

Scale up of Integrated Care for Chronic Patients

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*To my dear mother in law, Rosario.
1939-2014*

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Iván Dueñas

Barcelona, Julio 2016

“Standardized process guidelines belie the complexity of individual patient circumstances, and freeze care delivery processes rather than foster innovation. What is needed is competition on results, not standardized care. What is needed is competition on results, not just evidence-based medicine. There should be no presumption that good quality is more costly.”

*— Michael E. Porter,
Redefining Healthcare:
Creating Value-based Competition on Results*

ABSTRACT

Background: Chronic diseases (CDs) are leading causes of morbidity and mortality worldwide. They cost healthcare systems around EUR 125 billion each year; further, fragmented care of CDs contributes to inefficiencies. The Chronic Care Model (CCM) has been designed as the way out to avoid the triple fail of bad experience of care, high costs, and undesired health outcomes. Integrated Care (IC) – the operationalization of the CCM – represents a promising alternative for fragmentation with potential for cost containment. Successful experiences of deployment across EU identified the drivers for large scale adoption of IC: (i) Standard workflow definition, (ii) Stakeholder cooperation and change management, (iii) Definition of outcomes and innovative modalities of assessment, (iv) Adherence to treatment and citizen engagement for better management of CDs, (v) Health risk assessment and stratification, (vi) Business model and reimbursement initiatives, and, (vii) Technological support. Regional experiences of implementation are promising in terms of cost-effectiveness, but current heterogeneity of services/programmes precludes proper comparison and objective decision making, selection and replication. This PhD thesis contributes both to justify IC deployment, and to overcome well-known limitations to mainstream adoption identifying, at the same time, relevant gaps to be solved by future research.

Methods: In the context of two European Commission-founded projects, the “Physical Activity as a Crucial Patient Reported Outcome in COPD (PROactive)” project and the Advancing Care Coordination and Telehealth Deployment (ACT) programme, we performed three studies. First, we prospectively assessed the effect of symptoms of anxiety and depression on physical activity in COPD patients. The second study was an analysis of population-based health risk assessment and stratification strategies in place in the five EU regions of the ACT programme. The third manuscript was a protocol proposal, in which we explored the community-based integrated care for complex chronic patients (CCP) following an adaptive case management (ACM) approach, in order to facilitate management of multi-morbidity and to foster both professional and patient engagement, as well as to induce healthcare-value generation.

Results: Firstly, we found that depression symptoms are associated with reduced physical activity levels in COPD patients; specifically, after adjusting for age, exercise capacity, comorbidities, pulmonary function, and baseline physical activity, patients walked 81 fewer steps/day per extra point in HADS-depression score. Second, there was consensus on the need for a population health approach to generate health risk predictive modelling. We found marked differences among regions in health risk predictive modelling tools and health indicators, and identified key factors constraining their comparability. Thirdly, the adoption of ACM, to support collaborative work constitutes an innovative approach that would facilitate case managers planning at run-time using well-structured, but flexible, service workflows; finally, we encourage using implementation research tools, organized within the frame of the Model for ASsesment of Telemedicine applications (MAST), in order to accomplish implementation criteria and subsequent decision making.

Conclusions: (1) symptoms of depression are prospectively associated with a measurable reduction in physical activity 6 months later in COPD patients; (2) the implementation of current recommendations for population-health risk assessment, in terms of risk predictive modelling and health indicators, constitutes a priority for the on-going processes of adoption of IC at the European level; (3) there is a clear need to produce structured evidence on large scale deployment of IC services for CCP with potential for transferability to other sites. In summary, this thesis supports IC deployment and provides relevant data to overcome existing limitations to its mainstream adoption.

RESUM

Antecedents: Les malalties cròniques són la principal causa de morbimortalitat a nivell mundial. Costen als sistemes de salut al voltant de 125 mil milions d'euros cada any, i la fragmentació en la cura de les malalties cròniques contribueix a la ineficiència dels sistemes. El Model de Cures Cròniques (MCC) ha estat dissenyat com una solució per evitar la triple fallida de mala experiència de cura, alts costos i resultats de salut no desitjats. L'Atenció Integrada (AI) - l'operacionalització del MCC - representa una alternativa prometedora a la fragmentació, amb potencial per a contenir costos. Les experiències reeixides de desplegament a la Unió Europea van identificar els factors que comporten l'èxit per a l'adopció a gran escala de l'AI: (i) Definició estandarditzada dels fluxos de treball, (ii) Cooperació per part dels actors i decisors involucrats i el canvi en la gestió, (iii) Definició de resultats en salut i modalitats innovadores d'avaluació, (iv) Adherència al tractament i el compromís ciutadà per a una millor gestió de les EC, (v) Avaluació de riscos en salut i estratificació, (vi) Model de negoci i iniciatives de reemborsament, i, (vii) Suport tecnològic. Les experiències regionals d'implementació són prometedores en termes de cost-efectivitat, però l'heterogeneïtat actual dels programes / serveis impedeix una comparació apropiada, un procés de presa de decisions objectiva, una selecció i la replicació. Aquesta tesi doctoral contribueix a justificar el desplegament de l'AI i a superar les limitacions ben conegudes per la veritable adopció de l'AI, identificant alhora bretxes rellevants per ser resoltes en futures investigacions.

Mètodes: En el context de dos projectes co-finançats per la Comissió Europea, el projecte "Physical Activity as a Crucial Patient Reported Outcome in COPD (PROactive)" i el programa "Advancing Care Coordination and Telehealth Deployment (ACT)", hem portat a terme tres estudis. Primer, vam avaluar prospectivament l'efecte dels símptomes d'ansietat i depressió sobre l'activitat física dels pacients amb Malaltia Pulmonar Obstructiva Crònica (MPOC). El segon estudi va ser una anàlisi de l'avaluació de riscos en salut basada en la població i les estratègies d'estratificació dutes a terme en les cinc regions del programa ACT. El tercer manuscrit va ser una proposta de protocol en el qual vam

explorar l'atenció integrada basada en la comunitat a pacients crònics complexos (PCC), seguint un abordatge de gestió adaptativa de casos (GAC), per tal de facilitar la gestió de la multi-morbiditat, fomentar el compromís professional i del pacient, i induir la generació de valor en l'atenció de la Salut.

Resultats: En primer lloc, hem trobat que els símptomes de depressió s'associem amb nivells reduïts d'activitat física en pacients amb MPOC; específicament, després d'ajustar per edat, capacitat d'exercici, comorbiditats, funció pulmonar i activitat física basal, els pacients van caminar 81 passes / dia menys per cada punt extra en la puntuació HADS-depressió. Segon, va existir un consens sobre la necessitat d'un abordatge poblacional per generar modelatge predictiu de riscos en salut. Trobem marcades diferències entre les regions pel que fa a les eines de modelatge de predicció de riscos en salut i en els indicadors de salut; també identifiquem factors clau que impedeixen la seva comparació. En tercer lloc, l'adopció de la GAC per donar suport al treball col·laboratiu constitueix un abordatge innovador que podria facilitar als gestors de cas la planificació de la gestió de casos en temps real i la utilització de fluxos de treball ben estructurats però flexibles; finalment, recomanem la utilització de les eines de l'anomenada "ciència de la implementació", dins el marc del model "Model for Assessment of Telemedicine applications (MAST)", per tal d'aconseguir criteris d'implementació per a la subseqüent presa de decisions.

Conclusions: (1) Els símptomes de depressió estan prospectivament associats amb una reducció mesurable d'activitat física 6 mesos més tard en pacients amb MPOC. (2) La implementació de les recomanacions actuals per a l'avaluació poblacional de riscos de salut, en termes de modelatge predictiu de riscos i indicadors de salut, constitueix una prioritat per als processos - en curs - d'adopció de l'AI a Europa. (3) Hi ha una clara necessitat de produir evidència científica estructurada pel que fa al desplegament a gran escala dels serveis d'AI a PCC amb potencial per ser transferits a altres localitats. En resum, aquesta tesi avala el desplegament de l'atenció integrada i proporciona informació rellevant per a resoldre les limitacions existents cap a la seva adopció a gran escala.

RESUMEN

Antecedentes: Las enfermedades crónicas (EC) son la principal causa de morbi-mortalidad a nivel mundial. Ellas cuestan a los sistemas de salud alrededor de 125 mil millones de euros cada año; además, el cuidado fragmentado de las EC contribuye a ineficiencias del sistema. El Modelo de Cuidados Crónicos (MCC) ha sido diseñado como una salida para evitar la triple falla de mala experiencia de cuidado, altos costos y resultados de salud no deseados. La Atención Integrada (AI) – la operacionalización del MCC – representa una alternativa promisorio a la fragmentación, con potencial para contener costos. Las experiencias exitosas de despliegue a lo largo de la Unión Europea identificaron los factores que conllevan al éxito para la adopción a gran escala del AI: (i) Definición estandarizada de los flujos de trabajo, (ii) Cooperación por parte de los actores y decisores involucrados y el cambio en la gestión, (iii) Definición de resultados en salud y modalidades innovadoras de evaluación, (iv) La adherencia al tratamiento y el compromiso ciudadano para una mejor gestión de las EC, (v) Evaluación de riesgos en salud y estratificación, (vi) Modelo de negocio e iniciativas de reembolso, y, (vii) Soporte tecnológico. Las experiencias regionales de implementación son promisorias en términos de costo-efectividad, pero la heterogeneidad actual de los programas/servicios impide una comparación apropiada, un proceso de toma de decisiones objetiva, una selección y la réplica. Esta tesis doctoral contribuye, tanto a justificar el despliegue de AI, como a sobrellevar las limitaciones bien conocidas para la verdadera adopción, identificando al mismo tiempo, brechas relevantes a resolver en investigaciones futuras.

Métodos: En el contexto de dos proyectos co-financiados por la Comisión Europea, el proyecto “Physical Activity as a Crucial Patient Reported Outcome in COPD (PROactive)” y el programa “Advancing Care Coordination and Telehealth Deployment (ACT)”, llevamos a cabo tres estudios. Primero, evaluamos prospectivamente el efecto de los síntomas de ansiedad y depresión sobre la actividad física de los pacientes con Enfermedad Pulmonar Obstructiva Crónica (EPOC). El segundo estudio fue un análisis de

la evaluación de riesgos en salud basada en la población y las estrategias de estratificación llevadas a cabo en las cinco regiones del programa ACT. El tercer manuscrito fue una propuesta de protocolo, en el que exploramos el cuidado integrado basado en comunidad a pacientes crónicos complejos (PCC), siguiendo un abordaje de gestión de casos adaptativa (GCA), a fin de facilitar la gestión de la multi-morbilidad y fomentar el compromiso profesional y del paciente así como inducir la generación de valor en el cuidado de la Salud.

Resultados: Primeramente, encontramos que los síntomas de depresión están asociados con niveles reducidos de actividad física en pacientes con EPOC; específicamente, después de ajustar por edad, capacidad de ejercicio, co-morbilidades, función pulmonar y actividad física basal, los pacientes caminaron 81 pasos/día menos por cada punto extra en el puntaje HADS-depresión. Segundo, existió un consenso acerca de la necesidad de un abordaje poblacional para generar modelaje predictivo de riesgos en salud. Encontramos marcadas diferencias entre las regiones en cuanto a las herramientas de modelaje de predicción de riesgos en salud y en los indicadores de salud; así también identificamos factores clave que impiden su comparación. En tercer lugar, la adopción de la GCA, para apoyar el trabajo colaborativo, constituye un abordaje innovador que podría facilitar a los gestores de caso la planificación de la gestión de casos en tiempo real y la utilización de flujos de trabajo bien estructurados pero flexibles; finalmente, recomendamos la utilización de las herramientas de la llamada “ciencia de la implementación”, dentro del marco del modelo “Model for Assessment of Telemedicine applications (MAST)”, a fin de conseguir criterios de implementación para la subsecuente toma de decisiones.

Conclusiones: (1) Los síntomas de depresión están prospectivamente asociados con una reducción medible de actividad física 6 meses más tarde en pacientes con EPOC. (2) La implementación de las recomendaciones actuales para la evaluación poblacional de riesgos de salud, en términos de modelaje predictivo de riesgos e indicadores de salud, constituye una prioridad para los procesos – en curso – de adopción del AI en Europa. (3) Existe una clara necesidad de producir evidencia científica estructurada con respecto al despliegue a gran escala de los servicios de AI a PCC

con potencial para ser transferidos a otras localidades. En resumen, esta tesis avala el despliegue del cuidado integrado y provee información relevante para resolver las limitaciones existentes hacia su adopción a gran escala.

PREFACE

Current scientific evidence demonstrates that three factors contribute to the increasing burden of chronic diseases (CDs): *(i)* the ageing of the population, *(ii)* the increasing percentage of people with long term CDs; and *(iii)* the prevailing fragmented care of those conditions. These factors arise new perspectives about chronicity, enhancing the role of formal (*i.e.* healthcare) and informal (*i.e.* patient, families and communities) care on promoting healthy lifestyles, preventing morbidities, and adopting self-care and self-management in a coordinated way. Several efforts worldwide have been done to tackle against chronic diseases (CDs), and their negative impact on quality of life, patients' health outcomes, and on the economics of the society as a whole.

Specifically in Europe, the evolving needs towards healthcare-value generation, altogether with the development of information and communication technologies, contributed to prioritize the adoption of innovative modalities of care. At the same time, successful experiences across Europe indicate that Integrated Care (IC) for chronic patients would result in cost-containment, better health outcomes, and better experience of care.

IC has been defined as a “set of well standardised tasks to be carried out to a patient on the basis of his/her health condition and social circumstances to achieve target objectives aligned with the comprehensive treatment plan”. Unfortunately, IC is not easy to adopt given three main barriers: *(i)* heterogeneity in the health risk assessment, *(ii)* non-structure service workflows, and *(iii)* lack of a proper frame for evaluation subsequent replication and final large scale adoption.

This PhD thesis gives insight into the large scale deployment of integrated care in Europe, by exploring specific interventions to modulate each of the next key drivers: *(i)* relevance of psychological determinants of health of chronic patients and its importance on adherence to the therapeutics; *(ii)* health risk assessment and stratification; and, *(iii)* service workflow definition.

The current PhD thesis was developed between July 2013 and July 2016 in the context of two European Commission-funded projects: “Physical Activity as a Crucial Patient Reported Outcome in COPD (PROactive)” project and Advancing Care Coordination and Telehealth Deployment (ACT) programme. It consists in a compilation of three papers (two published and one submitted) developed under the direction of Dr. Judith Garcia Aymerich and Dr. Josep Roca, and co-authored by the PhD candidate according to the procedures of the Biomedicine PhD program of the Department of Experimental and Health Sciences. The thesis includes an abstract, a general introduction, the objectives, the results (the three original scientific papers), a general discussion, and final conclusions.

The three papers of current thesis were aimed to *(i)* assess the effects of anxiety and depression on physical activity in COPD patients, as a use case to explore the determinants of behaviour in chronic patients; *(ii)* analyze health risk assessment strategies in the 5 regions participating in Advancing Coordinated Care and TeleHealth (ACT): Scotland (UK), Basque Country (ES), Catalonia (ES), Lombardy (I) and Groningen (NL), and to explore the potential of population-based risk assessment to enrich risk assessment at individual level in the clinics; and, *(iii)* identify core characteristics of any given integrated care service and to generate a proposal for assessment of service outcomes using two use cases: complex chronic patients and patients requiring long-term oxygen therapy, in order to facilitate long-term follow-up of deployment at any given site and enhance comparability among deployment sites.

The PhD candidate has participated actively in both projects, has contributed to the data collection, has performed the analysis and was the responsible of the manuscripts elaboration of papers one and two, and contributed in the elaboration of the paper three. A summary of the research activities of the author during the development of the thesis is provided in the Annex.

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GENERAL INTRODUCTION

Integrated Care for chronic diseases

The growing burden of chronic diseases

Chronic diseases (CDs) are defined by the World Health Organisation (WHO) [1,2] as “diseases of long duration and generally slow progression”, not passed from person to person. They represent the major global health problem of the 21st century, and generate a high burden on healthcare systems worldwide [3–5]. In 2011, the General Assembly of the United Nations recognised the magnitude of the epidemics and the societal challenge that CDs represent [6]. In 2008, around 58% of the total deaths were due to CDs [7] and the percentage is expected to increase by 20% at 2030 [5]. The two root causes of the increasing prevalence of CDs are the unhealthy lifestyle (lack of physical activity and poor nutritional habits) and the ageing of the population, as broadly recognised by the WHO and the Centres for Disease Control and Prevention [8].

Evidence indicates that four types of CDs – cardiovascular diseases, cancers, chronic respiratory diseases and diabetes – make the largest contribution to mortality in all countries [1,9]. Briefly, during year 2008, cardiovascular diseases (CVD) - the leading cause of death worldwide - accounted for nearly 17 million of deaths [10,11], cancer contributed to 7.6 million deaths [12], chronic respiratory diseases were responsible for 4.3 million [10], and diabetes caused 1.3 million deaths [14]. In Europe, these three conditions cost healthcare systems around EUR 125 billion each year [11].

Importantly, these diseases are largely preventable by means of effective interventions that tackle shared risk factors, namely: tobacco use, unhealthy diet, physical inactivity, unbalanced nutrition and harmful use of alcohol. Furthermore, once the disease is established, there is evidence that improved management can reduce morbidity, disability and death, and may contribute to better health outcomes [3]. Broadly, this improved care is understood as widening the focus of the caring process towards the contexts of the patients, enhancing preventive strategies, supporting effective

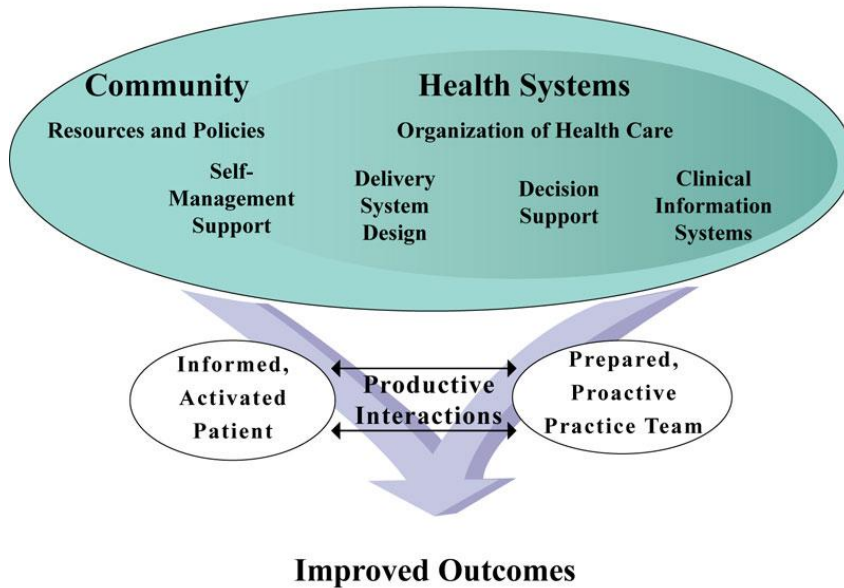
health and social care, and coordinating among different healthcare tiers and providers.

Last but not least, some patients with CDs require long-term involvement of multiple specialists, have functional decline and/or social deficits, and require highly specialized care with home-based technological support. These patients are labelled as complex chronic patients (CCP) and, despite being a small percentage of the general population, they use huge amounts of healthcare resources [12]. Therefore, any approach to tackle chronic diseases also must consider CCPs as a special group of patients.

The management of patients with chronic diseases. The Chronic Care Model

Current healthcare systems generally follow a fragmented approach [13], which has been defined as “focusing and acting on the parts [*i.e., diseases*] without adequately appreciating their relation to the evolving whole [*i.e., patient*]” [14]. Such fragmentation has been reported to predispose patients and health systems to a triple fail: bad experience of care, poor health status, and high healthcare costs [14,15]. Moreover, it has been demonstrated that fragmented care is associated with twice the cost than less fragmented care [16]. In the case of patients with CDs, there is an increasing recognition that healthcare outcomes can be improved without increasing costs if CDs were targeted comprehensively using a care coordination approach [17]. A conceptualisation of this idea was developed at late 90's by Wagner EH. *et al*, who proposed the chronic care model (CCM) (Figure 1) approaching holistically the patients and their contextual factors [18].

The Chronic Care Model



Developed by The MacColl Institute
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Figure 1. The Chronic Care Model.

Adapted from: Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? *Eff Clin Pract*, 1998.

The CCM was developed as a result of a review of interventions to improve care for various chronically ill populations. Research showed that the greatest improvements in health outcomes were achieved by changes in four categories of healthcare practices: (i) increasing providers' expertise and skills, (ii) educating and supporting patients; (iii) making care delivery team-based and planned; and, (iv) making good use of registry-based information systems [19]. Consequently, the CCM was designed to help practices to improve patient health outcomes through a combination of the elements mentioned above and other effective team care and planned interactions (Figure 1). All these elements working together allow strengthening the provider-patient relationship and improving health outcomes [18,20].

The potential of the CCM to result in effective interventions for a specific health problem at different healthcare settings was confirmed in a 2001 Cochrane Collaboration review [21] in which,

after analysing forty one studies (involving more than 200 practices and 48 000 patients), researchers found that a combination of inter-professional and multiple interventions, generated favourable effects on patients' health outcomes, in comparison with usual care. In 2002, the WHO launched the Innovative Care for Chronic Conditions initiative [22] adopting the CCM and formulating basic principles and strategies to improve management of patients with CDs.

Nevertheless, the CCM is not a defined, immediately replicable intervention. It is a model that care delivery organisations use as a frame to translate general ideas for change into specific, often locally distinctive, applications. As a result, the specific changes in health practice resulting from the application of the CCM vary from organisation to organisation and from country to country [23].

Integrated Care as the way out

The operationalization of the CCM for CDs is the Integrated Care (IC) [24]. The term IC covers a variety of different concepts, interventions, programmes or services intended to foster coordination within and between health organisations, with the goal to improve patients' participation and to enhance overall efficiency of health systems [25]. For the current PhD thesis, we define IC as a “set of well standardised tasks to be carried out to a patient on the basis of his/her health condition and social circumstances to achieve target objectives aligned with the comprehensive treatment plan” [26,27]. However, any theoretical definition of IC requires being translated into an operative intervention. How to operationalize and implement IC is not easy and requires a proper articulation of several stakeholders while keeping the patient in the very centre of the healthcare delivery [28].

A first important challenge towards IC adoption is the appropriate preparation of the healthcare workforce. IC constitutes a radically new manner of delivering healthcare, in comparison with traditional fragmented care, and most of the logistics relies on the workforce, who selects and harmonises new interventions to different types of patients, and across different contexts. The relevance of workforce preparation was recognised in 2005 by WHO in its statement

“Preparing a healthcare workforce for the 21st century” [29]. According to this consensus document, core competences of health professionals were classified into five major domains; namely, (i) Patient-centred care, which represents the need of acquiring enough communication skills to allow health professionals offering information from the patient’s point of view, and meet the patient at his/her unique level of understanding, (ii) Partnering, which means that health providers need skills allowing them to share power and involve patients in all aspects of healthcare continuum and decision making, (iii) Quality improvement, means improving workforce’s ability to design and test interventions with the goal of improving quality, safety and efficiency; and their ability to measure quality in terms of structure, process, and outcomes, (iv) Information and communication technology, which encompasses basic technological skills like using word-processing and data analysis software, searching online and internal databases, etc.; and, (v) Public health perspective, which is related to the necessity of the workforce of being aware of the different levels of the healthcare system: micro- or patient level, meso- or healthcare organisation and community level, and macro- or policy level. Certainly, such change and competences acquisition by health professionals remain a big challenge for healthcare systems and should be developed using a stepwise process of successfully incorporating new skills without neglecting previous backgrounds [29].

Another challenge for IC implementation is how to select best practices (*i.e.*, the above mentioned “set of well standardised tasks to be carried out to a patient”). This is because the deployment of IC services relies on an evidence-based selection of successful experiences and its contextualised replication into other environments. Unfortunately, the effectiveness of a given IC service is difficult to extrapolate to other services or settings because of the wide diversity in the content of interventions and their particular interrelations with the context. Briefly, according to a literature review [30] focused on analysing studies about effectiveness, definitions, and components of IC programmes on patients with heart failure, diabetes mellitus, rheumatoid arthritis, CVD, stroke, COPD and chronic illnesses in general, it was found that, despite considerable heterogeneity in IC interventions and population settings, IC reduced hospital utilisation, increased quality of life, functional health, and patient satisfaction, and improved process

outcomes, such as adherence to guidelines and compliance with medication. Regarding mortality, another review remarked that IC offers potential reduction in mortality, but extrapolation of conclusions was difficult given the diverse specificities of interventions [31]. Finally, another review [32] focusing on the economic impacts of IC as reported in seventeen studies found that, in general, quality of evidence was weak, and only eight of the studies reported cost-effectiveness of the IC interventions. Worth mentioning, these eight studies involved heterogeneous IC interventions and various chronic diseases.

Summarizing, IC must be considered as a promising strategy against CDs and, despite the fact that its implementation involves major effort, the change towards its mainstream adoption has been identified as a priority of developed health systems. Moreover, a comprehensive preparation of the workforce and a deep understanding of the IC initiatives are required for the scale up.

Deployment of Integrated Care services in Europe

The European Union has recognized IC as an appropriate strategy for tackling CDs and their deleterious effects, so major efforts are being invested in the selection of best practices (*i.e.*, components of IC) and their subsequent implementation [33]. According to WHO [34], this process of implementation -the so-called “scale up” of health service innovations- encompasses sequential phases of piloting (*i.e.* at project level), deployment (*i.e.* at the partner organisations), and mainstreaming adoption (*i.e.* at policy subsystems and external organisations level). Figure 2 shows graphically a multidimensional process of learning & policy change [35], it means a process which comes from individual learning to the EU level learning, considering organisational and policy levels [35,36].

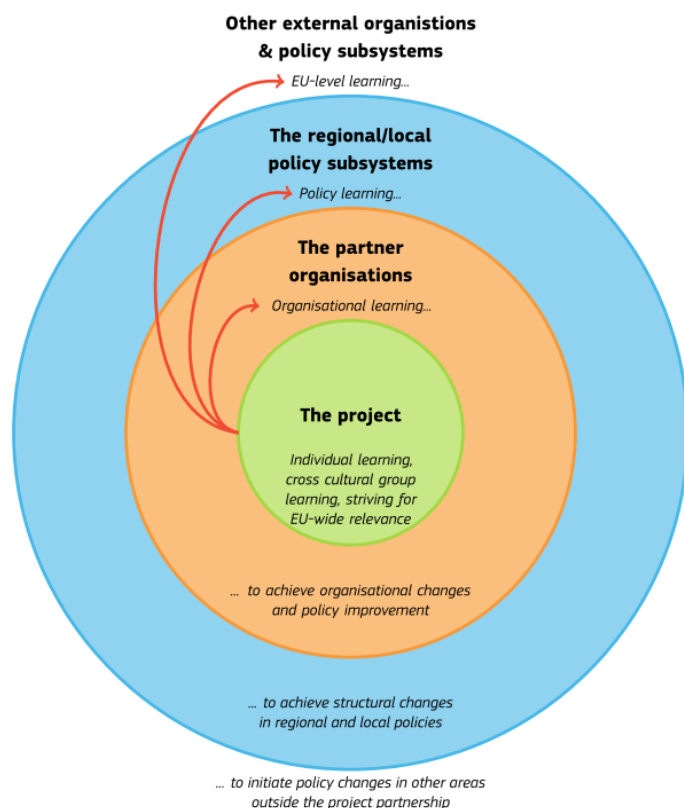


Figure 2. *Interregional exchange of expertise — a multidimensional process of learning & policy change. Adapted from an original INTERREG IVC Programme Table.*

In 2012, as an answer for handling the IC scale up, the European Innovation Partnership on Active and Healthy Ageing (EIP AHA) was created as an EU catalyst for fostering and implementing IC regionally. A number of IC experiences in real scenarios that were implemented between 2000 and 2012 had generated scientific evidence about the identification of key drivers – defined as “generic aspects of healthcare programmes determining their quality with respect to IC” [11] – for successful deployment as well as on barriers for its adoption [27,37]. Below we present a brief analysis of drivers and barriers of previous experiences of IC deployment in order to identify potential solutions.

Analysis of experiences of IC deployment

Integrated care deployment in Europe has been led by relevant initiatives across different countries. Some of these initiatives have resulted in positive impacts on health outcomes and cost containment [38]. However, the heterogeneity in interventions, outcomes, populations and health systems precludes a unique interpretation. Therefore, the current section presents a separate analysis of factors modulating IC deployment in each IC initiative. We selected the initiatives that allowed extracting information with potential for replication and transferability. A contextualisation of each experience is also provided to facilitate interpretation.

Basque Country, Spain – The Telemonitoring of Chronic Patients Care in Geriatric Centres

In order to cope with the phenomenon of aging in a context of deep economic crisis, the healthcare system of the Basque Country promoted a profound transformation of its model in 2009 to improve productivity in the sector at medium and long term. Among other changes, a system was created that allowed the continuity of care through health integration and care to people in the most appropriate and efficient place. In this context, a small pilot study, the Telemonitoring of Chronic Patients Care in Geriatric Centres (Telbil project) [39] aimed to transfer hospital care to primary care using telehealth, by reorganising health and social care, a process which involved design and application of new workflows. Patients were followed-up by telemonitoring, comprising personalised alerts set for each patient sent to the Web platform when the recorded biological parameters fell outside the pre-established limits. All formal and informal care professionals participating in the project were well informed about the management of the clinical conditions under study [40]. The study was designed as a randomized controlled trial funded by the Spanish Ministry of Health. It involved twenty-eight patients to the intervention group and thirty patients to the control group, all of them with chronic heart failure and/or chronic lung disease.

Results of the Telbil study showed that telemonitoring notably increased the percentage of patients with no hospital admissions, and there was a trend to reduce total and cause-specific

hospitalisations and hospital stay [41]. These findings support that reorganisation of health and social care (workflows, tasks and processes), as well as proper education/information and incentives to health professionals are key to the mainstream adoption of IC [42].

Catalonia, Spain – The Nexes project

The Nexes project, a four year project (2008-2012), (<http://www.nexeshealth.eu/index.html>) funded by the European Commission, was conceived to assess the deployment of four Integrated Care Services supported by Information and Communication Technologies in three sites (Barcelona in Catalonia, Spain, Trondheim in Norway, and Athens in Greece) with different profiles. The Nexes project in Barcelona was built on earlier proof-of-concept pilots (involving up to 3000 patients) led at Hospital Clinic and aiming to transfer these previous experiences from hospital to primary care and patients' homes with the support of information and communication technologies (ICT). The project involved and evaluated four types of services based on well-standardized patient-centred interventions, and including activities of self-management and prevention whilst enhancing the care continuum by the coordination across tiers of care. First, wellness and rehabilitation services were deployed with the aim to positively impact lifestyle, slow disease progression and reduce use of healthcare resources. Second, enhanced care was facilitated for frail patients, including complex chronic patients mentioned above, to prevent emergency room consultations and hospital admissions. Third, home hospitalisation and early discharge were implemented to investigate factors modulating extensive deployment of home hospitalisation and, in particular, the role that ICT plays as one of the components of a comprehensive chronic care program. Finally, remote support was provided to primary care for diagnosis and therapy in order to improve the efficiency of delivery of care and generate cross-fertilisation between levels of care.

The Nexes project identified positive effects of IC on health outcomes and enhanced use of healthcare resources with a reduction in inpatient services costs [27]. Interestingly, Nexes also proposed to redistribute the saved resources at hospital level (about 17%) to primary care, in order to transfer complexity efficiently [27]. Apart

from drivers of successful deployment already mentioned above, Nexes introduced new key elements: the interoperability with technological support and the reimbursement modalities.

England, United Kingdom – The Whole System Demonstrator (WSD) project

The challenge of providing care for an increasingly aging population prompted the publication in 2006 of a white paper [43] focusing on health and social care for people with long term needs by the Department of Health in England. The strategy proposed a series of pilots to redesign healthcare systems, supported by advanced technologies. The Whole System Demonstrator (WSD) project, designed as a randomized controlled trial and funded by the Department of Health, was deployed in three sites (Cornwall, Kent, and Newham) chosen for the diversity of their populations and involving over 6000 participants. The intervention participants received a package of telehealth equipment and monitoring services for 12 months, in addition to the standard health and social care services available in their area. The telehealth and monitoring devices varied among the three sites and were different for each chronic condition. Controls received usual health and social care [31].

Results of the WSD showed that telehealth is associated with lower mortality and emergency admission rates [31,42]. Nevertheless, the costs associated with the telehealth intervention were higher than in usual care, suggesting that telehealth is not a cost effective addition to usual care in a randomised controlled setting. Telehealth was identified as the key driver of health benefits and its costs could be recovered by reductions in the use of secondary healthcare, which has been a rationale for government willingness to test IC at large scale.

Germany – The Gesundes Kinzigtal (GK) initiative

In 2004, a German law facilitated the provision of financial incentives for developing and implementing IC models and fostering their deployment. As a consequence, the regional

government of Kinzig Valley, in cooperation with a network of physicians in the area and a German healthcare company, launched the Gesundes Kinzigtal (GK) initiative - literally, Healthy Kinzig Valley (<http://www.gesundes-kinzigtal.de/>).

The GK initiative is the only population-based IC intervention deployed in Germany. It provides integrated care to the general population covered by one insurer, reaching almost 50% of 69000 inhabitants. It consists in a set of organised interventions for people of all ages and care needs, targeting common chronic diseases through interventions well-coordinated at all health service sectors. The activities are performed according to the principles of: (i) individual treatment plans and goal-setting agreements, (ii) patient self-management and shared decision making, (iii) follow-up care and case management, and (iv) system-wide electronic health record. Apart from improving health outcomes, GK also aims to improve the margin for the contracting sickness funds by saving financial resources within the Kinzigtal region.

After 2.5 years of follow-up, the IC deployment resulted in a reduction of mortality by a half, using the non-enrolled population as comparison group [38]. Moreover, the margin costs per person per year improved in the IC population, compared to the non-enrolled population [38]. These results suggest that one key driver for implementing IC at the regional level is the legal consideration of providing financial incentives for fostering the adoption of the model.

Italy – The eCare project

After the occurrence of several deaths of elderly citizens caused by heat during the summer of 2003, some IC projects were born in Bologna, including the telesupport set of services eCare project. The eCare network covers 50 councils in the Bologna district, and delivers telemonitoring, teleassistance and other telecompany services to over 11000 elderly frail people through a specialized call service centre. Until 2007, eCare was funded through small financing and charity. With the establishment of the fund for non self-sufficient people – *Fondo regionale per la non Autosufficienza* – covered by the regional government, the service experienced a radical transformation enlarging both the services' scope and reach,

and becoming a network for tele-assistance company and support for the elderly with chronic conditions [44]. Currently eCare aims to prevent the aggravation of social and health frailty, and avoid unnecessary hospitalisations by: (i) enabling citizen empowerment, prevention, social and health service integration, (ii) providing hospital transition care and home care, (iii) personalising of care; and, (iv) integrating different domains of care, such as health and social services, allowing users to reach multidisciplinary management (including involvement of social workers, nurses and to some extent physicians) [45].

According to the assessments of the Bolognese regional health service, the impacts of eCare have been positive in terms of reduced hospitalization rates, cost containment, and 50% reduction of emergency department visits [42,44]. This experience allows identifying drivers for successful IC deployment, being the design of new processes and decision making flows like the integration of social and formal care in daily routines a core for such implementation, which is aligned with the WHO statement about the importance of workforce preparation for better tackling chronic diseases. Another identified driver for success was the fact that the project includes professionals who used to work in silos, virtually isolated of other domains of care, and they changed their perspective towards a more cooperative and team-based working. Importantly, researchers of the project concluded that “it is more than just an organisation issue; it is a cultural process that had to be triggered”.

The Netherlands

In 2009, the Dutch Parliament approved to implement bundled payment programs both for type 2 diabetes and cardiovascular diseases, as an alternative to previous fee-for-service reimbursement modality. The bundled payment system makes it possible for different elements of care to be purchased, delivered, and billed as a single product or service. As a result, IC interventions were deployed for patients with type 2 diabetes, cardiovascular diseases, or COPD. The interventions covered general modules including interventions on physical activity and smoking, as well as disease-specific modules targeting different phases of care (early detection

and prevention, diagnosis, individual care plan and treatment, and coordination, rehabilitation, participation, and secondary prevention).

The impact of these interventions was modest and more related to quality of care and clinical processes than health outcomes. There was no impact on mortality, and a higher usage of specialist care (with increased associated costs) was observed [38]. It is likely that a “disease-oriented”, rather than a “patient-oriented” approach, would be the responsible for the lack of positive effects, thus supporting the need of keeping the patient at the very centre of the healthcare delivery is a driver for skipping inefficiencies. The organisational change and the financial incentives for adopting the IC frame were other drivers for IC deployment in the Netherlands.

Scotland, United Kingdom – National Telecare Development Programme

In Scotland, the development and adoption of IC was closely related to the development of the *National Telecare Development Programme* (NTDP). Two main rationales for the creation of the programme were: (i) the projected increase of Scotland’s elderly population, of up to 81% of people older than 75 y by 2031, and (ii) the observed dramatic increase of burden of diseases associated to the elder population, persons with dementia, disabled and people with long term illnesses. The programme was introduced in 2007, initially as a two-year programme of £8.35 million (€10.6 million), and subsequently it was extended for a further 2 years and by a further £8 million (€10.1 million). This funding was provided by the Scottish Government. The programme consisted on tele-healthcare implementation and day-to-day activity, which were mainly driven by trained, community nurses, who helped to transfer the complexity to primary care, based on an adequate change of the tasks assigned to each provider. The technological support was relevant too; community nurses had facilitated access to electronic health records allowing them to assess better the condition of each patient. Nurses also coordinated with social care services [42].

In health terms, the NTDP found a transformational effect on service user and carer quality of life [46]. Two key drivers were identified, first, the willingness of the government to invest in tele-

healthcare in order to ameliorate the potential effects of the growing people at risk of high needs of care, and second, the workforce preparation for changing tasks and roles of the care personnel, including social support, through a coordinated manner along the care process.

Drivers of successful IC deployment

The pilot projects, randomised controlled trials and population-based strategies mentioned in the previous section allow identifying key drivers for the future deployment of IC. These have been aligned in seven groups and developed in detail following.

(1) Service workflow definition

Broadly, workflow is defined as “the processes involved in completing a job, including such functions as the organisation of human or other resources the design of tasks, and the development of procedures, followed by feedback, oversight and quality improvement” [47].

IC focuses on a patient centred approach, consequently it is necessary to model healthcare delivery from patient’s perspective and to organize the work around the patient [48]. Therefore IC workflow is not easy to implement. Recent experiences showed that workflows are widely various, precluding replication to other populations and environments [37]; furthermore, tailoring and contextualization are required.

Implementation of workflows depends on the specific feedback loops, starting conditions, and diversity of activities and outcomes [49]. Considering the dynamism of IC and the need for a change of the classical roles of caregivers at formal and informal levels, an alternative is to acquire proactive and flexible service processes modelling tools.

New processes modelling approaches offer some advantages over classical less flexible tools: *(i)* enable appropriate response to the needs of this population, *(ii)* improve the efficiency of the system in the context of clinical practice guidelines and care pathways; and *(iii)* modify the provision of services with a shared care model [11].

Summarizing, a proper workflow description is necessary for characterization of healthcare services [50], specifically IC scale up requires such process for adequate replication at large scale.

(2) Stakeholder cooperation and change management

A reorganisation of services and governance mechanisms, as well as the commitment of policy and/or health professionals, appeared as key drivers of success in previous deployments of IC services [37]. However, the assumption that “innovative solutions are more expensive” [51] precludes IC adoption.

Some relevant challenges to succeed in involving stakeholders have been previously remarked [33], and cover enhancing the willingness for change in professionals, introduction of comprehensive chronic integrated model, dissemination of best practices, improving support for the integrated care concept and enhancing availability of funding, public acceptance, alignment of health and social care strategic and operational objectives, benefits/profit realisation, and co-ordination between systems and care levels.

Therefore, it becomes clear that stakeholders should be well informed about benefits and boundaries of IC on patient and population health outcomes as well as about its potential for users’ satisfaction and cost containment.

(3) Definition of outcomes and innovative modalities of assessment

One of the most relevant limitations for the assessment of IC (services or programmes), is the lack of common indicators of results (e.g. processes and outcomes) [11], which precludes the possibility of comparing properly between them and across regions, with the subsequent difficult decision-making process. This was clearly shown in a recently published “cookbook” of good practices for IC installation [11]. The authors reported that, through the comparison of programmes of five EU regions, Basque Country (ES), Catalonia (ES), Northern Netherlands (NL), Lombardy (IT) and Scotland (UK), there were no common indicators for comparison of efficacy and cost effectiveness. Thus, data

availability and homogeneity appeared as the biggest challenges when evaluating the performance of the programmes. Also, although performance is essential, feasibility assessment through pilot projects is another challenge to consider [35].

A multi-sectorial and independent expert panel, set up by the European Commission, proposed that assessment of IC should cover *(i)* impact on common values, *(ii)* impact on outcomes, and *(iii)* a feasibility study. Such assessment should include safety, clinical effectiveness, patient perspectives, economic aspects, organisational aspects, and socio-cultural, ethical and legal aspects [35].

Therefore, IC at large scale requires not only a proper comparison of qualitative and quantitative indicators of IC performance, but also an analysis of feasibility in a comprehensive way.

(4) Adherence to treatment and citizen engagement for better management of CDs

A core structural difference between IC and other models of care is the assignment of new roles and tasks to both formal and informal carers. These include a culture of multidisciplinary teams, shared responsibility and joint working, and improved knowledge in topics such as targeted health and quality of life outcomes, identification of patient clusters, or targeted care plans [33].

The adherence of patients to therapies has been identified as a key factor for the success of the changes mentioned above. Adherence involves a complex set of domains: acceptance to the type of care, compliance of care plans, patient satisfaction, patient knowledge about his/her health condition, patient self-care, and self-management. Nevertheless, all of those domains depend on patients' contextual and individual factors, like accessibility to healthcare [52] and/or the presence of psychological comorbidity (anxiety or depression) [53] which negatively influence patients' ability to self-manage chronic diseases, resulting on complex treatment demands [54].

IC, including also social interventions, is postulated as a proper way for comprehensive consideration on the whole aspects involved in

adherence. In fact, there is evidence suggesting higher response to depression treatment in patients receiving integrated care when compared to those receiving usual care [54]. Therefore, understanding and improving adherence to treatment among IC users is at the top of the priorities for enhancing IC deployment.

(5) Health risk assessment and stratification

As some deployment experiences have found, one big challenge generated by large-scale deployment of IC is the need for dynamic health risk assessment and stratification, at both population and individual levels [11]. Risk assessment and stratification tools usually have two main aims: one, helping in the decision-making processes at clinical and individual level, by scoring an individual, according to the probabilities of having undesired outcomes (like hospital admission) or high usage of healthcare services; and two, to help to allocate resources in an efficient way [55]. Thus, the risk assessment and stratification strategy offers potential for maximizing efficiencies from IC [55]. Further, population- and individual- based health risk assessment and stratification, constitute a core aspect for proper comparison of the effects of IC practices, between and within health systems/programmes [12]. However, current risk assessment and stratification tools are diverse and heterogeneous [55,56] and need a deeper analyses of existing experiences to further propose the best approach to IC deployment.

(6) Business model and reimbursement initiatives

The German, Dutch, and Catalan experiences are good examples of how transferring complexity towards primary and informal care, could result in efficiencies and high quality in the provision of care. They also show that a change in the business model is necessary. In this sense, the change of the reimbursement model, from pay-for-fee modalities towards health value-based modalities (e.g. bundled payment, pay-for-performance, etc.), would enhance IC adoption at large scale [42]. However, lack of proper financial frame to incentivise IC adoption remains as a barrier for subsequent IC mainstreaming. It has been argued that IC implementation has high economic costs which result in cost containment only at the long-

term, and in turn affects how pilot experiences are conducted [11]. Importantly, the European Innovation Partnerships for Active and Healthy Ageing (EIP-AHA) B3 action group identified specific challenges in the area of financing IC: clinical and financial evidence to move from pilot to deployment, new funding models, willingness to invest of funding agencies, changes to insurance reimbursement schemes, financing for ICT solutions, and regional funding for integrated chronic disease care extension [33]. Summarizing, it seems that IC deployment will require complex schemes of financing and reimbursement models.

(7) Technological support

Although telehealth – one of the technological parts of IC – is considered by patients and clinicians as the way for intervening in real time, acting quickly, and providing flexible care; it is no less true that – resulting from previous experiences – technology is no longer considered the core of the IC interventions. In fact, platforms for information exchange and storage (*i.e.* electronic medical records) and system's support for clinical decisions, still remain as innovative fields for IC development. The European project Nexes made some recommendations for the utilisation of technology on the leverage of IC: (*i*) to select simple and robust supporting technologies well integrated into the clinical processes of the IC services, (*ii*) to use open and modular ICT platform supporting the clinical process logics of the IC services and providing organisational interoperability, (*iii*) including collaborative tools, clinical decision support systems (CDSS) and information sharing functionalities, (*iv*) the implementation of the ICT platform should not require replacement of pre-existing proprietary electronic health record; and (*v*) that interoperability of the ICT platform at health system levels must be ensured across healthcare tiers and among providers (Table 1) [27]. Future considerations of development should be able to identify advantages and boundaries of the technology during deployment.

Table 1. Recommendations for regional deployment of IC in the technological area.

1. Factors that may be limiting transferability of a given Integrated Care Service should be considered in the planning of the deployment phase.
 2. The overall strategy for deployment should be based on a building blocks approach aiming at short-term outcomes that generate continuous feedback and iterations that help to refine the deployment process.
 3. The setting of flexible organisational strategies based on complex adaptive changes theory constitutes the first priority to achieve an appropriate management of the human factor. New professional roles and corresponding curricula should be considered.
 4. Select simple and robust supporting technologies well integrated into the clinical processes of the ICSs.
 5. To use open a modular ICT platform supporting the clinical process logics of the ICs and providing organisational interoperability. Including collaborative tools, clinical decision support systems (CDSS) and information sharing functionalities.
 6. The implementation of the ICT platform should not require replacement of pre-existing proprietary Electronic Health Record. Interoperability of the ICT platform at health system levels must be ensured: across healthcare tiers and among providers.
-

Adapted from: Hernandez C, Alonso A, Garcia-Aymerich J, *et al.* Integrated care services: lessons learned from the deployment of the NEXES project. *Int J Integr Care* 2015.

Towards European Scale-up of IC: The ACT programme

As stated above, IC has not yet progressed substantially beyond pilots or test installations, likely because mainstreaming adoption of IC requires solving barriers such as those identified in the previous section.

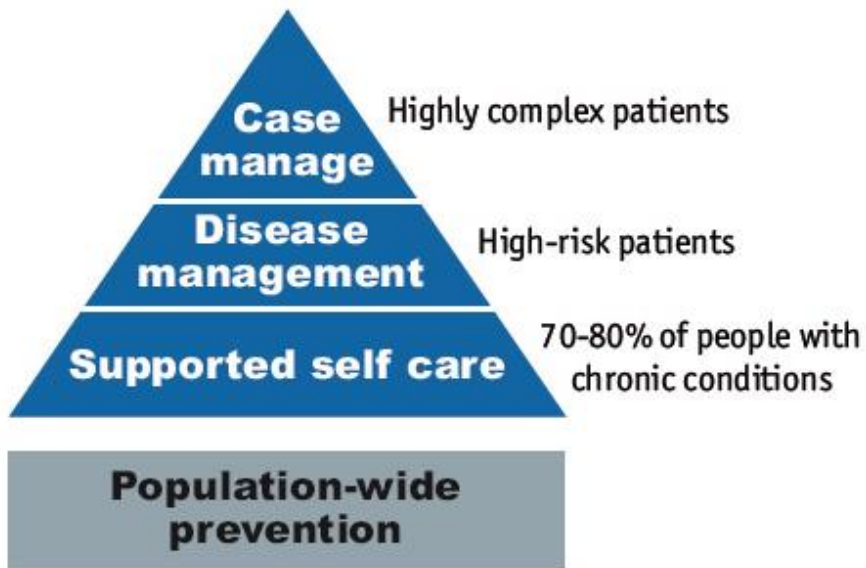
Some European institutions are investing big efforts to solve the dilemmas for translating evidence into practice in real scenarios. Among them, EIP-AHA brought together key stakeholders in this

health policy area, supported the good practices and “Reference Sites” developed by its partners, and aims to act as a catalyst to foster scaling-up of IC across regions and countries [57]. Moreover, the European Institute of Innovation and Technology (EIT), an independent body of the European Union, set up in 2008 to spur innovation and entrepreneurship across Europe to overcome some of its greatest challenges. EIT created a Knowledge and Innovation Community (KIC) on active living and healthy ageing. Among its core strategies, it is worth mentioning the ongoing InnoLife project, aiming to promote healthy living, support active ageing, and improve healthcare [58].

The ACT approach to Integrated Care scale-up

In this context, the ongoing EU funded Advancing Care Coordination & TeleHealth (ACT) programme [59] was selected by the EIP AHA as an example of best practices in the “European scaling-up strategy in active & healthy ageing”. The ACT programme started in February 2013 and is the first of its kind specifically designed to examine and overcome some of the key drivers and barriers learned from previous deployments.

ACT focuses on improving Coordinated Care & Tele Health (CC&TH) services for patients with chronic conditions, specifically Heart Failure, COPD, Diabetes, and multi-morbid patients. ACT aims at tailoring CC&TH services and solutions – as integrated care initiatives – to specific needs at all acuity levels set out in the Kaiser-Permanente Acuity Pyramid, [60] and not only in the 3%-5%, the highest risk (see Figure 3). The regions and the healthcare experts evaluate the integrated delivery of healthcare services between community care, primary care physicians, hospitals and informal care givers, and obtain feedback on how to organise these to provide optimal care.



Source: NHS and University of Birmingham.

Figure 3. The “Kaiser pyramid” illustrating different levels of chronic care.

In conjunction with the healthcare providers and the CC&TH expert team, ACT investigates how the abovementioned organisational and structural elements that influence effective deployment of IC are currently being used and how they can be optimised. Five European healthcare regions are involved: The Basque Country (SP), Catalonia (SP), Lombardia (IT), Scotland (UK) and Groningen (NL).

The areas considered as key drivers for successful scaling-up according to previous research that are addressed in the ACT programme are: (i) care coordination and organisation, (ii) patient & population stratification, (iii) staff engagement, (iv) patient adherence; and, (v) assessment of IC outcomes & efficiency. These areas are clearly aligned with EIP-AHA prioritized actions.

The ACT consortium, recognizing that the IC deployment experiences are widely various and that organisational barriers are

more relevant than technological issues, aims to overcome the abovementioned limitations and barriers for the proper mainstreaming of IC. ACT has organised its tasks according to the following five main drivers:

(i) Optimising organisation and workflow structures; by indicating how their pathways are integrated and accepted within the regions; by gathering and monitoring specific data using clinical and performance indicators to assess improved efficiency and quality and; by giving recommendations describing effective structures of how the care provider eco-systems can be organised as well as, information technologies support to patient-centric management.

(ii) Effective patient stratification, by analysing and comparing current concepts within the regions, in order to help to reach the long-term objective of moving from disease-oriented stratification models to more holistic approaches.

(iii) Staff engagement and education, which are prerequisites enabling health and care professional staff to effectively utilise CC&TH solutions. ACT approaches this driver by making a landscape of tools and incentive programmes that motivate staff to engage in the mentioned solutions.

(iv) Improving patient adherence, by assessing how CC&TH delivery improves patient and how patients can be empowered to more effectively self-manage their condition.

(v) Improving care provider efficacy and efficiency, by ensuring that CC&TH delivers adequate health outcomes for the eligible population in a cost efficient manner.

The current Thesis

The present PhD thesis is aligned with the rising need of defining better pathways for IC scale up in Europe and follows the principles of the ACT programme, in which it is nested. The thesis is focused on key current needs for IC deployment and organised in three topics with their corresponding manuscripts.

First, it has been highlighted in the introduction that IC places chronic patients at the very centre of interventions and approaches them holistically. Consequently, it could be hypothesised that IC also has the potential of being the standard care for psychological comorbidities which, at the same time, are relevant determinants of empowerment for self-management as well as to achieve adherence. The first manuscript focuses on stating a rationale for IC interventions on chronic patients with subclinical symptoms of anxiety and depression, enhancing the role of the patient and his/her mental status as a determinant of future health outcomes, using an epidemiological approach.

Second, there is a need of overcoming the problem of heterogeneous risk assessment and stratification strategies, given that this heterogeneity precludes healthcare forecasting, comparison of IC strategies and proper allocation of resources at population and individual level. The second manuscript analyses several risk assessment and stratification strategies at both the population and individual level.

Third, there is a necessity of better organisation of the workflow services and their subsequent assessment. The third manuscript proposes the deployment and assessment of a community-based integrated care program for complex chronic patients (CCP) following an adaptive case management (ACM) approach in order to foster professional and patient engagement, as well as induce healthcare-value generation.

Summarizing, this PhD thesis contributes both to support IC deployment, and to overcome well-known limitations to mainstream adoption, identifying, at the same time, relevant gaps to be solved by future research.

HYPOTHESIS

We hypothesise that the adoption of integrated care services at regional level may benefit from interventions modulating *(i)* patient engagement and self-management, *(ii)* health risk assessment and stratification, and *(iii)* service workflow definition. Specifically we hypothesise that:

- Patient engagement to a given integrated care service constitutes a key requirement to build up empowerment for self-management, as well as to achieve high degree of adherence to a given service.
- Population health risk assessment strategies provide information on the distribution of the population by risk strata in a given geographical area. This information is useful to define health policies, for service commissioning and for risk adjustment.
- Population-based risk predictive modelling may enrich individual health risk assessment with potential usefulness in the clinical scenario.
- The assessment of healthcare value generation of integrated care services is limited due to reduced comparability among different deployment sites.
- Community-based integrated care of CCP following an adaptive case management (ACM) approach with enhanced patient stratification will facilitate management of multi-morbidity, foster both professional and patient engagement, as well as induce healthcare-value generation.

OBJECTIVES

General Objective

This PhD Thesis aims to contribute to the large scale deployment of integrated care by generating specific interventions to modulate each of the key drivers alluded to above. That is: i) patient engagement; ii) health risk assessment and stratification; and, iii) service workflow definition.

Specific objectives

1. To assess the effects of anxiety and depression on physical activity in COPD patients, as a use case to explore the determinants of behaviour in chronic patients.

Manuscript 1:

Iván Dueñas-Espín, Heleen Demeyer, Elena Gimeno-Santos, Michael I Polkey, Nicholas S Hopkinson, Roberto A Rabinovich, Fabienne Dobbels, Niklas Karlsson, Thierry Troosters, and Judith Garcia-Aymerich, on behalf of the PROactive Consortium.

Depression symptoms reduce physical activity in COPD patients. A prospective multicenter study

Int. J. Chron. Obstruct. Pulmon. Dis. 2016; 11:1287-1295

2. To analyze health risk assessment strategies in the 5 regions participating in Advancing Coordinated Care and TeleHealth (ACT) (<http://www.act-programme.eu/>): Scotland (UK), Basque Country (ES), Catalonia (ES), Lombardy (I) and Groningen (NL), and to explore the potential of population-based risk assessment to enrich risk assessment at individual level in the clinics.

Manuscript 2:

Iván Dueñas-Espín, Emili Vela, Steffen Pauws, Cristina Bescos, Isaac Cano, Montserrat Cleries, Joan Carlos Contel, Esteban de Manuel Keenoy, Judith Garcia Aymerich, David Gomez-Cabrero, Rachel Kaye, Maarten Lahr, Montserrat Moharra, David Monterde, Joana Mora, Marco Nalin, Andrea Pavlikova, Jordi Piera, Sebastià

Santaeugenia, Helen Schonenberg, Jesper Tegner, Christoph Westerteicher, and Josep Roca
Proposals for enhanced health risk assessment and stratification in an integrated care scenario
BMJ Open 2016; 6:e010301

3. To assess implementation of integrated care services addressed to complex chronic patients (CCP), in order to facilitate long-term follow-up of deployment at any given site and enhance comparability among deployment sites.

Manuscript 3:

Isaac Cano, Iván Dueñas-Espín, Carme Hernandez, Jordi de Batlle, Jaume Benavent, Juan Carlos Contel, Joan Escarrabill, Juan Manuel Fernández, Judith Garcia-Aymerich, Miquel Àngel Mas, Felip Miralles, Montserrat Moharra, Josep M^a Nicolas, Jordi Piera, Tomas Salas, Sebastià Santaeugènia, Nestor Soler, Gerard Torres, Eloisa Vargiu, Emili Vela, and Josep Roca
Protocol for Regional Implementation of Community-based Collaborative Management of Complex Chronic Patients
To be submitted

RESULTS

Manuscript 1

Iván Dueñas-Espín, Heleen Demeyer, Elena Gimeno-Santos, Michael I Polkey, Nicholas S Hopkinson, Roberto A Rabinovich, Fabienne Dobbels, Niklas Karlsson, Thierry Troosters, and Judith Garcia-Aymerich, on behalf of the PROactive Consortium.

Depression symptoms reduce physical activity in COPD patients. A prospective multicenter study

Int. J. Chron. Obstruct. Pulmon. Dis. 2016; 11: 1287-1295

Manuscript 2

Iván Dueñas-Espín, Emili Vela, Steffen Pauws, Cristina Bescos, Isaac Cano, Montserrat Cleries, Joan Carlos Contel, Esteban de Manuel Keenoy, Judith Garcia Aymerich, David Gomez-Cabrero, Rachel Kaye, Maarten Lahr, Montserrat Moharra, David Monerde, Joana Mora, Marco Nalin, Andrea Pavlikova, Jordi Piera, Sebastià Santauegenia, Helen Schonenberg, Jesper Tegner, Christoph Westerteicher, and Josep Roca

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Manuscript 3

Isaac Cano, Iván Dueñas-Espín, Carme Hernandez, Jordi de Batlle, Jaume Benavent, Juan Carlos Contel, Joan Escarrabill, Juan Manuel Fernández, Judith Garcia-Aymerich, Miquel Àngel Mas, Felip Miralles, Montserrat Moharra, Josep M^a Nicolas, Jordi Piera, Tomas Salas, Sebastià Santauegènia, Nestor Soler, Gerard Torres, Eloisa Vargiu, Emili Vela, and Josep Roca

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Manuscript 2

Proposals for enhanced health risk assessment and stratification in an integrated care scenario

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BMJ Open 2016; 6:e010301

Dueñas-Espín I, Vela E, Pauws S, Bescos C, Cano I, Cleries M, et al. [Proposals for enhanced health risk assessment and stratification in an integrated care scenario](#). *BMJ Open*. 2016 Apr 15;6(4):e010301. DOI: 10.1136/bmjopen-2015-010301

Manuscript 3

Protocol for Regional Implementation of Community-based Collaborative Management of Complex Chronic Patients

Isaac Cano, Iván Dueñas-Espín, Carme Hernandez, Jordi de Batlle, Jaume Benavent, Juan Carlos Contel, Joan Escarrabill, Juan Manuel Fernández, Judith Garcia-Aymerich, Miquel Àngel Mas, Felip Miralles, Montserrat Moharra, Josep M^a Nicolas, Jordi Piera, Tomas Salas, Sebastià Santa Eugènia, Nestor Soler, Gerard Torres, Eloisa Vargiu, Emili Vela, Josep Roca

To be submitted

Cano I, Dueñas-Espín I, Hernandez C, de Batlle J, Benavent J, Contel JC, et al. [Protocol for regional implementation of community-based collaborative management of complex chronic patients](#). Supplementary material. npj Prim Care Respir Med. 2017 Dec 14;27(1):44. DOI: 10.1038/s41533-017-0043-9

GENERAL DISCUSSION

Main findings

The current PhD thesis is composed of three papers from different projects that, as a whole, were aimed to solve specific unmet needs about integrated care (IC) mainstreaming. First, we identified that major efforts are necessary for preventing and identifying early depressive symptoms, which may result in increased patients' adherence and self-management, both pivotal for IC. Second, we identified a window to improve health risk assessment of chronic patients in order to enhance care and commissioning. Third we proposed a protocol for real world implementation aiming at a proper evaluation of IC for complex chronic patients. The protocol aims to contribute to a roadmap for successful transferability of large-scale deployment of IC at EU level. The implications of these findings are discussed in next three subheadings.

Holistic patient-centered approach is a “must” for management of chronic patients

The main finding of the first paper is that symptoms of depression, as measured by the HADS, are prospectively associated with lower physical activity levels in patients with chronic obstructive pulmonary disease (COPD). This finding, using a highly prevalent chronic condition as a case study, reveals an opportunity for improved healthcare that is better approached under the IC framework. Specifically, a holistic patient-centered approach will likely provide the clinicians with the best tools for prevention, early identification, and proper management of depressive symptomatology.

First, health promotion activities in the frame of IC may facilitate a healthy lifestyle and improved self-care, which will likely revert in less depressive symptoms. Considering that major depression represents one of the most prominent causes of increased DALY's and reduced QALY's worldwide [61], and it is one of the most common comorbidities in chronic patients [62,63], a focus in depressive disorder should be a priority for health professionals clinicians when approaching chronicity [64].

The early detection of health risks, such as preclinical depression, by using case-finding strategies would result in a positive modification of the course of a given chronic disease [65,66]. Indeed, there is data suggesting that long term depressive disorders are more difficult to treat than acute conditions, and that early diagnosis and treatment enhance success and cure [67]. In some chronic conditions, like COPD, depressive symptoms also increase the risk of exacerbations [68–70], so early identification of depression becomes a key issue in the care of multimorbid populations.

Finally, a timely and proper management of established diseases or conditions, in a well-coordinated flux of information and along time lowers mortality and enhances quality of life when comparing treating advanced diseases, rehabilitating patients, and providing palliative care [2]. In this context, we used the case of depression as a mental health disorder which requires early multidisciplinary management [71]; indeed, social and family support show clear advantages for improving outcomes on depressive patients when compared with only-medical support [54]. Moreover, depressive symptoms are directly associated with loss of self-efficacy, treatment adherence, and empowerment [72]. Further, mental health assessment has been proven to improve risk characterization and stratification even after adjusting by “classical” variables like age, gender, comorbidities and previous healthcare usage [73]. Of additional relevance is the finding from the ACT focus groups that patients are often unaware of the impact of their own behaviour on their health [11]. They assume that they understand their diagnosis or what they can do to improve their health, but important uncertainties were disclosed, mainly related to misunderstandings and misconceptions regarding the organisational changes of care towards the holistic proposal [11].

In conclusion, our findings suggest that providing a holistic approach, as in the integrated care principles, will increase quality of care and will contribute to improved health outcomes of chronic patients.

EU regional consensus about health risk assessment and stratification

The second manuscript of the thesis reports that current characteristics of population-based health risk predictive tools are too different to allow comparability across EU regions. Moreover, health risk predictive tools should show flexibility to adapt to the evolving needs of IC scaling-up.

An important area of consensus is the population-health approach. The five ACT regions agreed on the relevant role of population-based health risk assessment for regional deployment of integrated care [11] and its usefulness for service commission, case finding and screening. Despite existing limitations of current stratification strategies, we found that health risk assessment and stratification may pave the way for efficient IC delivery by two main mechanisms: *(i)* proper allocation of resources, and *(ii)* potential contribution to individualized management in the clinical setting [55]. The latter must be prospectively assessed with an appropriate study design.

A second important finding is the central role of risk prediction tools. Predictive accuracy of existing tools should be enhanced. In this respect, we found enough evidence suggesting that risk predictive tools should include individual-based information (*i.e.* -omics, social and clinical information) as covariates [74]. Further, a frequent update of the modelling is needed to properly calibrate risk assessment of population [12]. We identified significant constraints for transferability of risk predictive modelling tools at EU level, namely: *i)* lack of algorithms transparency, *ii)* unnecessary rigidities for transferability (*e.g.* morbidity groups adjustment based on expert criteria); and, *iii)* license bindings constraining applicability of risk predictive tools to other EU regions.

Aligned with findings from the first paper of this thesis, results of the second manuscript give insights into a key driver for IC scale-up: the need to better assess individuals risk profile at an early stage of the disease. We postulate, therefore, that early and comprehensive assessment of the patient characteristics, by adding new covariates to the modelling technique (including biological, social and environmental factors) [74], is necessary for IC adoption. To this end, EU should evolve towards the adoption of the proposed “Digital Health Framework” (DHF) [75] in order to facilitate research and individualized care and to allow clinicians and case

managers allocating individuals into a specific healthcare. Further, given that the large majority of medical information generated today is consumed by clinically trained individuals and is therefore presented in a format which is not necessarily meaningful to patients or to informal care-givers, information technologies (IT) applications still need to be made more 'kind to people' and the use of visual analytics would facilitate interpretation by clinicians and patients during clinical visit [76]. The citizen, actively engaged in digital health, cannot become a reality without significant and sustained attention to this topic. Even professional stakeholders today 'struggle' with the user interface of current health IT systems, claiming the later generate more 'work' than immediate 'value'.

In summary, our data supports that there is a trend, within and between European health systems, towards improving risk assessment and stratification by adapting risk predictive modelling tools using a population health approach. Although risk distribution differences explain partially the low comparability of IC results [11], standardized risk assessment across EU region [for example by adopting open tools like the Catalan comorbidity grouper *Grupos de Morbilidad Ajustados* (GMA)] would facilitate decision making process for replicating experiences of IC and its subsequent adoption and mainstreaming [34,35].

Characterization and evaluation of IC experiences

The proposed protocol describes a comprehensive strategy for achieving regional adoption of IC for complex chronic patients (CCP). The main contributions of this protocol are the deployment of two pillars: (i) ICT-supported service workflows based on collaborative and adaptive case management of complex chronic conditions; and, (ii) A highly transferable enhanced clinical risk assessment & stratification strategy. The current protocol represents an innovative strategy for overcoming identified limitations of regional experiences of IC.

The third paper of the thesis focused on improving characterization of IC services in order to compare IC experiences better. With this aim, we propose two protocols for the assessment of two programs for complex chronic patients (CCP).

As clinical workflows for CCP require health professionals that perform complex tasks autonomously, novel approaches for service workflow modelling, like Adaptive Case management (ACM) play a role balancing structured and unstructured processes to facilitate creative aspects, which are indispensable for solving such complexity. We support that ACM for development and implementation of IC interventions is an innovative tool for characterizing workflows, by proper representation of well coordinated processes across healthcare tiers. Adaptive case management approach let the user (patient or healthcare professional) to navigate in the continuum of the care provision, by flexible selection and accomplishment of discretionary tasks properly selected by well informed providers.

Strengths and limitations

The strengths and limitations of the papers of this thesis have been deeply addressed in each of the manuscripts. In this section, we focus on strengths and limitations of the thesis as a whole.

The main strength of current thesis is the innovative approach to the complexity of “hot topics” on integrated care scale-up. Our research is convergent with world class scientific literature by raising relevant questions about IC and its mainstreaming. Europe is looking for efficiencies to contain chronic conditions and complexity [11,51,77]; IC, therefore, represents a challenge in different ways: reorganisation of the services, re-assignment of roles and tasks, health risk assessment and stratification, and improving communication across tiers by simple technologies [28,42]. Further, the thesis supports the rationale for IC adoption and proposes several steps for mainstreaming the IC principles, based on research under real conditions. The European width of all the included research adds to strengths, since so far IC development and evaluation had been limited to local settings, precluding proper extrapolation of the methods that would allow IC benefits worldwide.

A limitation of the thesis is that the third and part of the second manuscripts include proposals rather than results of IC experiences. However, these proposals are the result of a comprehensive evaluation of the state-of-the-art under real conditions. This offers a

better understanding of IC potentialities, difficult to emulate during controlled trials. Although some methodological gaps could not be solved, we offer a scientific-based repository of tidy, operative and well defined strategies for paving the way towards IC scale-up. A health risk assessment of clinical outcomes will be further tested in longitudinal studies and in outsource populations. Similarly, the implementation and evaluation of the protocol for IC for complex chronic patients was not possible during this thesis lifespan but will be conducted and reported.

Implications of current thesis for research

This thesis raises some issues that are relevant for future research:

Since the presence of depressive symptoms relates significantly to health outcomes of chronic patients, it will be useful to identify and evaluate the existing strategies for the detection of these symptoms in routine clinical practice, and to propose and test novel patient-centered approaches. How quality of life, socio-economic status and mental health are measured and managed in clinical practice, as well as their relation to patient empowerment, self-care and self-management, are relevant areas for future research. The role of self-care, self-management and self-efficacy on health outcomes and as covariates of risk predictive models needs to be explored. Further, the update of risk assessment tools when risk is a rapidly changing characteristic needs to be defined and tested.

The new Adaptive Case Management, should be evaluated using both qualitative and quantitative research. This approach represents a shift towards an overarching redesign of IC interventions. Successful European experiences have shown that very few projects combine all relevant stakeholders during healthcare of complex chronic patients. Therefore, it is necessary to resolve the challenge of designing IC for the very different type of stakeholders. New research should focus on this issue to obtain a more comprehensive template for services design.

Implications of current thesis for risk assessment and stratification tools

In order to achieve an efficient commissioning of resources to IC programmes, risk assessment and stratification should be based on dynamic and flexible tools. Moreover, in the clinical scenario, risk prediction of well-defined medical problems can support health professionals in the decision making process. Clinical risk prediction may also contribute to patient allocation in the optimal healthcare tier, helping to define shared care arrangements between primary care and specialists and in a longitudinal way. The PhD thesis generates a clear proposal to explore inclusion of outcomes of population-based health risk assessment into the clinical scenario in order to generate enhanced clinical decision support systems.

Implications of current thesis for IC deployment

Some results of the current thesis help to build on requirements for the next IC deployment strategies.

Our finding that subclinical mental symptoms – e.g. depressive symptoms – have consequences on certain health outcomes – i.e. physical activity – demonstrate the need for assessing patients holistically and not only according to patients’ diagnosis. Unfortunately, current models of care are not able of achieving such pre-clinical “syndromes”; therefore, chronic patients will be benefited by holistic assessment which detects timely early conditions. Recent evidence suggests that mental health has deleterious effects on self efficacy, self management, empowerment, adherence to therapeutics, among other factors [78], which in turn are related to higher usage of healthcare interventions [73]. Given that integrated care implies changing roles and tasks from clinicians and technical staff, we propose to build IC interventions taking advantage from experience of knowledge workers. Therefore, all processes in a given IC intervention should be the result of a consensus between providers and stakeholders during the design of such IC service or programme.

CCP often show a dynamic evolution over time in terms of both health risk and care requirements [28], such that their management requires a balance between structured (predefined and repeatable) and unstructured processes (depending on evolving circumstances and ad-hoc decisions) [79]. Considering this principle, we propose using community-based care coordination of CCP following an

ACM approach with support of information and communication technologies in order to enhance both professional and patient engagement, as well as induce healthcare-value generation.

Implications of current thesis for assessing IC deployment

In current thesis, we propose that methodologies for assessing IC should follow the frame of implementation research [80–82]. The science of implementing innovative care modalities has been described relatively recently. Peters and cols, defined it as the “... scientific inquiry into questions concerning implementation — the act of carrying an intention into effect, which in health research can be policies, programmes, or individual practices” [82]. Research on implementation has different indicators – or criteria – of success: *(i)* acceptability, *(ii)* adoption, *(ii)* appropriateness, *(iii)* feasibility, *(iv)* fidelity, *(v)* implementation cost, *(vi)* coverage, and *(vii)* sustainability [82]. We propose to use them on IC deployment adapting them to real case scenarios:

Acceptability – We have identified a clear trend for adopting IC as a priority. The ACT cookbook [11] describes this trend across different scenarios, even in those in which IC has not been proven as successful as expected, for example the case of the Netherlands. Specifically, other programmes like Embrace, Badalona Serveis Assistencials, etc. have been tested at the provider level, and have achieved acceptability. This fact is mainly explained because of the involvement of frontline staff and patients perspectives in the development of the interventions.

Adoption – Regional adoption of IC has demonstrated that overcoming pilot phases results in cost containment. That is the case of Telbios, Gesundes Kizingtal, MPOC IC, and others [45]. Although lack of a proper classification of IC interventions remains as a predominant barrier, local research may adopt IC in a “building blocks” approach, tailoring IC interventions into the specificities of local context.

Appropriateness – ACT found that providers accepted and appropriated IC when the design and iterative improvement of the intervention considered their opinion [11]. Experts propose including continuous quality improvement processes during IC design and testing, as it is stated in the third paper; it represents a higher possibility of success in terms of acceptability and empowerment from providers' point of view [11]. Unfortunately, some cultural barriers preclude changing the workforce's role towards a more proactive role. ACT found that prejudice causes difficulties in terms of communication, proper referral, or adequate discussion of complex cases [11]. Dealing with these cultural factors is essential prior to adoption of IC interventions in a given site.

Fidelity – Some well described IC interventions have been tested outside source population, but the result is various, not only for the difficulty in replicating processes; but for the diverse scenarios and populations [32,84,85]. As an example, the WSD tried to demonstrate favourable differences in terms of cost-effectiveness from IC, but only modest results were achieved [86]. Even in this controlled scenario, replications of interventions were not as effective as expected. Then, it is reasonable to expect that IC assessment, in real scenarios, will require more accurate description of IC processes. Our proposal, from third paper, is to use a process description using the innovative ACM, which could result in an easier way for replicating frames, avoiding rigidities from classical methods.

Implementation cost – According to Nolte et al. around 50% of studies about cost-effectiveness of IC have demonstrated successes, the rest of the studies failed in achieving this target [32]. It has been argued that to estimate costs containment from IC a similar comparator needs to be taken into account, as well as adequate methodology and a population comparable to previous experiences [32,84]. Thus, experts suggest that cost-effectiveness analyses in real scenarios, using risk profiles maps at population level for stratifying the analyses would help to obtain realistic results in terms of more accurate costs estimation [87,88]. Moreover, cost-based decision making is narrow and potentially unreal; so we added the multiple criteria decision analysis as a parameter for holistic approach of the intervention, widening the spectrum for IC

assessment as it is proposed in [84]. We believe that the implementation of the protocol proposed in the third paper is aligned to these principles.

Coverage – Providing health, by a total population health approach [89], enhances the relevance of implementing IC in order to provide interventions according to the specific risk profiles. Health promotion and prevention for low risk, disease management for intermediate risk and case management for complex patients are, widely, the general principle. Nevertheless, efficiencies in healthcare are more suitable of being achieved if adequate coverage is warranted. This involves: *(i)* better predictive modelling from large cohorts (totality of population of a given place), *(ii)* more fair healthcare provision resulting from universal health coverage, *(iii)* solidarity, or *(iv)* reducing expenses at individual level for covering highest risk population. These facts imply the need of assuring universal coverage as the only way for IC mainstreaming.

Sustainability – Basic principles about sustainability of health systems have highlighted that large investments in health are not the answer for achieving sustainability, but that the key driver for this target is improving quality of care at the provision level [24,51,77]. At a wider view, this implies breaking the general idea that quality comes with a higher cost. In this context, IC is a major priority given the high potential for cost containment from the population health perspective.

Beyond these criteria, a realistic assessment and subsequent improvement of IC besides on choosing proper methodologies and should be based on the deployment in real scenarios. Some key elements for the assessment are: *(i)* a proper case ascertainment by assuring enough coverage, *(ii)* selecting adequate health outcomes like mortality or survival; *(iii)* establishing indicators of clinical management goals and processes outcomes; *(iv)* stating specific indicators of service utilization for optimizing resources, like assessing the readmissions at 30 days; and *(v)* selecting accurate economic outcomes like transitions of resources to primary care.

In summary, although IC has not broadly adopted the implementation criteria, we propose these should be used in the

future as parameters of success, in order to warrant IC mainstreaming in EU.

Implications of current thesis for IC stakeholders

There is a complex relationship between the different drivers of IC. The ACT programme [59] showed that no single intervention is enough for acquiring efficient results. The qualitative analysis of perceptions from healthcare professionals and patients, performed by the ACT programme [11] facilitates the understanding of the relationship between drivers and outcomes in the context of IC scale-up at regional level. Nevertheless such relation is a complex process of tailoring, involving clinical staff, adding quality improvement processes, and involving professionals in the design of services [11].

ACT found that clinicians believe in IC interventions when they experiment its benefits [11]. Moreover, early communication with clinical staff during the modelling of processes will identify barriers for implementation and enables the development of clinical champions. Another point to argue for involvement of staff in the design of services is the extra value of adding creative solutions and dynamics from experienced workers. Such knowledge workers are able to create new processes in the context of IC development, adjust their tasks in order to solve problems using an innovative repository of processes, based on their previous experiences. Luckily, it is not difficult to obtain input from clinicians. According to findings from ACT [11], qualitative feedback is enough to provide tips for improving services of IC and gives a voice to the healthcare workers, recognizing the need from staff support to the general management of the IC intervention.

Another recommendation for successful IC scale-up is considering the active role and empowerment of the patient in his or her care. Healthcare professionals need to be aware that involvement of the patient, and shared decision processes are crucial for higher therapeutic adherence rates. ACT found that patients specifically valued: *(i)* high degree of sense of urgency, *(ii)* some form of self management, *(iii)* self care or patient empowerment, *(iv)* patient satisfaction with communication channels, *(v)* shared decision

making, and (vi) a committee that represents the views of patients and/or carers.

Finally, future ACM of IC will provide a platform for dynamic changes and assignment of roles in a more efficient way.

As a summary, from clinical and patient perspective, we believe that current thesis has contributed to understand that IC mainstreaming will facilitate chronic care, not only by cost-effectiveness approach but by patient and clinician enhanced adherence and participation.

CONCLUSIONS

1. Symptoms of depression are prospectively associated with a measurable reduction in physical activity 6 months later in COPD patients.
 - Whereupon, and since the current management guidelines for patients with COPD include the treatment of comorbidities, our study suggests that the management of symptoms of depression need to be considered, including in subclinical states, to prevent decline in PA over time.
2. The implementation of current recommendations for population-health risk assessment, in terms of risk predictive modelling and health indicators, constitutes a priority for the on-going processes of adoption of integrated care at the European level.
 - The current study proposes novel strategies for enhanced clinical risk assessment and stratification, together with a roadmap for evaluation and future implementation of the novel approach.
3. There is a clear need to produce structured evidence on large scale deployment of integrated care services for complex chronic patients with potential for transferability to other sites.
 - The proposed program articulates lessons learnt in previous experiences, as well as different technological developments carried out and validated in Catalonia during the last years. This generates a collaborative ecosystem with high potential for transferability to other geographical areas.
 - The scale up of IC requires assessment in real scenarios for proper forecasting of successful replications of local experiences.

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ANNEX

About the Author

This thesis was written at Centre for Research in Environmental Epidemiology (CREAL) and at the Institut D'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS) in Barcelona-Spain, between July 2013 and July 2016. The thesis has been directed by Dra. Judith Garcia Aymerich and Dr. Josep Roca and consists of a compilation of three scientific original manuscripts co-authored by the PhD candidate according to the procedures of the Biomedicine PhD program of the Department of Experimental and Health Sciences.

This thesis was done in the context of two projects: the European Commission-funded PROactive project (www.proactivecopd.com), which aims to develop and validate patient-reported outcome (PRO) instruments that capture the dimensions of physical activity in daily life relevant to patients with chronic obstructive pulmonary disease (COPD), and the European Commission-funded Advanced Care-coordination and Telehealth ACT project (www2.med.auth.gr/act) which aims to identify 'best in class' organisational and structural procedures, supporting effective implementation of Care Coordination & Tele Health services in the routine management of chronic patients.

Currently, the author is the Manager of the Implementation of Family and Community Medicine in the National Health System, Ministry of Public Health in Quito–Ecuador and is part-time professor at the *Universidad Técnica Particular de Loja* (UTPL), Loja–Ecuador.

List of publications

List of manuscripts or books co-authored by the PhD candidate about IC for chronic patients

- Dueñas-Espín, I. *et al.* Depression symptoms reduce physical activity in COPD patients: a prospective multicenter study. *Int. J. Chron. Obstruct. Pulmon. Dis.* Volume 11, 1287 (2016).
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List of manuscripts co-authored by the PhD candidate about other topics

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