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Annex C to Deliverable 3 :

WP5 - Top indicators for risk assessment and stratification

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Part I – ACT project lifespan

1.1 Conceptual approach and scope of the document

The principal aims of health risk assessment and stratification are to explore and generate instruments, risk predictive models, fostering the transition from reactive care to predictive/preventive medicine. Consequently, it constitutes a highly relevant area of the project **Advancing Care Coordination and Telehealth** (ACT).

The two core concepts developed in the work package are: (i) **population-based stratification**, addressing health risk assessment of groups of citizens; and, (ii) **patient-based stratification**, aiming at supporting subject-specific risk assessment in the clinical arena.

Population-based stratification serves to two principal purposes. Firstly, it is a key factor to assess the health status of a population and a necessary step for the design of specific public health and healthcare programs in a given territory. A second important use of population-based predictive risk models is the identification of high-risk subjects for presenting undesirable health events (i.e. life threatening situations, unplanned hospitalizations, etc…) that may deserve cost-effective preventive interventions.

It is well accepted that, by stratifying populations according to each person's risk and anticipated response to an intervention, health systems could more effectively target different preventive interventions at particular risk strata.[1]

Patient-based stratification in a coordinated care scenario should help to optimally allocate patients in the healthcare system. Subject-specific predictive modelling should contribute to identify the most appropriate healthcare layer for a given patient, as well as to define shared-care arrangements between specialized care and primary care. It can also help in the decision making process of patient-assignment to a given integrated care program or service.

Part I of this document sequentially describes: (i) the method followed to select indicators for stratification and baseline of stratification; (ii) the results of the baseline comparison of top indicators across ACT regions; (iii) conclusions on the study of indicators; and, (iv) recommendations for the second period of the project.

Part II of Annex C describes the role of health risk assessment in an “ideal” coordinated care scenario and generates proposals to be debated within the consortium aiming at generating recommendations for further actions beyond the current project. The ultimate aim of Part II is to pave the way for a future 4P scenario wherein: (i) personalized medicine should be deployed; (ii) with a strong role of patients co-design of healthcare; (iii) risk assessment and stratification will not rely on past-history of use of use of healthcare resources; (iv) biological, behavioural, societal and environmental factors modulating disease occurrence, activity and severity will be jointly considered for subject-specific predicting modelling; and, (v) dynamic update of predictive modelling tools with synergies between population and patient-based approaches will be a reality.

We believe that the exercise undertaken in Part II of the document may provide useful elements that should contribute the internal debate within the consortium, but also with the B3 group of EIP-AHA. Thus, we hope that Part II may somehow contribute to define future directions and requirements for developments in this area.

The analysis of population-based risk prediction tools currently used in the 5 ACT regions is the core content of Annex D. For clarity, it has not been included in the current document.

1.2 Population-based risk assessment: method

This type of stratification will generate a map of the distribution of the population by health risk in a given sector or region. It serves the purpose of defining specific policies and interventions at population level. It will also serve for the generation of indicators useful for the follow-up of health outcomes. Moreover, a relevant application of population-based risk assessment is to identify individuals with high-risk for presentation of undesirable events like life-threatening health problems, unplanned hospitalization or death. Thus, population-based risk predictive modelling may serve to allocate specific subjects in cost-efficient preventive healthcare and/or social support programs aiming at avoiding such undesirable health events.

As part of the strategy to perform population-based stratification, we consider five different domains, some of them including several sub-domains indicated in **Figure 1** and defined below:

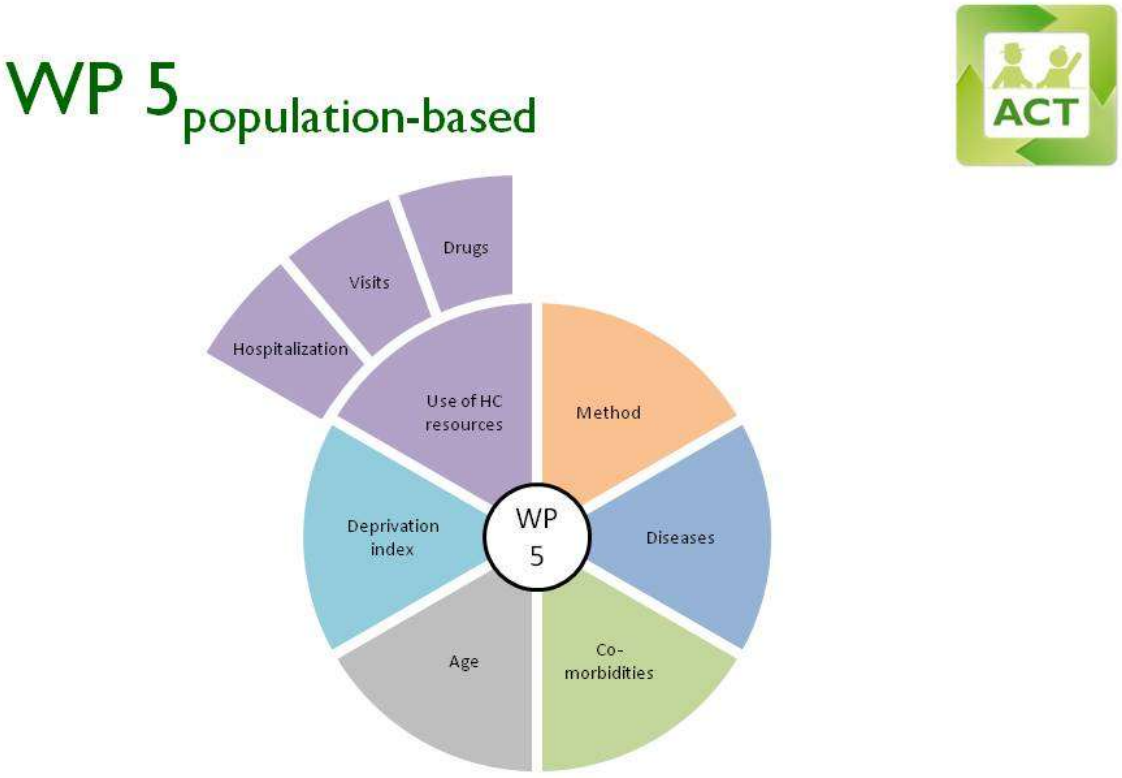

Figure 1 – Display of domains considered for population-based stratification. Domain and sub-domain definitions are indicated in the text below.

1. **Method** - The domain includes the conceptual definitions guiding the population-based stratification and the description of the methodological steps followed to obtain the population-based indicators
   1.1. **Purpose** – In the sub-domain, we state the primary objective to be achieved with the population-based stratification. The purpose of the stratification strongly modulates the method followed to obtain the indicators. As examples, population-based stratification can be done for public health purposes, cost-savings, enhance efficiencies of services, etc…

   1.2. **Process** – It refers to the sources of information and the method used to generate the indicators. The sources of the information can be existing registries with different characteristics requiring specific methods for data exploitation. Alternatively, periodic epidemiological studies of randomly selected samples from the general population are used in some European regions, mainly for public health purposes (i.e ESCA in Catalonia is done every 5 years). The indicators can be primary variables, indices composed by different primary variables or mathematical modeling.

   1.3. **Frequency** – Indicates time-related characteristics of the population-based stratification: time frame of the analyses and its periodicity.

   1.4. **Combination method** – Conceptually, it could be considered a sub-domain of Process (1.2) describing the methodological approaches followed to obtain complex indicators, either indices composed by different primary variables or mathematical models, from one or several information sources.

2. **Diseases** – Disease domain indicators provide information on the epidemiological impact of targeted diseases and their combination (co-morbidities) at population level (1). Two different sub-domains are considered

   2.1. Severity – Disease severity is conceptually defined as a loss of function due to the organs affected. Consensus classification of severity for major chronic diseases is reported in international clinical guidelines (i.e. NYHA, New York Heart Academy classification for heart failure; GOLD stages for Chronic Obstructive Pulmonary Disease, COPD). Population-based stratification by disease severity is considered in the sub-domain.

   2.2. Co-morbidities – Co-morbidities are defined as concomitant diseases in a given patient. It is a common condition in chronic patients with a significant impact on health risk. A classical variable to be considered to assess the impact of co-morbidities at population level is the Charlson index.

3. **Age** - Age domain indicators include age as primary variable, but also age used as part of composed variables to assess the impact of age on survival, healthcare and use of technologies (2).

4. **Deprivation Index** – To be used to characterize socio-economical and/or educational status of the population. Deprivation index indicators characterize the poverty in an area. Poverty is related to health, education level, availability of means to sustain a healthy lifestyle and social support from the environment, and the availability to utilities, e.g. a network. Hence poverty is expected to impact outcomes and adherence to the program (3).

5. **Past use of healthcare resources** – Use of healthcare resources within a given period of time (i.e , past 12 m) are indicators of disease burden on the health system. Three main sub-domains are currently considered, but it may need to be expanded to include novel modalities of interactions of the patient with the healthcare system using telehealth.

   5.1. Hospitalization – Several primary variables such as hospitalization rate, early re-admission rate, emergency room admissions, etc… should be considered in the domain. Also combination of these primary variables with other domains/sub-domains may be of interest (i.e, by disease, by disease-severity, by co-morbidity, by age, etc..)

   5.2. Visits – Frequentation to primary care physician, home visits by health professionals, outpatient visits to specialized care as primary variables or in combination with other domains can be taken into account

   5.3. Drugs - Indices related with drug consumption, poli-medication, desprescription programs, etc… will be considered

The domains and sub-domains defining defined above were explored in order to identify a complete list of potential indicators. An initial comprehensive list of potential markers to be used for stratification purposes was subsequently trimmed to achieve a list of top indicators, as described in **Table 1** of the results section. But the status of harmonization of the data did not allow comparison across regions.

The final selection of top indicators was based on an empirical approach of the available list of indicators (WP5 Overview.xls), derived from the engine developed by WP3. The selection was performed using a score from 0 to 10 points, 0 was the less relevant to 10 the more relevant for stratification purposes. So, selected indicators were those with a score equal or higher than 5 points (intermediate to completely relevant). Additionally, the indicators were categorized according to the potential usefulness as an outcome or as an explanatory variable. Certainly, most of the indicators should be used as explanatory, given their predictive potential for explaining risk (core objective of WP5).

1.3 Patient-based risk assessment: method

Patient-based assessment of health risk is used to allocate the patients into specific integrated care programs aiming at optimizing care and generating efficiencies. Allocation into a program will depend on two main factors: i) health status and associated risk level; and, ii) target health goals planned. A given patient can be simultaneously included in one or more programs.

As part of the strategy to perform patient-based stratification, we initially considered four main domains, all of them including several sub-domains, as indicated in **Figure 2** and defined in the text below.

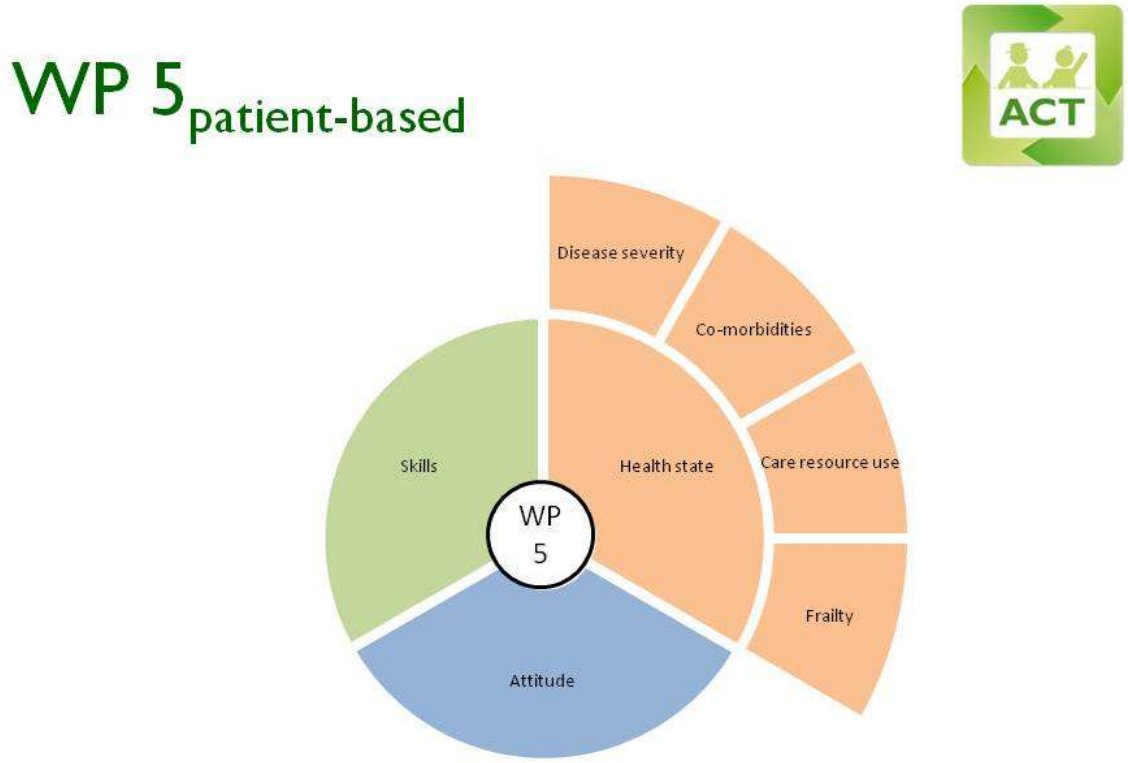

Figure 2 – Display of domains considered for patient-based stratification. Domain and sub-domain definitions are indicated in the text below.

1. **Health Status** – Disease domain indicators provide information on the individual impact of the disease on the patient's health status, as defined below by different dimensions indicated by the sub-domains.

    a. **Disease severity -** Within the disease domain, we should also take into **Severity** conceptually defined as a loss of function due to the organs affected. Consensus classification of severity for major chronic diseases is reported in international clinical

guidelines (i.e. NYHA, New York Heart Academy classification for heart failure; GOLD stages for Chronic Obstructive Pulmonary Disease, COPD). But also **Activity** – defined as the level of the biological process activation that drives disease progression. Disease activity can be expressed by frequency & intensity of exacerbations.

b. **Co-morbidities** – Co-morbidities Chronic disorders are often clustered in the same patient. Co-morbidity number and severity increase with age. Co-morbidities (Charlson index) are associated with worse health outcomes and disease burden.

c. **Use of healthcare resources**. Frequency of use of healthcare services and costs associated to services are pivotal elements for stratification purposes. The integrated care programs will be guided by the principle of fostering efficiencies at health system level. That is, achievement of enhanced health outcomes without augmenting overall healthcare costs.

d. Frailty – It includes three different aspects: i) impact of disease on daily life activities; ii) loss of muscle strength and coordination that are associated with risk of fall; and, iii) needs for social support. The frailty score shows an independent association with disease burden such that its assessment plays a pivotal role for patient stratification in primary care. Moreover, the interplay between frailty and complexity of care is a major determinant in the design of shared care management strategies across healthcare tiers, defining the role of specialized care.

2. **Attitude**– It is the patient's perception of the disease and its impact on adherence.

3. **Skills (capabilities)** – It encompasses several indices reflecting external factors that have proven influence on health status and accessibility and use of healthcare services. It includes attitudes and skills toward integrated care programs and use of technology. But also considers factors such age, educational background and poverty score.

The aim of the project is to refine the conceptual aspects of these domains/sub-domains and to generate recommendations for future assessment. It is of note, however, that specific indicators for patient-based stratification were not collected in the initial phase of the project, as explained in the conclusions.

1.4 Results of the baseline assessment

The summary of the selection of population-based top indicators following the method described above is displayed in **Table 1**.

Table 1. – Selected indicators for population-based stratification (an indicator was considered relevant when the score was ≥ 5).

Selected Indicators			
Indicator name	**Potential usefulness of the indicator[i]**		**Relevance**
	Outcome	**Explanatory**	**scale 0 to 10**
Methods Domain			
Are you considering disease severity in the stratification?		X	10
Are you considering disease co morbidities in the stratification?		X	10
Are you considering age in the stratification?		X	10
Are you considering deprivation index in the stratification?		X	10
Are you considering past hospitalizations in the stratification?		X	10
Are you considering past healthcare visits in the stratification?		X	10
Are you considering past drug usage in the stratification?		X	10

[(i)]The indicators have been classified according to the domain (Method, Co-morbidities, etc...). **Potential usefulness** of the indicator was expressed by two dimensions: (i) **Outcome** indicates the potential impact of the covariate to explain a given outcome (risk of death, unexpected hospitalization, etc...); and, (ii) **Explanatory** indicates that the indicator shows potential as explanatory variable. By definition, all the indicators considered in the table have potential as covariates, its estimated weight is indicated by the score in the rightest column (**Relevance**).

Co morbidities Domain				
	The prognosis (in years) on life expectancy in 2012	X	X	10
	The prognosis (in years) on healthy years in 2012	X	X	10
	Charlson comorbidity index in 2012		X	10
	Prevalence (in %) of COPD in 2012		X	5
	Prevalence (in %) of DM type II in 2012		X	5
	Prevalence (in %) of HF in 2012		X	5
	Incidence (in %) of COPD in 2012		X	5
	Incidence (in %) of DM type II in 2012		X	5
	Incidence (in %) of HF type II in 2012		X	5
Age Domain				
	Population size age <65 years in 2012		X	9
	Population size age ≥65 and age ≤75 years in 2012		X	9
	population size age >75 years in 2012		X	9
Deprivation index Domain				
	The education level in 2012		X	10
	The accessibility to healthcare in 2012		X	10
	The derived deprivation index in 2012		X	10
	The education level for COPD in 2012		X	5
	The education level for DM in 2012		X	5
	The education level for HF in 2012		X	5
	The education level for COPD + DM in 2012		X	5
	The education level for COPD + HF in 2012		X	5

	The education level for DM + HF in 2012		X	5
	The education level for COPD + DM + HF in 2012		X	5
	The accessibility to healthcare for COPD in 2012		X	5
	The accessibility to healthcare for DM in 2012		X	5
	The accessibility to healthcare for HF in 2012		X	5
	The accessibility to healthcare for COPD + DM in 2012		X	5
	The accessibility to healthcare for COPD + HF in 2012		X	5
	The accessibility to healthcare for DM + HF in 2012		X	5
	The accessibility to healthcare for COPD + DM + HF in 2012		X	5
	The derived deprivation index for COPD in 2012		X	5
	The derived deprivation index for DM in 2012		X	5
	The derived deprivation index for HF in 2012		X	5
	The derived deprivation index for COPD + DM in 2012		X	5
	The derived deprivation index for COPD + HF in 2012		X	5
	The derived deprivation index for DM + HF in 2012		X	5
	The derived deprivation index for COPD + DM + HF in 2012		X	5
Past use of health resources Domain				
	Hospitalisation rate (per 1000), last 12 months	X	X	10

	Hospitalisation rate (per 1000), last 12 months, COPD	X	X	10
	Hospitalisation rate (per 1000), last 12 months, DM	X	X	10
	Hospitalisation rate (per 1000), last 12 months, HF	X	X	10
	Average length of stay (days), last 12 months	X	X	10
	Number of ED consultations, last 12 months	X	X	10
	Number of readmissions, last 12 months, COPD	X	X	10
	Number of outpatient visits, last 12 months	X	X	9
	Hospitalisation rate (per 1000), last 12 months, COPD + DM + HF	X	X	8
	Average length of stay (days), last 12 months, COPD + DM + HF	X	X	8
	Number of ED consultations, last 12 months, COPD + DM + HF	X	X	8
	Number of readmissions, last 12 months, COPD + DM + HF	X	X	8
	Number of visits to primary care, last 12 month	X	X	8
	Number of home visits, last 12 months	X	X	8
	Number of visits to primary care, last 12 months, PP [BAS]	X	X	8
	Number of outpatient visits, last 12 months, COPD + DM + HF	X	X	7
	Drug consumption last 12 months	X	X	7
	Hospitalisation rate (per 1000), last 12 months, COPD + DM	X	X	5

	Hospitalisation rate (per 1000), last 12 months, COPD + HF	X	X	5
	Hospitalisation rate (per 1000), last 12 months, DM + HF	X	X	5
	Average length of stay (days), last 12 months, COPD	X	X	5
	Average length of stay (days), last 12 months, DM	X	X	5
	Average length of stay (days), last 12 months, HF	X	X	5
	Average length of stay (days), last 12 months, COPD + DM	X	X	5
	Average length of stay (days), last 12 months, COPD + HF	X	X	5
	Average length of stay (days), last 12 months, DM + HF	X	X	5
	Number of ED consultations, last 12 months, COPD	X	X	5
	Number of ED consultations, last 12 months, DM	X	X	5
	Number of ED consultations, last 12 months, HF	X	X	5
	Number of ED consultations, last 12 months, COPD + DM	X	X	5
	Number of ED consultations, last 12 months, COPD + HF	X	X	5
	Number of ED consultations, last 12 months, DM + HF	X	X	5
	Number of readmissions, last 12 months, COPD	X	X	5
	Number of readmissions, last 12 months, DM	X	X	5
	Number of readmissions, last 12 months, HF	X	X	5

	Number of readmissions, last 12 months, COPD + DM	X	X	5
	Number of readmissions, last 12 months, COPD + HF	X	X	5
	Number of readmissions, last 12 months, DM + HF	X	X	5
	Number of visits to primary care, last 12 months, COPD + DM + HF	X	X	5
	Number of home visits, last 12 months, COPD + DM + HF	X	X	5
	The number of patients using ≥5 and <10 drugs, last 12 months, COPD + DM + HF	X	X	5
	The number of patients using ≥10 and <15 drugs, last 12 months, COPD + DM + HF	X	X	5
	The number of patients using ≥15 drugs, last 12 months, COPD + DM + HF	X	X	5

1.5 Conclusions

1.5.1 Population-based health risk assessment and stratification

1. A list of top indicators for population-based stratification can be realistically recommended, despite the reported high heterogeneity among regions. It is of note that most of the indicators are part of the "past use of health resources" domain, which implies a high weight of these variables on current stratification techniques.
2. Overlap between outcome indicators (WP7) and predictors for population-based stratification requires further analysis.
3. Reported information was not harmonized, such that comparisons across regions for the purposes of the current baseline analysis was not possible due to data heterogeneity (lack of common denominator and data aggregation following different criteria). An analysis of these limitations should be done. It may not necessarily mean lack of available information. However, harmonization of data is clearly requested for comparison purposes.

1.5.2 Patient-based health risk assessment and stratification

4. Although consensus on domains and sub-domains defining subject-specific stratification was achieved during the period, we concluded that a strategy aiming at identifying top indicators for patient-based health risk assessment and stratification, at the current stage of conceptual development, could likely generate unmanageable complexities and be unproductive.
5. The consortium acknowledges that, for the targeted chronic disorders, patients show marked heterogeneities both in terms of clinical manifestations and disease progress. It is fully accepted that disease heterogeneities have a significant influence on patient management and prognosis with a marked impact on the design of care coordination. Consequently, further debate on key conceptual aspects of coordinated care, namely: (i) disease-oriented versus patient-oriented coordinated care programs (or services); (ii) role of patient-based risk assessment and stratification in integrated care services; and, (iii) interplay and potential synergies between population-based and patient-based risk assessment, is needed in order to define operational aspects of patient-based risk assessment for clinical purposes.
6. The WP identified that an alternative approach was to build-up a strategy for subject-specific health risk assessment through the generation of a consensus report. As indicated in the current document, a patient-based stratification proposal should be closely linked to our understanding of the integrated care services and the corresponding workflow definitions.

1.6 Recommendations

Population-based risk assessment and stratification

- Generate consensus on a final list of top predictors after trimming for outcome indicators.

Actions:
1. Joint proposal from WP3, WP5 and WP7
2. Criteria for data harmonization before requesting information to regions
3. Debate in the General Assembly to reach consensus

Patient-based risk assessment and stratification

- Clarify conceptual aspects of patient-based stratification and its boundaries with population-based stratification

Action: Use Part II of the current document to generate a debate in the General Assembly

- Generate recommendations on patient-based risk assessment

Action: Produce a consensus document describing the roadmap toward operational patient-based stratification, as an intermediate step for future personalized care. The immediate step is to generate debate in the General Assembly on these prioritized areas, such that the two publishable consensus reports with proposals for the second period of the project, and beyond, can be produced and agreed with EIP-AHA within 2014.

2. Part II – Beyond ACT

The transition from current healthcare practice to novel modalities of care for chronic patients based on articulation of Integrated Care Services (ICS) with support of Information and Communication Technologies (ICT) is driven by three main forces: the epidemics of non-communicable diseases [2]; the need for containment of healthcare costs [3]; and, emerging concepts on chronic diseases leading to early preventive interventions based on enhanced knowledge on disease mechanisms [4], [5].

Some of the statements described below are well beyond short-term deployments in the clinical scenario and clearly pertain to the research domain. The purpose of this section is to highlight future healthcare directions and foster a double role for the ACT project. That is, (i) define strategies for a short-term the transition toward coordinated care at European level; and, (ii) indicate future long-term developments in terms of risk assessment and stratification policies. To this end, and to avoid confusing messages, the refinement of current population-based risk assessment tools is being analyzed in the different document (Annex D).

2.1 Recommendations for future coordinated care programs

We define an Integrated Care Service (ICS) [6] as a set of well standardized actions to be applied to each case on the basis of his/her predefined health condition and social circumstances. Each individual ICS targets specific objectives; and any given patient can be associated to one or more ICS [7]. Specific differential characteristics of an integrated care service (ICS), as compared to usual care, are: (i) patient centeredness; and, (ii) the longitudinal nature of the interventions which duration depends on the type of ICS.

The novel integrated care scenario, based on the articulation of different ICS covering the spectrum of severity and needs of chronic patients, has shown potential to enhance health outcomes with cost-containment [8]. These goals can be achieved through patient-based health risk assessment and stratification, such that patient care is delivered into the most appropriate healthcare tier. Overall, the integrated care approach favors the transfer of complex services from hospital-based specialists to the community that facilitates cost savings.

For extensive deployment, the ICS should be chosen because their adequate articulation can cover the longitudinal care requirements of the entire spectrum of severity of chronic patients. Consequently, they should not be envisaged as silos. ICS's effectiveness, complementarities, costs and barriers for adoption must be considered prior the process of deployment in a given healthcare sector.

Multi-morbidity, as the central biomedical problem, because of its high impact on healthcare and its potential for improvement if systems-oriented strategies are properly designed, requires patient centeredness of the healthcare design.

2.2 Health risk assessment and stratification

Current risk assessment approaches are based on past-use of healthcare resources as main predictors. It is hypothesized that future health risk assessment (subject-specific predictive modelling) will be based on the use multiple sources of information (multilevel omics, biological, physiological, clinical, behavioural, sociological and environmental) with a systems medicine approach, to anticipate, for the individual patient, the development or progression of disease.

One of the central objectives is to generate subject-specific predictive modelling for health risk assessment and stratification aiming at facilitating allocation of interventions in the most adequate layer. The approach includes the transfer of complex services to primary care and to the community, promoting a proactive role of the citizens/patients, as well as their participation in healthcare co-design.

It is accepted that, by stratifying populations according to each person's risk and anticipated response to an intervention, health systems could more effectively target different preventive interventions at particular risk strata. Consistent with the building-blocks approach proposed for integrated care deployment, patient stratification is envisaged as an optimal realistic strategy to pave the way for true personalized health.

Dynamic articulation between subject-specific risk assessment and stratification and population-based stratification is needed. The hypothesis is that by addressing both approaches (subject-specific and population-based) in a coordinated manner, we will be generating synergies and prevent some of the current limitations of available stratification tools.

2.3 Underlying mechanisms and biomedical assessment: need for a systems approach

Multi-morbidity should be considered as an expression of patients' heterogeneity. That is, well identified risk factors (tobacco, sedentarism, etc…) may not generate disease (i.e. asymptomatic smoker), may trigger one organ disease (i.e. chronic obstructive pulmonary disease, COPD) or, in some cases, may prompt two or more accompanying disorders (i.e. cardiovascular disorders, CVD, and/or type 2 diabetes mellitus). A proper understanding and management of multi-morbidity cannot be done with a disease-oriented approach, nor without taking into consideration the interactions between biology and environmental/risk factors. These two main limitations prompt the need for adopting a new paradigm to adequately understand and manage multi-morbidity.

Principles of network medicine (i.e. concept of endotypes) [9]–[11] need to be considered as a tool to overcome one major limitations in the understanding of complex chronic diseases. That is, current disease classification, as well as the analysis of disease heterogeneity (i.e. clinical phenotypes), is based on three elements: (i) identification of aetiology; (ii) clinical manifestations (signs and symptoms); and, (iii) specific diagnostic testing often organ-centered. But, it does not take into account the underlying mechanisms of disease at molecular level. Nor the potential combination of abnormalities in biological pathways (i.e. endotypes), that may be shared by different diseases. Thus, explaining multi-morbidity (refs). It is hypothesized that endotypes are the end result of complex interactions among: (i) genetic susceptibility; (ii) transcriptional regulation; and (iii) multilevel transcriptional regulatory phenomena wherein the interplay between subject and environment must be considered. Such a complexity explains the limitations of genomewide association studies (GWAS) in: (i) assessing patients' heterogeneity, as well as (ii) providing information on underlying mechanisms of disease [12].

The upcoming monograph [13] generated by the Synergy-COPD consortium analyses achievements/limitations and recommendations of the novel approach using COPD as a use case to address the analysis of both disease heterogeneity and multi-morbidity.

2.4 Transfer to healthcare

The design and validation of cost-effective preventive interventions based on subject-specific predictive modelling is a key component of future strategies for personalized care. The final aim is early detection and modulation of the progress of the phenomenon in order to reduce its burden on healthcare. Subject-specific predictive modelling should be used to feed clinical decision support systems (CDSS) embedded into ICT-supported integrated care clinical processes.

The personal health folder (PHF), articulated with regional ICT systems ensuring interoperability, will have a twofold core aim in the project: (i) to provide support to a proactive

role of citizens/patients on self-management [14]; and, (ii) to ensure interoperability between healthcare and informal care/social support.

Refinement of current regional models for population-based risk assessment and stratification is needed with inclusion of dynamic analysis of stratification. As indicated above, articulation of strategies for population-based and patient-based prediction of risk is a must.

The cross-talk between ICT-supported integrated care (healthcare and informal care) and systems-oriented biomedical research will also constitute a core component of the new model of care. To this end, further developments of the recently reported Digital Health Framework (DHF) (Cano I et al. Journal of Translational Research, late September 2014) [15] should be taken into account. Identification of indicators for continuous assessment of deployments (regional and healthcare sector level) of the novel approach should rely on the DHF concept further developed in Annex D and in [15].

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