercise. It will be piloted during an expert peer review/site visit of at least three European Comprehensive Cancer Centres. The findings regarding content, governance and implementation can have relevance for other clinical and research fields.
BACKGROUND

Translational research can be defined as a complex process of transforming scientific discoveries, arising from laboratory, early clinical, or population studies, into clinical applications to reduce incidence, morbidity, and mortality [1]. On average, it takes over a decade to deliver patient benefits [2, 3]. After the 2007/09 financial crisis healthcare providers find it harder to justify funding for translational research in cancer but also other fields. The Stockholm Declaration recognises that creating a strong case for funding translational research in Europe, needs proof of excellent performance by Cancer Centres that are engaged in it [4]. Assessing excellence can stimulate continuous improvement in the way an organization perceives, plans, and performs translational research for the benefit of patients. It can also help to develop a network of excellent Centres that can focus their collaboration and share best practices through regular benchmarking.

In the last decade, we have begun discussing the idea of translational research in every field of medicine without ever clarifying exactly what this entails and how it should be assessed (Researcher)

To date no assessment framework has specifically focused on excellence along the entire continuum of translational research. Previous frameworks have focused on criteria/questions mainly for the self-guided assessment of the success of translational research organizations and/or projects [5] [6]. But there are a number of limitations to those frameworks: (i) not every success may necessarily be a sign of excellence; (ii) self-assessment is not sufficient to benchmark the performance of different Centres. Although success in translational research may be assessed by the organization itself, for the sake of credibility, excellence assessment requires an expert judgement (preferably at an international level) that is completely independent to the organization. To date, no formal framework exists that supports peer-reviewers to judge excellence in translational research; (iii) previous frameworks were informed by a few experts but did not engage key stakeholders in setting criteria. Achieving excellence in translational research relies on people from different disciplines and functions working together to improve overall performance. Consensus building helps achieve common understanding, commitment and collaboration and is recommended for criteria development [7].

This study provides an excellence assessment framework that was developed using a consensus building exercise with key stakeholder groups and experts from the European cancer community. The framework will be used to identify and assess excellent translational research in a number of European Comprehensive Cancer Centres (CCC’s) (combining basic, translational and clinical research and patient care activities). The framework will be thoroughly piloted with a number of CCC’s in 2013-2014.
METHODS

Consensus building took 18 months using several methods to fully engage stakeholder groups (See Figure 1). These included clinicians, researchers, senior management and patient representatives, representing around 70 European organizations including: CCC’s, Cancer Research Centres, Clinical Cancer Centres, Cancer Units, Patients Organizations and Cancer networks. Recruiting a small group of seven acknowledged experts to provide informed review and reflection at key points complemented this process. Development of the excellence assessment framework can be summarized as follows:

- **Literature reviews** – The European accreditation standards for CCC’s (from the Organization of European Cancer Institutes) and a report from the National Cancer Institute’s (USA) Translational Research Working Group on improving translational research performance [8] were taken as a starting point. A systematic literature review followed to identify and critically appraise translational research models most suitable for performance assessment of CCC’s [9]. The result was a list of 59 excellence criteria covering inputs, processes and outputs of basic, translational and clinical research & clinical care.

- **Stakeholder survey and focus group discussion** – This initial list of 59 criteria was scored by stakeholders (N=78) in an online survey. Evaluation of criteria by participants identified criteria as critical (if selected by more than 60% of the participants as important), optional
(if selected by 40-60% of the participants as important) or not relevant (if selected by less than 40% of the participants as important). 12 of the 59 criteria scored critical (e.g. early stage clinical trials; effective transfer of innovations from basic research to clinical practice); 36 optional (e.g. improved Quality of Life from innovations implemented; innovative prevention services) and 11 not relevant (e.g. number of surgical/paediatric/radiotherapeutical subspecialities; number of radiotherapy units). Quantitative criteria generally scored lower than qualitative criteria. Next, a focus group was assembled with a representative sample of survey participants (N=30). Participants clarified that the criteria that scored critical and optional should be considered when developing excellence criteria and the criteria that scored not relevant should be discarded with the exception of Health Technology Assessment.

- **Expert Group meeting** – The updated list was sent to an expert group (2 basic, 2 translational 2 clinical experts and 1 senior management expert). Their selection reflected more than 30 years of experience in basic, translational and/or clinical cancer research, prestigious awards and memberships in Oncology, significant current roles in European Comprehensive Cancer Centres and willingness to contribute to excellence framework development. The experts suggested a comparative review of the adapted list against recent external peer-reviewed evaluation reports from two CCC’s (see acknowledgements) to check if the criteria were reflected in these reports and to what extent additional criteria can be identified. The revised list was sent back to the experts who scrutinized each criterion, added specific points, and placed them under 10 categories that shaped an excellence assessment framework. The expert group stressed the importance of using expert peer-review when assessing the quality of translational research in combination with the assessment framework being developed.

- **Final validation by stakeholders** – The revised version of the assessment framework was sent to the same stakeholders who had previously participated in the consensus building exercise. The participants (N=34) made suggestions to improve criteria clarity in terms of being to the point, having short sentences, avoiding connectors such as “and”/“or” to make them less risky for misinterpretation. Ultimately, stakeholder feedback helped filter and refine the list down to 20 excellence criteria to assess excellence in translational research in CCC’s during a peer-review process and 6 additional criteria to be considered according to the preference of the CCC’s.

- **Critical review of excellence criteria by an external committee within an independent body, the European Academy of Cancer Sciences (EACS)** - The excellence criteria that evolved from the stakeholder consensus building were critically reviewed by a committee (see endnote for the composition) that has been formed in the EACS to give external input and govern the excellence assessment. This committee will be responsible for assessing excellence in CCC’s including a site visit/peer-review process. The committee
suggested minor re-structuring to the excellence criteria. They reduced the criteria to 18 core excellence criteria placed them in 6 themes and merged all additional criteria with the core criteria (see Table.1).

**Table. 1 Excellence framework for assessing translational cancer research**

<table>
<thead>
<tr>
<th>Excellence Criteria</th>
<th>Sub-criteria/questions to help peer-reviewers assess Cancer Centres</th>
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<tbody>
<tr>
<td><strong>Theme 1. Organizational Policies and Strategies</strong></td>
<td></td>
</tr>
<tr>
<td>Evidence for integration of Basic, Translational, and Clinical research with excellence in all areas</td>
<td>Effective communication between multidisciplinary teams?</td>
</tr>
<tr>
<td>Centre is treating patients in at least 3 major cancer types at an internationally competitive level</td>
<td>Sufficient patient volume?</td>
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<tr>
<td></td>
<td>Appropriate infrastructure?</td>
</tr>
<tr>
<td></td>
<td>Internationally recognized medical specialists?</td>
</tr>
<tr>
<td></td>
<td>Expertise level?</td>
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<tr>
<td>Mechanisms in place for continuous quality assurance.</td>
<td>Defined protocols for:</td>
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<tr>
<td></td>
<td>Output monitoring?</td>
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<td></td>
<td>Peer review programs?</td>
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<td></td>
<td>Ethical standards?</td>
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<td></td>
<td>Teaching good practices?</td>
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<td>Scientific misconduct provisions?</td>
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<tr>
<td><strong>Theme 2. People management</strong></td>
<td></td>
</tr>
<tr>
<td>Clear recruiting strategy to promote excellence</td>
<td>Internationally competitive recruiting?</td>
</tr>
<tr>
<td>Independence of PIs is clearly defined</td>
<td>Attention for gender issues?</td>
</tr>
<tr>
<td>The research program of PIs is regularly evaluated</td>
<td>Defined institutional support for PIs?</td>
</tr>
<tr>
<td></td>
<td>Incentives to improve leadership competencies in place?</td>
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<td></td>
<td>Scientific output?</td>
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<tr>
<td></td>
<td>Multidisciplinary activities?</td>
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<td></td>
<td>Regular site visits?</td>
</tr>
<tr>
<td>Mechanisms in place to involve basic researchers and clinicians in translational research</td>
<td>Active participation of clinicians in basic/translational research?</td>
</tr>
<tr>
<td></td>
<td>Institute clearly facilitates participation?</td>
</tr>
<tr>
<td></td>
<td>Interaction between clinicians and basic research is effectively stimulated?</td>
</tr>
<tr>
<td></td>
<td>Number of clinicians participating in MD-PhD programs during last 5 years?</td>
</tr>
<tr>
<td>Mechanisms to promote collaboration with research teams outside the Centre</td>
<td>Number and quality of joint output?</td>
</tr>
<tr>
<td></td>
<td>Partners are internationally leading?</td>
</tr>
</tbody>
</table>
Theme 3. Research infrastructure/Competencies

Centre has internationally competitive facilities and proven forefront expertise in a substantial number of key areas.

Prominence in number of the following areas:
- Identifying, validating, and designing rational Rx strategies directed at key molecular cancer targets?
- Surgery, innovative operation theaters.
- Radiotherapy infrastructure?
- Next generation sequencing and other "omics"?
- Bioinformatics and computational biology (both infrastructure and innovation)
- Robotic screening (drugs, shRNA, siRNA)?
- Advanced microscopy facilities (e.g. confocal, lifetime imaging, flow cytometry etc)?
- Clinical imaging and innovative modalities?
- Prominence in area of animal model systems?
- State of the art biobank with clinical informatics linked with genomic and other data?
- Patient registry with strong biostatistical support?
- PK, PD monitoring phase 1/2 clinical trials?
- Pharmaceutical production/formulation?
- Production biologicals for use in patients?
- Molecular pathology?
- Good interface with chemistry, physics, engineering, mathematics etc?
- Population studies and resources such as cohorts?
- Health economics; primary care links; early detection programmes?
- Technology Transfer support?
- Other?

Theme 4. Clinical (trial) management

Clinical trials are well designed

Number of innovative aspects:
- Has it performed groundbreaking? Proof of Concept trials?
  Were these based on molecular tumor parameters?
- Innovative stratification of patients (adaptive trial design)?
- Investigator-initiated trials?
- First in man?
- Substantial fraction of phase I/II trials?
- Advanced modeling (e.g. PDX)?

Centre utilizes an internal review system to select for the most innovative and promising protocols.

Evidence that this has lead to innovative trials over a 5-year period?

Patients enrolled in clinical trials

A substantial fraction (>10%) of patients is enrolled in phase I/II trials?

Continuous improvement of the quality of patient care

Appropriate monitoring with patient participation in the process?

Outcome is at forefront and based on patient mix treated

Proper benchmarking?

Theme 5. Internationally recognized excellence

Research has resulted in changes in clinical thinking and practice – emphasis on physician investigators.

- Examples to be listed.
- Best in class young and mid career physician-investigator faculty recruited and retained by the Centre;
  Is the Centre training and recruiting ever better physician/oncologist-investigators?
The Centre has an international reputation ranking it in the top 10% segment Evident from:
- Output related to size and expenditure based on independent benchmarking performed within last 3 years.
- Substantial impact is evident in all three research areas (basic, translational, clinical).
- High rating by international peers
- Prestigious collaborations
- Accreditation status
- National/international awards
- Prestigious competitive grants obtained

Theme 6. Financial expertise

Efficient financial management and support Appropriate support for managing external grants and clinical research projects including contracts with industry.

A substantial fraction of income is obtained through funding bodies that employ a critical review process. Objective success in open competition for grants.

RESULTS

The consensus building exercise clearly identified a need to assess excellence in translational research based on qualitative rather than quantitative criteria. Stakeholders and experts felt that whilst for instance state-of-the-art infrastructure is important to perform excellent translational research, the assessment of excellence itself should focus more on how efficiently they are being used by the organization and the quality of their outputs.

*The numbers of services/units or treatments required to be assessed as “Excellent” appear to me to be somewhat arbitrary. Quality rather than quantity should prevail.* (Researcher)

There was unanimous support for the need to minimize the bureaucracy of the excellence assessment and to have an external expert-based governance system that is independent to the organization being assessed in order to maximize transparency. The experts suggested that reports regularly prepared by the CCC’s for existing national and/or European level assessment programmes should be first assessed against the excellence criteria (Table.1). These reports contain sufficient qualitative and especially quantitative data and only data missing in such reports needs collecting. A European excellence assessment framework can only be established if the procedure exceeds the current national accreditation efforts within the European Union (EU) member states and carries sufficient credibility.

*CCC's in the European Union member states already go through different expert based peer-reviewed national evaluations, how are we going to justify the need for and reduce the bureaucracy of a European excellence assessment?* (Experts)
It was emphasised that assessing the translational research “process” along the entire continuum from basic research upto clinical practice and back is as critical as assessing inputs and especially outputs. However, it was decided that the assessment does not have to encompass population based outcomes because that stage goes beyond the scope of most European CCC’s and is the responsibility of different authorities within the European Union member states. Furthermore, it has a very long lagtime and is influenced by several non-institutional related factors which makes it difficult to access data on time. A focus on organizational level assessment was preferred. However, for certain issues, such as those related to prevention and early detection, translational research should extend its scope beyond current organizational boundaries to optimize its relevance on population level. Stakeholders can be made aware of this through relevant contacts with Europe-wide organizations such as the European Public Health Alliance (EPHA) [10] who act as gatekeepers to the national and regional authorities across the EU-28 member states.

*It is important to establish an excellence assessment, which helps assess the highest levels of translational research quality through the innovation, productivity and efficiency of an organization (Manager)*

Another example of careful qualitative assessment instead of quantitative data collection is the use of the scientific infrastructure that CCC’s offer to other institutions. Such criteria cannot be imposed on all CCC’s as the nature of demand depends on specific regional/national contexts.

Of course, an excellent Centre should be willing to make these facilities available if asked for on a collaborative basis. But at my Centre, while we make some of these facilities available across the rest of city, we have not in the past five years had any requests to make these facilities available to other Centres in the nation because these Centres have their own access to these facilities (Manager)

Finally, excellence criteria on patient-related aspects were perceived to be specifically important.

*We must not only look at efficacy and safety in clinical study setting but even more to the value in the everyday practice of products/technologies/therapies (Patient representative)*
DISCUSSION

By undertaking a consensus-building exercise to develop an excellence assessment framework it was clear that while consensus can exist at a general level, some disagreement is unavoidable due to the different backgrounds, experiences and interests of the stakeholder groups. For instance, clinicians and patient representatives felt that excellence assessment does not need to involve basic research and should focus more on clinical care, but basic researchers and managers felt that unless basic research is included, the entire continuum of translational research cannot be fully assessed. Furthermore, the question whether the right stakeholders and experts are involved was carefully addressed at each stage of the criteria development process. For each excellence criterion, we considered having consensus when 60% or more of the stakeholders that participated agreed and we did not consider single votes by an individual stakeholder as sufficient. However, we cannot exclude that some perspectives may have been left out that might still show to be critical. Excellence assessment requires a degree of flexibility, which is possible to implement in a transparent manner by using an independent peer review panel. While a common format is desirable, rigid formats may be unsuitable for organizations operating in different health systems and can introduce significant bureaucracy.

Qualitative excellence criteria increase the challenge for objective rating. A flexible and meaningful rating system is therefore needed. For the final decision, strengths and weaknesses across all criteria as well as individual criterion should be considered with an agreed minimum score on each criterion. However, to what extent should there be flexibility in accommodating the limitations imposed on individual CCC’s because they have to operate in different European health systems? Regarding health care, the EU operates on a subsidiarity principle. It means that all clinical and some research fields operate within nationally set frameworks. However, transnational cooperation is valued to share knowledge and improve performance and this brings some specific rules into play. Most EU member states have their competitive national level assessments but none would be easily accepted for use in another member state. Instead, considering best practices from across all member states in identifying and assessing excellence in translational research is far more transparent and can give wider acceptance of such assessments across the EU. Essentially, it is about an individual Centre making its own case of why it deserves to be designated as excellent given its own operating environment. And then the peer-reviewers can check whether the case made by the Centre is valid during a site visit. This will be done with the help of the excellence criteria (Table 1) to some extent but experts should also be prepared to come across areas of excellence that the Centre may have forgotten to mention during its application for excellence designation. A related issue raised by some experts was about discarding or “killing” insufficiently promising translational research projects, because of insufficient innovation, a low chance of clinical implementation or probably
very unfavourable clinical effectiveness. Of course, identifying those is a risky matter, as it is often very difficult to predict the actual clinical potential in early stages of research. Nevertheless and increasingly, early stage Health Technology Assessment techniques are being developed and applied to aid decision makers to decide about further research investments or researchers to set the specifics/demands that the research and development process should meet [11]. One should consider looking into the availability of mechanisms to assist early stage decision-making on adequate translational research progress. It seems advisable to develop specific knowledge and development of a norm or reference material on this topic.

“Research is also a matter of intuition, intellectual flexibility and aptitude to identify opportunities. Excellence assessment must go beyond putting a tick against criteria and needs to consider the local context in which institutions operate.” (Manager)

For example, for high impact of publications it was hard to establish a minimum level because it varies greatly between the different disciplines within Oncology and among CCC’s across the member states of the European Union. However, the average scores for each discipline can still be considered to make this criterion inclusive. Further, a range of bibliometric index other than just impact factors should be considered i.e. citation factor, cumulative impact factor and the quality and impact of individual publications to be rigorously judged by an expert peer review team.

“One publication that shows the 100% cure of a cancer is enough. Ten publications of one-month prolongation of survival mean nothing.” (Clinician)

In Europe, the current excellence assessment primarily intends to evaluate team science due to the multifaceted nature of translational research where collaboration of different disciplines is critical to its success. The criteria that have emerged through the consensus building exercise, support this statement for example by focusing on multidisciplinary team collaboration, communication and joint publication efforts, participation of different department staff in various research projects and the outputs. A specific product of work may involve biologists, medical chemists, pharmacologists, imaging physicists and clinicians. Thus it can be difficult to identify the exact contributions made by each single member of the team and this could raise issues when individuals are evaluated for tenure or promotions etc. However, the consensus building exercise revealed that also monitoring individual efforts to some extent is needed for excellence.

This could help promote a competitive attitude among researchers within and outside a Centre and help identify and reward excellent contributions of specific researchers to science that might otherwise go undetected. The individual efforts will be evaluated taking into account a range of factors: the quality of scientific outputs by clinicians pursuing a
PhD in translational research; the quality of the research programs of PI’s and if they are regularly evaluated; prestigious awards, discoveries and memberships attributed to specific individuals from the Centre; investigator-initiated trials and their success rate etc. Currently, national assessment programs within some EU member states conduct these evaluations but there is no formally agreed assessment on European level. Finally, this consensus building exercise revealed a need to get some obvious basics right that might otherwise be ignored. For example, to ensure that the criteria are both meaningful and easily understood by organizations, words such as “high”, “well”, “minimum”, “significant”, “cutting-edge”, “state-of-the-art”, “substantial” etc. unless carefully explained can be easily misinterpreted by stakeholders. Stakeholders accepted to start developing an excellence framework with these words/definitions but suggested refining them based on pilots.

Piloting of the excellence framework

A committee consisting of internationally respected and renowned experts in Oncology will govern the excellence assessment process. In the EU, members of the European Academy of Cancer Sciences satisfy such requirements, and international experts (from the National Cancer Institute, USA and Accreditation Canada) will be invited to join the committee and the official peer review team. A Centre that applies to be assessed as excellent should provide documentation to the committee. This will include recent external peer reviewed evaluation reports in English that the Centre has produced for national and/or international evaluations in the past 3 years, covering basic, translational and clinical areas with specific achievements in translating innovations from bench to bedside and/or vice versa. Further documentation may be requested if the initial material is found insufficient. After an initial screening of the documents against excellence criteria (Table.1) the committee will decide if the Centre qualifies for site visit/peer review in which again the excellence criteria will be used to evaluate Centres. A minimum of three European CCC’s will pilot the excellence framework.

CONCLUSION

Assessing excellence requires a mix of quantitative and qualitative criteria retrievable through different data sources. But we need to recognise that the consensus building exercise showed strong support for qualitative criteria. This is because it will build on existing evaluation systems across the EU and other international systems (e.g. US, Canada) that already provide the necessary breadth of quantitative data. The assessment framework that we have developed will need to be thoroughly tested with European CCC’s to prove that it can help identify excellence in translational research. Although, the framework was primarily developed for Oncology, it can probably be translated to other research and/or
clinical fields after rigorous validation. Allocating governance to an external entity that has credibility and is independent of the organizations being assessed is a key ingredient. Finally, the success of the assessments will depend on minimized bureaucracy and maximized transparency and accountability during the evaluation process.

Endnote

The composition of the committee formed in the European Academy of Cancer Sciences is: Prof. Dr. Anton Berns (Senior Group Leader Molecular Genetics, Netherlands Cancer Institute), Prof. Dr. David M. Livingston (Chairman, Executive Committee for Research, Dana-Farber Cancer Institute and Emil Frei Professor of Genetics and Medicine, Harvard Medical School), Prof. Dr. Daniel Louvard (Director of Research Centre at Institut Curie France), and Prof. Sir Bruce Ponder (Head of Department, Oncology at University of Cambridge, UK).

Acknowledgement

This research was funded by the European Commission FP7 programme as part of the Eurocan Platform project. Contributions by the following are valued: (i) all stakeholders and experts from the Eurocan Platform, the Organization of European Cancer Institutes (OECI) and the European Cancer Patient Coalition (ii) the Netherlands Cancer Institute and the Oslo University Hospital, Norway for sharing external peer-reviewed national evaluation reports by The Dutch Ministry of Health, Welfare and Sport-Dutch Cancer Society (2004-2008) and the Research Council of Norway, Norwegian Ministry of Education & Research (2010-2011), respectively (iii) the OECI Accreditation Standards.
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Excellent Translational Research in Oncology: a Journey
Towards Better Clinical Outcomes

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Submitted
ABSTRACT

Comprehensive Cancer Centres (CCCs) serve as critical drivers for improving cancer survival. In Europe, we have developed an Excellence Designation System (EDS) consisting of criteria to assess “excellence” of CCCs in translational research (bench to bedside and back), with the expectation that many European CCCs will aspire to this status.

Key messages
Assessing excellence of translational research is essential to improving its performance so that the time lag in bringing results of research to practice will be reduced.
We have developed and piloted a set of excellence criteria that can help identify and designate Comprehensive Cancer Centres that perform excellent translational research. The criteria include assessing the organizational strategy for translational research; the depth of research programmes from bench to bedside and back; team science; commitment to collaboration; shared resources; commitment to develop and maintain state-of-the-art infrastructure; utilization of bio specimen banks; staff education and training in translational research; hypothesis-driven and hypothesis-generating studies; critical patient mass; investment in high-risk/high-gain research projects; ability to acquire and utilise available funding; and the involvement of patient advisory committees.
Assessment needs to be flexible because excellent translational research can be found also in areas that are outside the scope of the assessment and/or the “typical” definition of translational research. The assessment framework was piloted in several cancer centres in Europe and is ready to be implemented. We expect that fine-tuning during its implementation will further improve the procedure and also generate added value for translational research at large.
There is a growing awareness of the importance of identifying conditions that can contribute to translational cancer research success. A need to improve performance is also a priority, in order to reduce the time taken to translate successful innovations from the laboratory into the clinic, and to take observations made in clinical studies back to the lab for further investigation or for the discovery of new biology. The increasing cancer burden and the fact that the performance of European cancer research could be considerably improved were the underlying drives for the EU Sixth Frame Work Programme (FP6) to fund clinical research for the first time.

The Eurocan+Plus project, funded in October 2005 (FP6), carried out a comprehensive analysis of European cancer research to identify barriers that hampered collaboration between various stakeholders, nationally as well as between European countries. One of the main conclusions of this project was the need to strengthen the collaboration between cancer research centres in order to achieve critical mass and share the infrastructure necessary for innovative translational cancer research. The concept of a Comprehensive Cancer Centre (CCC) was considered of great importance, being the only organisational form in which cancer treatment and care are closely integrated with research and education and, therefore, optimal for translational research.

As a follow-up to the Eurocan+Plus project, in 2011, the European Commission (EC) funded the EurocanPlatform, which brings together 23 European cancer research centres and 5 cancer organizations to structure translational cancer research. The long-term goal of this platform is to create a sustainable translational cancer research platform with the critical mass of expertise, resources, infrastructures, and patient numbers that are needed to facilitate innovation and improve performance in all areas of cancer research, particularly translational research. Recently, six EurocanPlatform centres established Cancer Core Europe (CCE) as a significant first step towards establishing such platform.

As requested by the EC, a work package was dedicated to developing a methodology to quality assure and designate “CCCs of Excellence” that could qualify for future European funding. Developing a methodology for identifying and assessing CCCs of Excellence in translational research was one of its primary goals. Towards this aim, we previously reported the steps that were taken to develop a draft Excellence Designation System (EDS). This included evidence from current literature and a European stakeholder consensus exercise, covering a 2-year (2011-2013) period and involving researchers, managers, clinicians and patient representatives from cancer institutions across Europe. Now, we describe a final EDS that has been developed in collaboration between the EurocanPlatform and the European Academy of Cancer Sciences (EACS) and that has been piloted with three European CCCs. Its relevance for CCCs and translational research is discussed.

Translational research has rapidly evolved in the past decade and numerous definitions currently exist. However, only few cover the complete cancer research continuum from...
bench to bedside and vice versa. One definition that does, was put forward by the staff of the National Cancer Institute (NCI) while working with Dr. Richard Klausner, its former Director:

“Translational research uses knowledge of human biology to develop and test the feasibility of cancer-relevant interventions in humans OR determines the biological basis for observations made in individuals with cancer or in populations at risk for cancer. The term “interventions” is used in its broadest sense to include molecular assays, imaging techniques, drugs, biological agents, and/or other methodologies applicable to the prevention, early detection, diagnosis, prognosis, and/or treatment of cancer.”

We present this perspective in three parts: (i) an introduction to the EDS that we piloted with 3 European CCCs, in September 2014 at Helsinki University Central Hospital Cancer Center, Cambridge Cancer Centre and The Netherlands Cancer Institute; (ii) a summary of the pilot results (see Table 1) as well as the experiences of CCCs and the peer-reviewers from taking part in the pilot; and (iii) a discussion of the relevance of the system for translational oncology and an overall conclusion.

**Excellence Designation System (EDS) in translational research for CCCs**

European CCCs already go through several assessments at the national level. In addition, they undergo European/international assessments such as the accreditation and designation system developed by the Organization of European Cancer Institutes (OECI). Hence, it was felt that the EDS should not reinvent the wheel nor add bureaucracy by creating a totally new assessment system. So, it takes the existing national/international assessments as a basis for developing and testing EDS. The assessments were conducted with impartial evaluation involving independent experts using existing reports available in English and not older than 5 years. This allowed the reviewers to check the validity, feasibility and relevance of the excellence criteria, and to formulate questions (see supplementary file) to be addressed at the on-site meetings.

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1. Following the pilot, a roundtable meeting was held in Amsterdam 05-09-2014 where the final EDS was scrutinised with peer-reviewers who took part in the EDS pilot as well as these experts: Prof. Anton Berns PhD, Prof. Sir Bruce Ponder PhD, FRCP, Henri van Luenen PhD, Femke Boomsma M.A, Prof. John F. Smyth MD, FRCP, Tuula Helander PhD, Prof. Julio Celis PhD, Prof. Olivier Delattre PhD, Prof. Ulrik Ringborg PhD, and Prof. Wim van Harten MD, PhD. In December 2014, the final set of excellence criteria was sent to 199 fellows of the EACS to critically appraise the EDS. A positive reaction was obtained.

2. The peer-reviewers who piloted the EDS are: Prof. David Livingston MD, PhD (Dana-Farber/Harvard Cancer Center, USA), Toby T. Hecht PhD (Translational Research Program, National Cancer Institute, USA), Prof. Robert Bristow MD, PhD (Princess Margaret Cancer Center, Canada), and Prof. Thomas Tursz MD, PhD (Honorary Director Institut Gustave Roussy, France). The review team was selected by the EACS.
1. Articulation of a vision of the Cancer Centre’s philosophy, scientific directions, and goals for the next 5 and 10 years; and which projects and translational science studies are expected to change the paradigms of clinical oncology.

2. Demonstration (with organisational data and publications) of at least three multidisciplinary programmes that are being pursued in great depth from basic discovery through pre-clinical development to clinical studies. These may be disease or discipline-based but must address major unanswered questions in the field and unmet clinical needs.

3. Experience with and commitment to a team science approach with basic and more applied scientists working together to achieve translational goals.

4. Tangible evidence of a commitment to collaboration both within the Cancer Centre’s own country and internationally, as a single Centre usually will be less effective in developing and testing new approaches that lead to changes in clinical practice.

5. Establishment of shared resource facilities (Cores) to support the research Programmes.

6. National and international peer review systems (including evaluation by funding and government bodies) assess the Centre on a regular basis to help maintain and improve the overall quality of the programmes, leadership, shared facilities (e.g. biospecimen banks) and research/clinical studies.

7. Commitment to a program of training of new translational scientists and re-training of established basic, clinical, or population scientists who wish to redirect their careers into translational cancer research.

8. Establishment of an up-to-date fully and clinically annotated biospecimen bank (or banks) with an information technology system or network for tracking specimens and linkage to clinical outcome and follow-up data. To optimize the impact of the bank, specimens should be shared with other researchers or collaborators.

9. Ability and commitment to perform hypothesis-driven and hypothesis-generating clinical and population studies.

10. Demonstration of a sufficient patient population to support bench to bedside studies in all the programmatic areas cited. Smaller cancer units should collaborate in their clinical trials in an effort to reach large enough numbers of patients to render the outcomes of these studies valid and effective.

11. Commitment to funding high-risk/high-reward projects to seize new and exciting research opportunities.
12. A detailed demonstration of the ongoing ability and a clearly articulated intention to 
leverage funding and/or resources obtained as a result of an “excellent” designation.

13. Involvement of patient advocates in advisory committees.

Pilot experience of the Excellence Designation System in 3 European CCCs

Participants in the piloted CCCs, as well as the peer-reviewers/experts, felt that the excellence criteria for CCCs in translational research were very helpful in identifying areas of existing excellence as well as areas for further improvement. Below we highlight relevant quotes from the pilot participants.

“For us, to be designated as an Excellent CCC should not be a mere honorific or demographic distinction, but should, above all, induce and result in new translational research missions, roles, and high value/high clinical impact discoveries for such institutes” Peer Reviewers

“There is no need to be anxious about the detailed Excellence Designation System even at the smaller and younger institutes. Yes, it will likely identify weaknesses. True, your institute may not shine as brightly yet as some older institutes. But detection of the weaknesses may allow improvement, and identification of the strengths may allow networking with the best cancer centres in Europe.” Helsinki University Central Hospital Cancer Center

“Preparing for the pilot of European CCCs in translational research helped us identify our strengths and weaknesses and where translational research can contribute to better treatment and care for cancer patients. The interaction with and the feedback from the site visit committee were essential and highly appreciated in this process. The pilot has stimulated internal discussion, which will lead to further strengthening of our translational cancer research programme. Other Centres can benefit from the best practices being identified in this process.” Cambridge Cancer Centre

“A high level review such as this (but without a large burden of paperwork) is useful in catalyzing discussion among colleagues as to the priorities and performance of the Centre, and identifying things that need attention. The discussions with the panel were lively and to the point; they reinforced some things we knew about but should attend to, and highlighted new ones. The pilot was well designed to elicit characteristics and metrics of the Centre that are truly relevant and a reflection of excellence, rather than the more usual measures of volume without examination of excellence. It will create a network of centres where ideas and scientists can be shared making it ideal for high quality collaborative science” The Netherlands Cancer Institute
How can we ensure that these criteria are suitable for identifying and improving excellence in translational cancer research?

The EDS was developed based on multiple sources of evidence: existing literature; expert opinion from inside and outside Europe (from certain National Cancer Institute-designated Comprehensive Cancer Centres in the US and similar institutions in Canada and from the Cancer Research UK assessment process); stakeholder views (researchers, clinicians, managers and patient representatives across Europe) through a survey and a focus group discussion; as well as reports of existing national assessments for CCCs in Europe. To our knowledge, this is the first systematic attempt to exclusively focus on identifying and designating excellent performance of CCCs in translational cancer research. We used available evidence to develop and pilot these criteria. The site visitors, the expert team and the involved institutions were unanimous in their opinion that excellent performance can be identified in CCCs using the EDS.

We feel that a flexible approach is needed to identify and assess excellence that may also fall outside the scope of the excellence criteria used. All piloted CCCs shared a strong emphasis on the physician-scientists career. Similarly, increasing the quality and number of academic trials and making better use of different features of Information Technology were common opportunities in all CCCs (see Table 1 and Figure 1). Distinctive examples of strengths and opportunities were also identified.

Outputs such as publication impact and citation are certainly important. In our systematic literature review\(^\text{13}\) we found process-related criteria to also be suitable for performance assessment. The EDS focuses on evaluating excellence based on key inputs (e.g. facilities and human/financial resources), outputs (e.g. publications) and outcomes (e.g. effect of innovations in addressing unmet clinical needs and the patient/population impact) but also on evaluating and improving the process of translational research (e.g. creating a suitable environment for conducting translational research).

Aristotle said: “We are what we repeatedly do. Excellence, then, is not an act, but a habit”. Thus, excellent performance of CCCs in translational research should be a habit, built into the mind-sets of the CCCs rather than a one-time qualifying act for an assessment. Experts strongly believe that CCCs should have a sustainable organisational culture of excellence across the continuum of basic research, development, education and patient care and connect all individual parts in order to succeed. This starts with having a strong organisational vision for translational research.
Figure 1. Examples of excellence identified in the European CCCs
<table>
<thead>
<tr>
<th>Dimensions</th>
<th>Helsinki University Central Hospital Cancer Center</th>
<th>The Netherlands Cancer Institute</th>
<th>Cambridge Cancer Centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot designation status</td>
<td>Actual potential for excellence</td>
<td>Excellent</td>
<td>Excellent</td>
</tr>
<tr>
<td>-Small country with excellent global survival statistics</td>
<td>-Extraordinary examples of deep translational science based on mechanistic basic science in a continuum to clinical care and back again particularly regarding resistance mechanisms</td>
<td>-Extraordinary conduit between basic, translational and clinical trials and back again to the laboratory</td>
<td></td>
</tr>
<tr>
<td>-Attracting the best people in the country</td>
<td>-26% of patients on clinical trials</td>
<td>-Superb leadership in bringing in basic science departments within the virtual cancer centre</td>
<td></td>
</tr>
<tr>
<td>-Strong position in Nordic research</td>
<td>-Strong investigator-driven clinical trials with biomarkers</td>
<td>-Exciting primary basic research leading to clinical trials (BET, DNA repair) and clinically driven projects with important implications for outcome-Barrett’s and endoscopy studies and Breast</td>
<td></td>
</tr>
<tr>
<td>-Outstanding population-based registry</td>
<td>-Three programs developing based on a decision by the Translational Research Board: immunotherapy, image-guided radiation therapy, precision medicine</td>
<td>-Solid approach to innovation and creative collaborations with pump priming projects, research sessions for National Health Services staff and director’s funds</td>
<td></td>
</tr>
<tr>
<td>-Young centre with opportunity to embrace rapidly evolving technologies and huge potential in precision medicine</td>
<td>-The model of twinning (pairing basic and clinical scientists) is successful, based on the projects, the fact that there are 39 MD-PhD students and 200 PhD students – provides an exciting model and a third of publications are generated from this mechanism</td>
<td>-Impressive backing of clinician-scientist careers and input to oncology research across training schemes—the trainees were committed to hypothesis-based clinical trials and have clinical support and protected time</td>
<td></td>
</tr>
<tr>
<td>-General direction—open to change, translational research and international collaborations</td>
<td>-Shared labs, monthly staff meetings, clinical rotations for PhDs</td>
<td>-External networking within European partners with up to 70,000 new patients per year for trials</td>
<td></td>
</tr>
<tr>
<td>-Strong individual leaders in research (angiogenesis, precision medicine, hematology)</td>
<td>-Open, strong and visionary new leadership for the institute and candid views regarding ways to improve the program</td>
<td>-First approach to network within major UK Cancer Centres with harmonization of trial and e-health infrastructure</td>
<td></td>
</tr>
<tr>
<td>-Bench to bedside &amp; back programs</td>
<td>-National collaborations within the context of Centre for Personalized Cancer Treatment are exciting and lead to further opportunities for novel clinical trials</td>
<td>-Impressive 16-50% entry into trials across departments and all histology</td>
<td></td>
</tr>
<tr>
<td>-Evidence of research reducing mortality</td>
<td>-Also allows for the development of biobanking and IT</td>
<td></td>
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</table>
Opportunities for further excellence

- Biobanking – annotation and real time acquisition of samples – priority for sites.
- New money for high risk/high gain innovative collaborations in house: has infrastructure but not resources for novel collaborations; integrated neurology; immunobiology; obesity should be integrated in cancer
- Improved relationship with university regarding discovery: protect intellectual property
- Combination drugs testing
- More academic trials (proof of concept studies, First in Human trials, testing drug resistance), phase I-II Clinical trials network/opportunity to become a national early phase center – need improved accrual –

Biomarker driven trials

- Selection of 3 cancer types; use of 3D cultures, patient derived xenografts, genomics; precision medicine (Hematologic oncology, Colorectal, Breast)
- Query lack of clinical scientist translational training
- Regular scientific advisory board meetings (monitoring/closing/opening trials)
- Strategic vision of a global architecture of an integrated information system
- Strong vision statement taking into account the unique strengths/needs of the cancer centre
- Explicit support from the clinical research/medical oncology
- Establishment of a foundation to support translational work (transformative donor)

- Increasing the time commitment to research for clinician-scientists beyond 50%. Recognize it is a priority; strong thrust in molecular pathology
- Efforts to engage basic cancer researchers in translational cancer research where this is relevant and possible. This should take into account that basic research creates the foundation on which to build translational research.
- Continue strong, new biological studies combining radiotherapy research (especially image guided radiation therapy) with basic and translational research fields such as targeted agents, DNA repair, immunotherapy and mechanistic studies regarding tissue side effects.
- Transparent and branding approach (used by Foundation) to practice-changing publications (i.e. develop metrics of intramural and extramural interest)
- IT systems need to be operationalized to prospective collections and auditing and working out the bugs in next year

- Great expectations for national and international leadership in cancer research driving to the clinic
- Unique opportunities from strengths (e.g. marry genomics to imaging with respect to tumour heterogeneity)
- Opportunities to marry strong immunobiology to immunotherapy
- 15% trials were the biology was discovered by the cancer center (30% of investigator initiated) – should be improved
- Consider resources for increased control over robust biomarkers leading to increased patient stratification for trials (e.g. using patient derived xenografts models to test the DNA repair inhibiting studies)
- Have an integrated structure to supervise all the clinical trials in terms of scientific interest, feasibility, costs and decide opening/follow-up and closing if low/no patient accrual and/or if question is not relevant
- Ratio between academia and industry initiated trials is still not clear. Mostly focused on discovery done here (Being original is important) can be more! Figure should increase.

- Opportunities for IT and e-hospital in which there in direct links to genomics and imaging and outcome databases across all histology (in addition to breast)
CONCLUSION

The positive experience of the piloted European CCCs as well as the acceptance of these excellence criteria among the EACS membership and key international experts in oncology cause us to believe that the EDS is sufficiently validated to be implemented. We have applied available knowledge, existing evidence and past experience of experts to develop and pilot this system. Our experience has already shown that assessment of translational research excellence can deliver positive impacts and added value to future developments in oncology. We conclude that this system is ready to be implemented through European and international excellence initiatives in translational cancer research. However, it will need close monitoring to be further adapted to cover different approaches in developing and sustaining excellence during and beyond implementation.
REFERENCES


5. EurocanPlatform http://eurocanplatform.eu/


SUPPLEMENTARY MATERIAL

Related questions for each criterion are placed in boxes 1-13. Reviewers asked questions to each CCC depending on the clarity and depth of evidence visible in the submitted documents. We provide a rationale for each criterion based on experience obtained from the pilot. Additional references used in the rationale for criterion are provided at the end of the supplementary material section.

1. Articulation of a vision of the Cancer Centre’s philosophy, scientific directions, and goals for the next 5 and 10 years; and which projects and translational science studies are expected to change the paradigms of clinical oncology.

   **Box 1 Questions**

   - Describe your vision for the next 5 years that will change the paradigms of clinical oncology.
   
   - Describe your vision for the next 10 years that will change the paradigms of clinical oncology especially in view of the expected collaborative funding to be obtained as a consequence of being designated an Excellent CCC in Europe.
   
   - Is there an internal and/or external scientific advisory board? List the individuals in your scientific advisory board. Please describe why they have been chosen for inclusion in your board and what responsibilities they will have in shaping the 5 and 10 year vision of your Centre. Also describe how often the advisory board meets and provides specific examples of advice given by the advisory board in the past three years.
   
   - Is there a committee that regularly meets to help maintain the overall standards of the programmes, leadership, shared facilities (e.g. bio specimen banks) and clinical studies?
   
   - Provide proof from the past 10 years that the absence/retirement/transfer of excellent leaders (either research clinical care or management) from your Centre has not affected output of your research and/or the overall operation of your Centre. Please provide examples of publications, awards, staff-enthusiasm that shows that excellence is uninterrupted.

   **Rationale for criterion:** Clear vision, policies and an action plan are vital to maintain a high standard and promote improvements in an organization as part of an organisational strategy for translational research. It should be part of a tangible culture, part of its history and future plans.

2. Demonstration (with organisational data and publications) of at least three multidisciplinary programmes that are being pursued in great depth from basic discovery through pre-clinical development to clinical studies. These may be disease
or discipline-based but must address major unanswered questions in the field and unmet clinical needs.

**Box 2 Questions**

- **Give examples of at least 3 cancer types where you have a comprehensive research programme (basic research to the clinic & back). Explain how the focus of your research in the 3 tumour types chosen reflects the unique patient distribution/population needs (including cancer prevention) within the following levels of your operating environment: regional, national and European.**

- **For each of the 3 cancer types state the following:**
  - Patient population
  - Scientific expertise
  - Internationally recognized experts (list your basic/translational/clinical specialists)

- **Provide examples of at least 3 clinical trials (within the past 5 years) that were initiated in your clinic that were based on the basic research discoveries at your centre.**
  - State how many academia-led trials and how many pharma-led trials are ongoing (and have been completed in the past 5 years) in each of these 3 cancer types?
  - What is the patient accrual for clinical trials? Mention at least for each of the 3 cancer types.
  - Describe your future plans for research in these 3 cancer types with regard to greatest possible impact in the practice of oncology.

- **Give examples (if available) as to how the clinical studies were reverse-translated into the laboratory to feed further mechanistic study or biomarker development.**

- **How does your Centre deal with patient comorbidities in clinical trials?**

- **Give examples to show how you deal with clinical trials in which patient accrual is slow. Who decides to stop or continue these trials and/or to relocate resources from these trials to other areas?**
  - How many trials are initiated on the basis of experimental data or of innovative hypotheses generated in the Centre?

- **What proportion of the research programmes funded by your Centre is cancer relevant?**

- **Do you include molecular pathology in addition to histological analysis in the three tumour types? Give examples.**

- **Describe your novel/innovative research using next generation sequencing.**

- **Give examples of innovative use of genomics and other “omics” in research/clinical settings.**

- **Give examples of your excellent research in immunotherapy/radiotherapy/surgery.**

**Rationale for criterion:** Programmes with great depth from bench to bedside and back- A Centre should focus and/or specialize in several tumours. This may include rare cancers. However, there should be at least 3 programmes that go from bench to bedside and back. Proof should be available that “home grown” innovations in those programmes are applied within the Centre. These programmes should address local, regional, national and European population clinical needs.
3. Experience with and commitment to a team science approach with basic and more applied scientists working together to achieve translational goals.

**Box 3 Questions**

- Provide specific examples of how different research teams/investigators that represent basic/translational/clinical research at your Centre work together effectively. The examples should give us an idea of excellent collaboration/communication between those staff members, e.g. basic and clinical scientists planning individual projects, brainstorm sessions, nature/scope/frequency of meetings.

- What are your future plans (in the next 3-5 years) to further improve the interaction between these team members?

- How are the clinicians trained in basic research and how are basic researchers trained to understand translational/clinical research at your Centre? Specify the number of clinicians already trained/currently in training in basic research? Also specify the number of basic researchers already trained/currently in training in translational research?

translational research. The centre needs to foster and catalyse interactions between different disciplines.

4. Tangible evidence of a commitment to collaboration both within the Cancer Centre’s own country and internationally, as a single Centre usually will be less effective in developing and testing new approaches that lead to changes in clinical practice.

**Rationale for criterion:** There is a need for critical mass, e.g. to speed up patient accrual especially in view of patient stratification based on genomic subtyping of tumours and specific and unique predictive biomarkers that are being developed. This complexity calls for stronger collaboration between excellent CCCs, especially in the area of rare tumours.

5. Establishment of shared resource facilities (Cores) to support the research programmes.

**Box 5 Questions**

- Specify any formal agreements with one or more universities concerning the use of shared resources and shared funding of resources.

- Give specific examples of the ease of researchers from different research programmes at your Centre to gain access to shared resources (Cores), e.g. do researchers from certain research groups have more access than the others? Are there written guidelines/policy to facilitate timely, efficient and equal access?

**Rationale for criterion:** The speed with which technology is being developed and the knowledge required to run state-of-the-art core facilities on an excellent level, makes it almost impossible for individual CCCs to cover all areas of technological innovation. This requires effective collaborations between CCCs, other academic institutions and industry.

6. National and international peer review systems (including evaluation by funding and government bodies) assess the Centre on a regular basis to help maintain and improve
the overall quality of the programmes, leadership, shared facilities (e.g. bio specimen banks) and research/clinical studies.

**Box 6 Questions**

- How often are your research programmes evaluated?
- What kind of peer-review programmes exist internally (intramural) within your Centre and externally (extramural)? Please give names and expertise of key peer-reviewers who have participated in the review of your Centre in the past 5 years. Please provide a summary of the reviewers’ recommendations for improvement in each of these review programmes. Which of these recommendations have you implemented and how? Was your Centre designated as excellent in your national (and/or international) context by any of these peer-review programmes?
- What metrics (criteria and/or indicator) were used by peer-reviewers for translational research programmes? Which of these peer reviewed programmes led to competitive funding nationally/internationally?

**Rationale for criterion:** The depth and thoroughness of existing evaluations can be used to assess the excellent quality of ongoing translational research. Other important issues to consider include: who judges the performance and based on what criteria/indicators? What is the value of such assessments in improving translational research excellence in CCCs? The evaluations should include identifying how a programme works, who benefits from it and how, and how it will be implemented.

7. **Commitment to a program of training** of new translational scientists and **re-training** of established basic, clinical, or population scientists who wish to redirect their careers into translational cancer research.

**Box 7 Questions**

- What incentives are available at your Centre to improve the leadership competencies of individual investigators with respect to training and re-training scientists wishing to conduct translational research?
- How many of your graduates (PhDs) have gone on to become leaders in oncology research? What are these graduates doing now? Give specific examples. This question will be evaluated taking into consideration the length of time the Comprehensive Cancer Centre has been established.
- What specific translational research training programmes exist for PhDs. Are they regularly evaluated by internal and/or external peer review programmes?
- Do the graduate students report that they receive excellent mentoring?
- Does the Centre have flexible mechanisms in place that will allow clinicians whose primary role is service delivery to devote some component of protected time to involvement in research programmes?
- Is it easy for students to stay connected to the research of other students? Are there regular retreats, joint symposia and/or meetings where students get to share/discuss their work with each other?
- Do the students state that they are able to make an impact in benefitting patients through their research?
- Do the students know what they want to do after graduation? Where do they see themselves in 5-10 years?
- Do they want to return to their own country in the future for work/studies? Or, do they specifically want to return to this Cancer Centre in the future for studies/work?
- Who are the role models for students in their own field of work and why?
- Is there anything that the students would like to improve in their own research group/department and/or in the Centre?
- Is there a concept of real team-building spirit, with regular exchanges among the students?

**Rationale for criterion:** In terms of human resources, there is an urgent need to train and retrain staff towards achieving and maintaining competence not just in science, but also in dealing with the practical issues that underlie translational research complexity in a dynamic, multidisciplinary, international setting.

8. Establishment of an **up-to-date fully and clinically annotated bio specimen bank** (or banks) with an information technology system or network for tracking specimens and linkage to clinical outcome and follow-up data. To optimize the impact of the bank, specimens should be **shared** with other researchers or collaborators.

**Box 8 Questions**

- Provide evidence that the quality of your bio specimen banking is excellent through demonstration of guidelines, SOPs, storage, collection, retrieval, full annotation, and access to different research teams in the Centre.
- Is the quality of the bio specimen bank excellent (as outlined above) for all tumour types or only for certain tumour types?

**Rationale for criterion:** Translational cancer research increasingly relies on human tissue (both tumour and normal) bio specimens and this requires a well-defined bio specimen banking approach. There are differences in collection, storage and usage of bio specimens in many cancer centres. Common SOPs are needed to improve research quality and for the sharing of resources.

9. Ability and commitment to perform **hypothesis-driven** and **hypothesis-generating** clinical and population studies.

**Box 9 Questions**

- Please give specific examples of at least three hypothesis-driven clinical and population studies in each of the three tumour types or themes that took place in your Centre during the past 10 years.
- Please provide evidence that those studies (and/or other research programmes) have led to increased survival in cancer within your region, nation, Europe and globally. This question will be evaluated based on the length of time for which your Centre has been established.
- Give examples of Quality of Life studies/studies that focus on cancer survivorship at your Centre.

**Rationale for criterion:** Novel therapeutic innovations should be based on lessons learned from previous successes and failures. Translational research can improve its performance if it is informed by experiences gained through informative (early phase) clinical trials. However, hypothesis-generating studies are equally important.
10. Demonstration of a **sufficient patient population** to support bench to bedside studies in all the programmatic areas cited. Smaller cancer units should collaborate in their clinical trials in an effort to reach large enough numbers of patients to render the outcomes of these studies valid and effective.

**Box 10 questions**

- Specify the patient population to support bench to bedside studies in the three tumour types or themes from your Centre that you have chosen.
- Within each of these 3 tumour types or themes, how many in-house discoveries, patents, commercialization of patents, spin-offs, clinical practice guidelines, and high-impact factor publications has been made in the past 10 years? This question will be evaluated taking into account the length of time for which your Centre has been established.
- Give examples of studies at your Centre which may have a direct/indirect impact on patient and population outcomes but that cannot be commercialized or patented for a specific reason. Please explain the reasons.
- How many phase 0/I/II/III trials are ongoing (or have been completed within the past 5 years) in each of these 3 tumour types or themes? And, what is the percentage of patient accrual in each clinical phase trial for each tumour type or theme?

**Rationale for criterion:** Despite innovative trials, a major challenge for translational research is to achieve effective accrual and retention of patients in trials/clincial research studies. This is far more challenging for rare tumours.

11. Commitment to **funding high-risk/high-reward** projects to seize new and exciting research opportunities.

**Box 11 questions**

- Give us three specific examples of unique collaborative (novel/high-risk/high-gain) types of research programmes currently on going at your Centre.
- How are these unique collaborations funded? Is there a designated yearly budget for investing in those unique collaborations (e.g. pump-priming grants)?

**Rationale for criterion:** The risk-taking aspect is essential to really advance translational research. Investing in creativity and accepting the possibility of failure is a critical ingredient of translational research. Innovations should include the development of high-risk/high-gain technologies that have the potential to empower research.
12. A detailed demonstration of the ongoing ability and a clearly articulated intention to leverage funding and/or resources obtained as a result of an “excellent” designation.

**Box 12 questions**

- Describe your expected inflow of funds for the next 5 years (both nationally and European funding).
- How do you intend to use the funds? (Will they be used for any of these: building new infrastructure/training and development of staff/recruiting new staff/pump-priming research projects/other)
- Is there flexibility in your management to relocate funds to other areas (e.g. pump-priming/high-risk/high-gain projects) if the need arises?

**Rationale for criterion:** There is a need to explore alternative models of funding, e.g. can the private sector be motivated to support high-throughput elements of research. CCCs themselves can set aside funds to conduct translational research and should incentivise basic researchers and clinician scientists to work together on translational cancer research projects as well as to acquire funding for their ideas.

13. Involvement of **patient advocates** in advisory committees.

**Box 13 questions**

- Provide evidence that patients receive timely/adequate information about the clinical trials that are open in which they can participate for a range of tumour types at your Centre.
- Describe the role of the patient advocates in your advisory committees? Give specific examples of how they have contributed to bringing patient perspectives to the discussion and what decisions they have led to?
- Give examples of instances where patient experience (and monitoring) in the 3 tumour types or themes led to new and/or refinement of research questions?
- Provide examples of philanthropic fund-raising. If this is not possible in your context, then tell us how your Centre will be able to accommodate potential donations gifted by individual patients/cancer survivors towards your research.

**Rationale for criterion:** Involvement of patient advocates is crucial to ensure that patient needs are met during the entire translational research process. Empowering and educating patients can lead to better accrual rates and give cancer centres better guidance on how to deal with patient co-morbidities.


17. J.L. Talmon, G.R. Maurits, D.A. Legemate, PSI: The Dutch Academic Infrastructure for shared biobanks for translational research. For the Dutch Federation of University Medical Centers (NFU) PSI, Summit on Translat Bioinforma 110-114 (2008).


SUMMARY, GENERAL DISCUSSION AND CONCLUSIONS
SUMMARY AND DISCUSSION OF THE MAIN FINDINGS

Existing assessment frameworks for European CCCs

Based on the responses from 19 cancer centers from 18 member states, there are 109 assessments in Europe. The numbers have steadily increased from 1990's till 2015. The number of patient care assessments have risen most rapidly in Europe, followed by the mixed assessments of patient care and research aspects. The rise in pure research assessments has not increased much. Some mixed assessments (combining research and care elements) may involve assessing translational research, which translates research to practice. However, not all existing assessment reports of EU CCCs are available in English and/or easily accessible. Hence, it is hard to know the exact criteria that are being used in these assessments.

The majority of assessments (n=63) are done at the national level, followed by international level assessments (n=38). There are only a handful of regional assessments (n=9). Almost all mandatory assessments are national and are mainly related to keeping license and/or receiving public funding. In contrast, most voluntary assessments seem to be international, and mainly aim at quality improvement and are seldom directly tied to licensing or funding.

Staff perceptions of change resulting from participation in the OECI European cancer accreditation program

A qualitative evaluation of the OECI Accreditation and Designation programme was conducted to understand the experiences of staff from the 8 Centers. Four of five change categories as described by Pawson et al., 2014 in their change theory were found. These are mentioned in brackets: (i) growing importance of nursing and supportive care field (role change). Nurses gained more autonomy/clarity on their daily duties. Importance was given to hiring and training of supportive care personnel (ii) critical thinking on data integration (strategic change). Managers gained insight on how to integrate institutional level data (iii) improved processes within multi-disciplinary team meetings (procedural change). Clinical staff experienced improved communication between multidisciplinary teams (iv) building trust (organizational change). Accreditation improved center’s credibility with its own staff and externally with funders and patients. We did not find motivational change, which seems to be like a basis for all other changes and is difficult to trace exclusively.

Pawson et al’s (2014) theory seems to be a useful guide for our categorization of changes taking place in cancer centers as a result of their participation in an accreditation program. The statement that dovetailing of types of changes is responsible for ever-lasting changes is justified. Different types of changes in cancer centers are interlinked. For example, according to staff perceptions, critical thinking about data-integration (strategic change) is a major source for better communication and alignment of processes within multi-disciplinary
teams (procedural change). The strategic change also has an impact on the organizational change e.g. data integration improved trust with other cancer centers.

Stakeholder input at the development stage of assessment criteria/indicators seems to be very important. Some stakeholder groups such as researchers do not feel very engaged in assessments. This disinterest may be generated because very few assessments focus on judging the quality of excellent research (especially translational research which is the bridge between basic research and clinical practice) and also in part, due to the bureaucracy required by assessments.

The added value of being a CCC

A number of criteria were identified (through a (systematic) literature review) with the potential to help understand the added value of being a European CCC. We conducted a survey to identify the most important criteria. Almost all criteria were scored important but three seemed to be most important in adding the value of a CCC: ‘Internal collaboration between research and clinical department’, the ‘availability of state of the art resources (staff skills, equipment)’ and ‘patient satisfaction’.

In staff interviews with 6 CCCs to clarify the criteria, we noticed some differences among clinicians, researchers, managers and nurses in terms of how they view added value of a CCC. However, this should not be interpreted as being hard to obtain a consensus on added value and a universal definition of added value. Rather, variances in staff perception (from different staff groups) even within a CCC can be taken as a positive impact with added value experienced in both shared and group specific ways among stakeholders.

To evaluate how far a CCC performs differently from other organisations involved in cancer research and/or patient care, the findings should be tested more broadly to benchmark different types of cancer organisations. However, there also needs to be better consensus to define the terminologies added value and CCC.

Existing frameworks suitable for assessing the performance of translational research in European CCCs

A systematic literature review was conducted to check whether there are any existing frameworks/models that can be used to assess the excellent performance of translational research in European CCCs. Models were assessed for: linkage between research & care components; new knowledge; systems integration; performance assessment; review of other models.

Performance assessment can help improve the process of translational research by identifying areas for improvement in its management, knowledge exchange and engagement of multidisciplinary teams to deliver efficient and effective translational research. This would
help reduce unnecessary time lag.

The fear regarding such assessments among some stakeholder groups is that it might: jeopardize serendipity that is characteristic for many research processes; fail to capture research excellence that might exist partially or completely outside the scope of assessment criteria and; enable bureaucrats to take control of fields they do not really comprehend. A cautious and stepwise approach is therefore advisable if cancer centers are to use these models for performance assessment.

**Consensus building with European stakeholders to develop an excellence framework**

To develop the framework, a draft set of criteria set was prepared (also with the input of the literature review in Chapter 5) and a consensus was achieved on key criteria using a consensus building exercise across Europe.

The resulting excellence assessment framework had 18 criteria categorized in 6 themes. Each criterion had a number of questions/sub-criteria. Stakeholders favoured using qualitative excellence criteria to evaluate the translational research “process” rather than quantitative criteria or judging only the outputs. Critically, the framework supports reduced bureaucracy by building on existing European evaluation systems, a critical issue for clinicians (also a finding from Chapter 2).

Excellence assessment requires a degree of flexibility, which is possible to implement in a transparent manner by using an independent peer review panel. While a common format is desirable, rigid formats may be unsuitable for organizations operating in different health systems and can introduce significant bureaucracy. The assessment framework that we developed had to be thoroughly tested with European CCC’s to prove that it can help identify excellence in translational research.

**Pilot results of excellence framework with 3 CCCs**

3 CCCs volunteered to take part in piloting the excellence framework. A review team of experts (from NCI, Canada and Europe) assessed these CCCs (both from the documents that CCCs submitted and by site-visiting them) against these criteria: the organizational strategy for translational research; the depth of research programmes from bench to bedside and back; team science; commitment to collaboration; shared resources; commitment to develop and maintain state-of-the-art infrastructure; utilization of bio specimen banks; staff education and training in translational research; hypothesis-driven and hypothesis-generating studies; critical patient mass; investment in high-risk/high-gain research projects; ability to acquire and utilize available funding; and the involvement of patient advisory committees. Strengths and opportunities were identified for each CCC. Some of them were
unique. After the pilot, the final draft set was shared with experts from the EACS (n=200). They approved this piloted set.

Assessment needs to be flexible because excellent translational research can be found also in areas that are outside the scope of the assessment and/or the “typical” definition of translational research. The assessment framework is ready to be implemented. We expect that fine-tuning during its implementation will further improve the procedure and also generate added value for translational research at large.

KEY METHODOLOGICAL ISSUES

**Strengths**
There are two overall methodological issues: does this framework really measure excellence in translational research? And is the pilot enough to prove the validity of this framework? To answer to these issues first a number of methodological strengths of this thesis can be highlighted that show a positive response to these questions. It is the first systematic attempt to construct an excellence assessment framework exclusively in translational research for Comprehensive Cancer Centers (CCCs). We developed this assessment framework by involving stakeholders from across Europe throughout the development and piloting phases. This has helped ensure acceptability and accountability among stakeholders. We thoroughly piloted this framework with 3 European CCCs with the help of an international peer-review team (from the National Cancer Institute, the US, Canada and Europe). This has given credibility to our findings at an international level. We have used the past experiences, knowledge and opinion of experts from both inside and outside Europe.

**Limitations**
A couple of methodological considerations also need to be taken into account. For example, in chapter 2, we wanted to identify the existing assessment frameworks for European CCCs. However, the data presented by some of them was difficult to access and/or to interpret, as they are not available in English. Similarly, data was confidential in many cases. In chapter 4, we conducted a (systematic) literature review to identify criteria that can define the added value of a CCC. But, we found that very limited evidence is available on this topic. We assume that it is because the terminologies “added value” and “CCC” need an international common definition or consensus by experts. In chapter 6, a draft criteria set was prepared and consensus was achieved on key criteria using a stakeholder exercise across Europe. We took a series of steps: survey, focus group and expert meeting till we arrived at the draft set. An ongoing issue we had with doing this consensus building process was that we noticed that some stakeholders wanted to make the excellence framework easily achievable for their institution. For instance, at first some stakeholders suggested that we should set
quantitative measures such as (an excellent CCC should have a minimum number of ‘x’ publications in a given year exceeding an impact factor of minimum 10). Whereas, a majority of the stakeholders did not think that only quantitative numbers can tell us anything about excellent performance of a CCC in translational research. Besides, the current assessments for many CCCs gather a lot of quantitative data. Hence, qualitative criteria were preferred which increased the challenge of objective rating. However, expert judgment was sought for the piloting of the assessment process, which showed that qualitative criteria could identify strengths and opportunities for excellence in CCCs.

IMPLICATIONS FOR FUTURE RESEARCH

The findings have implications for future research as well for a wide range of stakeholders (i.e. Comprehensive Cancer Centers as an entity, translational research and clinicians within CCCs and policy makers).

The excellence framework can promote the integration of research and patient care by enhancing the performance of excellent translational research in CCCs. We strongly recommend the monitoring of the performance in CCCs using this framework and also to keep track of the planning and implementation cycles of changes (using these excellence criteria) to inform and facilitate necessary changes without delay in order to improve the performance of translational research. This will allow monitoring the impact of changes that have occurred. This provision and feedback of information can form the basis of regular review meetings to be held within CCCs (and also with necessary external stakeholders e.g. other CCCs, organizations, funders and government agencies) that can initiate further discussion and improvement of translational research.

Researchers and clinicians need to be better motivated to participate in assessment programmes and activities. For this the assessment programme has to minimize bureaucracy and maximize transparency. Also the added value of assessments should be demonstrated to stakeholders who do not understand the value of such assessments.

Currently there are different definitions and interpretations of the terms “CCC”, “translational research”, “added value of a CCC” and “excellent performance”. These depend on the context. Even within a CCC there are variances in these definitions among different stakeholder groups. To improve excellent translational research in CCCs, all stakeholders must agree on a common working definition. We have managed to establish a common excellence framework for assessing and improving translational research excellence in CCCs. Future research can take this thesis as a reference to develop definitions and frameworks based on consensus among key stakeholders. This thesis explains what techniques and methods are useful especially for building transnational consensus (in our case it was done
across Europe) in any context.

**Proposed process for selection and conducting the assessments for CCCs using the excellence framework**

The proposal is to start a multi-phase approach for conducting the assessment of CCCs for the excellence framework (see Figure 1). Phase 1 will require a pre-screening of CCCs. This will consist of an international team of experts reading the application of the CCCs. If needed, webcam/Skype/phone interviews will be conducted with staff from the CCCs to clarify any questions that the experts may have on the provided documentation. If the experts are convinced that the CCCs will make it to the next round (some will be rejected at this stage and a reason for rejection will be conveyed), experts will invite the lead representatives of those CCCs to a formal reverse site visit (e.g. to Amsterdam or Brussels where the expert team will interview key staff of the applicant CCCs). If not, a clear advice on an attainable schedule will be given (and also the impossibility, if applicable)

The interviews can lead to one of three scenarios:

1. The applicant CCC directly qualifies for a formal site visit by a review team of international experts; acceptance in principle provided they live up to the criteria of excellence in the actual site visit;

2. The applicant CCC is asked to provide minor revisions; the CCC needs minor improvements in specific areas before it can apply for the excellence designation system. This can take up to 3 years. The experts will convey their recommendations to those CCCs identifying specifically what needs to be improved within the next 3 years

3. The applicant CCC is asked to make major revisions; the CCC needs major improvements in specific areas before it can apply for the excellence designation system. This can take 5 years or longer. The experts will convey their recommendations to those CCCs identifying specifically what needs to be improved within the next 5 years)

All recommendations will be conveyed through the European Academy of Cancer Sciences and never directly to the CCCs during the reverse site visit. The CCCs that gets an acceptance in principle, will qualify for a formal site visit to be conducted by a team of international experts. Only upon validation, the CCC will get a formal excellence designation certificate, which will be valid for 5 years. After 2.5 years, the CCC can submit a progress report on how it has used the excellence designation and should notify the panel of significant changes/developments that may have occurred with respect to one or more excellence criterion. A review team will assess this report virtually and give feedback. The CCC can put in a fresh application after the 5-year designation term is over.

Future research needs to test whether a pure qualitative judgment will be able to sufficiently
identify excellence or if it can be combined with other types of rating systems (e.g. semi quantitative-qualitative or even purely quantitative).

The role of European Academy of Cancer Sciences (EACS) and the Organization of European Cancer Institutes (OECI)

With respect to the governance of this system, the European Academy of Cancer Sciences (EACS) will recommend international and European experts as auditors for the process. And the OECI can provide logistical support to organizing and conducting the pilot. The auditors’ feedback will be first checked and discussed in the governing body/task force of the EACS and later on be disseminated to the CCC via OECI.

![Excellence Designation System Process](image)

**Phase 1.** If the result of step 5 is a minor revision then start with step 1 after a minimum of 3 years. If the result of step 5 is a major revision then start with step 1 after a minimum of 5 years.

**Phase 2.** If the result of step 5 is a provisional acceptance then proceed with Step 6

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Figure 1. A two-phase approach to conducting the assessment of CCCs for the Excellence Designation System
IMPLICATIONS FOR COMPREHENSIVE CANCER CENTERS

The excellence framework has the potential to help improve the performance of translational research in CCCs. As a result of excellent performance one can expect a CCC to improve the various intricate processes involved in translating research into practice. The peer-reviewers for this assessment who will conduct the site visit will be renowned international experts. They can give credible expert advice on the changes and improvements that a CCC needs to improve its performance to international standards.

Free promotion and international exposure are immediately available to CCCs that will enter into the excellence assessment process and especially to those that will be designated as excellent. Through this necessary awareness can be raised with public e.g. to publicize clinical trials that are active and recruiting, to publicize clinical performance to patients and others (e.g. by showing examples of how excellent and efficient translational research improves personalized medicine and/or improves survival).

Being successful in a European excellence assessment can lead to an enhanced stature that can increase the ability of a CCC to attract specific research grant funds (locally and internationally) and especially funding from the European Commission (EC). International/European prestige can also attract top physicians and scientists from around the world to the CCC, which can further strengthen its value.

The excellence framework will designate European CCCs that will meet excellent standards in scientific leadership, resources, the depth and breadth of their research in basic, translational, clinical, and/or population science. They demonstrate an added depth and breadth of research, as well as extensive transdisciplinary research that links these scientific spheres. This can attract other CCCs that are aiming to collaborate in specific research areas. For example, in the pilot we saw that one of the pilot CCCs could benefit from collaborating with other CCCs that have excellent MD-PhD programmes. The two other piloted CCCs have excellent MD-PhD programmes. In this way, identifying strengths and weaknesses can easily lead to European collaboration thus boosting competitiveness as well as collaboration among European CCCs. For example, a recently formed a ‘translational research working group’ as part of EU-LIFE², an alliance of thirteen research institutes with the common goal of promoting excellence in European life sciences (See Annex – I) have found common ways to improve the process of translational research and as EU-LIFE² and would like to share their experience in an attempt to identify measures to promote translational research without undermining basic exploratory research and academic freedom. Five ways to foster translational research that are proposed by this working group include: promoting interdisciplinary research; collaborating to target unmet medical needs; nurturing international collaborations; creating and sharing the required resources; and encouraging a cultural change. The excellent framework can help identify excellent translational research.
performance (among CCCs and non CCCs within the EU-LIFE network).

Participation in the excellence assessment enables a CCC to benchmark its performance against CCCs of similar standing. Reports and other resource tools can help a CCC to compare its quality of translational research and improve performance based on internationally (and European) recognized quality measures and standards of research.

OVERALL CONCLUSIONS

1. European CCCs go through several assessments at the national and international levels and some also at the regional level. Few of these assessments focus on evaluating or sustainably improving the performance of research (especially translational research). On the contrast, a lot more assessments currently exist for improving clinical performance.

2. CCCs and assessment bodies should make an effort to track changes that occur in CCCs as a result of participating in assessment (e.g. accreditation) programmes: whether and how peer-reviewer’s suggestions are taken up/implemented in the CCCs and how long it takes to implement them, what are the obstacles for change implementation etc.

3. CCCs seem to provide an added value in a number of areas including: availability of state of the art resources, excellent interdisciplinary collaboration between researchers and clinicians, high patient satisfaction. Based on feedback from staff from a number of CCCs, other areas also seem to distinguish a CCC’s performance from other types of institutions providing cancer research and patient care but this requires further evidence. These areas may include: active participation in guideline development, improved patient outcomes, better career development possibilities especially for nurses, speed of research and clinical processes, high patient accrual in clinical trials etc.

4. The accreditation programme of the Organization of European Cancer Institutes (OECI) seems to bring many positive changes in European CCCs such as, giving nurses more autonomy/clarity on their daily duties, importance to hiring and training of supportive care personnel, integrating institutional level data, improving communication between multidisciplinary teams, improving center’s credibility with its own staff and externally with funders and patients. Researchers perceived no changes. Auditors suggested many areas for improvement (to implement changes) but it seems that some of these changes are yet to be implemented and/or some may have been implemented but will take time to become visible.
5. There are several definitions of translational research depending on the context and which organization is using it. Some definitions only focus on mere descriptive presentation, thus they are not very helpful for assessing and improving the performance of translational research in CCCs. Some models focus on outlining the processes and show the blockages from research through to clinical practice and back. These models are potentially useful to improve the performance of translational research in CCCs. However, they are from business management background and so, they should first be thoroughly tested in healthcare setting preferably in Oncology setting.

6. Developing an assessment framework required the engagement of researchers, managers, clinicians and patient representatives and subject (international) experts in a range of methods to arrive at a consensus. Excellence assessment requires a degree of flexibility, which is possible to implement in a transparent manner by using an independent peer review panel. While a common format is desirable, rigid formats may be unsuitable for organizations operating in different health systems and can introduce significant bureaucracy.

7. During the pilot of the draft framework with 3 CCCs on a voluntary basis (The Netherlands Cancer Institute, Helsinki University Central Hospital Cancer Center and Cambridge Cancer Center), a number of common and unique examples of strengths and opportunities were identified. For example, whilst MD-PhD career development was emphasized in all 3 CCCs, two of the 3 CCCs had excellent programmes to support and conduct MD-PhD training. This shows that the CCC that is on the path towards excellence can learn from the best practices of excellent CCCs and even collaborate with them to transfer some of those practices.

8. To our knowledge, this is the first systematic attempt to exclusively focus on identifying and designating excellent performance of CCCs in translational cancer research. We used available evidence to develop and pilot these criteria. The site visitors, the expert team and the involved institutions were unanimous in their opinion that excellent performance can be identified in CCCs using the excellence assessment. It needs to be flexible because excellent translational research can be found also in areas that are outside the scope of the assessment and/or the “typical” definition of translational research.
1. Rajan A, Wind A, Saghatcian M, Thonon F, Boomsma F, van Harten WH. Staff perceptions of change resulting from participation in a European cancer accreditation program: a snapshot from 8 cancer centers. ecancer. 2015, 9; 547


5. ‘Translational research working group’ as part of EU-LIFE (www.eulife.eu)
Stimulating translational research: several European life science institutions put their heads together

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ABSTRACT

Translational research leaves none indifferent and everyone expects a particular benefit. We as EU-LIFE (www.eu-life.eu), an alliance of 13 research institutes in European life sciences, would like to share our experience in an attempt to identify measures to promote translational research without undermining basic exploratory research and academic freedom.
INTRODUCTION

“There does not exist a category of science to which one can give the name applied science. There are sciences and the applications of science, bound together as the fruit of the tree which bears it” (1). This quote emphasizes the interconnection between basic and applied sciences. We propose that in the biomedical sciences there are six major phases: a) Open-ended research, aimed at understanding the core principles governing biological systems; the ensuing discoveries may have short-term, long-term or no direct applications at all. b) Disease-oriented research aimed at understanding the pathogenesis and/or evolution of maladies, referred to as use-inspired basic research (2), and includes research in animal models aimed at validating specific targets as causative drivers of disease. The results may only apply to the studied disease, may have far-reaching relevance for other diseases and may also elucidate fundamental principles of biology. c) Research aimed at treating a disease and testing it in preclinical models. d) Clinical research for testing diagnostic tools and treatment modalities in patients. e) Research for monitoring the effects of therapies: refining the mechanism of action, and understanding side effects and potential resistance mechanisms. f) Finally, research into the social-economic impact of a new treatment. Although this suggests one-way traffic from bench to bedside, in practice it is a continuous back and forth between the different phases (Figure 1). The realm of translational research has blurred boundaries and there is a plethora of definitions of translational research (3). However, one thing is certain: it is important to almost everyone (4), as it attracts strong opinions and wide-ranging expectations, and everybody agrees that the process of translating findings from the lab to clinical application should be faster and more (cost) effective. How can one advance biomedical translational research, phase b to f of the above-described continuum, and make it optimally benefit from exploratory research and vice versa?

We propose seven recommendations (Box 1) and five measures discussed below.

Although this paper focuses on improving translational research, we would like to stress its tight dependence on exploratory research, like a mill that without water cannot grind any grain. As such fostering open-ended research in life sciences, from molecules to cells to model organisms, is a key measure any stakeholder should take to ensure translational research a bright future.

Measure 1: Interdisciplinary research and training

Translational research requires interdisciplinary scientists who speak the same language and understand the common problems. We need to train a new generation of researchers for whom translational research is ‘second nature’. Institutes in our alliance do this successfully through a variety of mechanisms including: themed translational research PhD and MD-PhD programmes, industry-sponsored PhD projects, postdocs jointly supervised by academia and
industry, interdisciplinary education for clinician scientists and basic researchers, mentoring of clinician scientists by leading experimental teams and visits of researchers in hospital wards, and research opportunities for physician scientists by giving them protected research time. The Knowledge Exchange & Commercialization programme at the Babraham Institute promotes scientific exchange not only between academics and clinicians, but also between charities, industry and policy makers. VIB recently launched its “Stellar” project where senior academics are welcomed for sabbatical stays in Johnson & Johnson Labs. In a pure academic setting, embedded Translational Departments at the NKI, FIMM, Curie Institute or the Experimental and Clinical Research Center on MDC campus create a collaborative atmosphere between basic scientists and clinicians. Recently, MDC and Charité - Medical Faculty Berlin created a shared research space and joined forces in the Berlin Institute of Health. Such co-location in “clusters” helps to bring different disciplines together.

Measure 2: Collaborate to identify and address unmet clinical needs

Once clinicians and scientists speak the same language they can identify unmet medical needs in the field of diagnosis, prevention or treatment of a disease, guided by the daily experience of clinicians with patients. These efforts can be further stimulated by “twinning”
schemes or seed funding to reward translational research projects involving both researchers and clinicians. Ultimately they should lead to relevant translational research programs enabled by progress made in fundamental research and advances in technologies. Such initiatives should bring the best and most urgent ideas forward.

**Measure 3: Nurture international translational research**

Having teams of excellent research groups with complementary expertise improves high quality translational research. Increasingly, these involve cross-border partnerships so geography should not be a barrier to progress. We must have mechanisms to identify relevant cross-border expertise-matching collaborations and engage with national and international stakeholders including academic centers, hospitals and biotech and pharma companies. EU-LIFE is an example in which academic centers capitalize on each others expertise and experience to link basic research findings to drug discovery programmes, clinical trials and ultimately new diagnostic and therapeutic products. Last but not least, such international partnerships is only efficient when legal and regulatory issues about clinical trials, data protection, exchange of data and human samples, IP, etc. are harmonized.

**Measure 4: Create shared research resources**

Translational research requires shared resources as one group or one institute cannot recruit enough patients for trials in a reasonable period, have enough data to perform important analyses, and have in-house all the research facilities and expertise to execute the research. Most EU-LIFE partner institutes incorporate Core Facility Programmes with high-end infrastructure that benefit all. Notably, the EU-LIFE partners have all benefited from long-term strategic public and private support, which has allowed them to make sustainable, long term investment to facilitate their exploratory and translational activities.

**Measure 5: Stimulate a cultural change**

Cultural change at the individual and organizational level is critical to support translational research. Awareness and motivation is needed from all staff and groups (not just basic researchers and clinicians) including managers, nurses and other groups. More combined efforts and ‘exposure’ to translational research will educate on the benefits and possibilities. Fostering interactions with hospitals, industry and entrepreneurs and other relevant stakeholders will enable faster progress to benefit patients. Schemes to facilitate cultural change, better dialogue and working together are needed. For example, joint appointments with hospitals, Advisory Boards with representatives from industry, visiting professorships for researchers from industry. Activities and environments that facilitate ‘mingling’ further enable interactions; for example, shared cafeteria and shared offices, tandem basic scientist-clinician seminars and science networking events. Promotion of entrepreneurship, such as start-up ‘incubators’ attached to academia, strengthens cross-sector interactions and
encourages research that can be commercialized to benefit patients. No matter what efforts are made, financial support to foster interactions is critically required, for example seed funds for proof-of-concept studies and emergent translational research projects. But maybe the biggest cultural change has to come from the fact that translational research is really a team effort. This requires another way of appraisal and recognition of researchers.

**Box1: Seven recommendations for policy-makers and funding agencies to stimulate translational research:**

1. Provide interdisciplinary training to basic and clinical scientists
2. Protect research time for clinicians
3. Create specific evaluation and rewarding systems for scientists doing translational research
4. Fund schemes for joint basic-clinical research projects
5. Foster continuous interactions between basic and clinical scientists, and between, academia and industry
6. Promote cultural change among all actors in translational research
7. Facilitate cross-border partnership
REFERENCES

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ABOUT THE AUTHOR

Abinaya Rajan (alias Abi) was born in Chennai, India on 9 March 1987. After completing her Bachelors degree in Nutrition & Dietetics from India and interning with the UNICEF India she moved to Europe to take part in an AIESEC intercultural traineeship in the Czech Republic. Her main duties included teaching English and Spanish languages to high school students in a small school in the industrial town of Karvina. She pursued a European Masters degree in Sustainable Regional Health Systems (2008-2010) from 4 EU universities: Deusto University (Spain), Corvinus University (Hungary), Vilnius University (Lithuania) and University of Verona (Italy). This was undertaken with a prestigious Erasmus Mundus scholarship awarded by the European Commission for her academic excellence. The Masters taught her a variety of subjects including: Health Technology Assessment (HTA), health economics, health policy and decision-making, patient safety and quality, managing innovation, entrepreneurial mind-set, financing and managing healthcare organizations. From 2010-2011, she worked as a policy research assistant in Brussels with a European patient NGO (European Patients Forum). Here she researched on how to effectively involve patients in decision making on health technologies. From May 2011 she has pursued a PhD at the Netherlands Cancer Institute (NKI-AVL) in Amsterdam in collaboration with the University of Twente in Enschede. Her thesis focuses on identifying and designating excellent performance in translational research in European Comprehensive Cancer Centers (CCCs). This PhD was performed as part of the EurocanPlatform project funded by the European Commission under the FP7 framework programme. Alongside her PhD, she took an active role in coordinating the entire project (work package) and communicating with/disseminating knowledge to a wide range of stakeholders across Europe and in the US and Canada. Her professional interest lies in areas of qualitative research, policy implementation, stakeholder engagement, performance assessment of organizations and sustainability of services. Her passion in life and hobbies include: abstract painting, photography, singing and listening to Indian classical music, playing acoustic guitar, dancing tango, learning new languages, cooking, yoga and meditation, spirituality, creative writing and travelling.
LIST OF PUBLICATIONS

Published (as part of this thesis)


Submitted (as part of this thesis)


6. Wind A.* Rajan A.* van Harten WH. An overview of quality assessments for cancer centres in Europe (shared first author with Wind A.)

7. Rajan A, Nagel J. van Harten WH. Understanding the added value of being a European Comprehensive Cancer Center.

Other publications


Meaning of the book cover

Identifying and improving excellence in translational research in Comprehensive Cancer Centers can be compared to the notion of the tree of life that has its branches downwards and roots upwards. Thorough reflection of the roots (core mission, vision and values) is necessary in order to focus improvement in all organizational processes. This ultimately leads to excellent outcomes.

Assessing translational research excellence in European Comprehensive Cancer Centres

Abinaya Rajan

Dear professors, colleagues, family and friends,

With great pleasure, I would like to invite you all to the public defense of my Ph.D. thesis entitled:

“Assessing Translational Research Excellence in European Comprehensive Cancer Centres”

The defense will take place on Friday, 11 September at 14.45 at the Prof. Dr. G. Berkhoff-zaal, Waaier building, University of Twente, Enschede, The Netherlands.

Looking forward to your presence!

Kind regards,

Abi

(Abinaya Rajan)