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Annex D to Deliverable 3 :

WP5: Analysis of predictive modelling tools currently used in the ACT regions.

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1. Conceptual approach and scope of the document

It is well accepted that **Population-based health risk assessment and stratification** covers two principal needs:

Firstly, it is a key factor to describe and assess the health status of a population which constitutes a necessary step for the design of specific public health and healthcare programs in a given territory. To this end, **predictive risk models** are mathematical tools useful for descriptive and monitoring purposes.

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. In this area, predictive risk models have shown to be superior to other "case finding" approaches.

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.

Population-based predictive models should be considered an approach complementary to subject-specific predictive modelling. While the former (population-based) is ready for standardization and deployment at European level, the latter (patient-based) is focused on clinical use and it is rapidly evolving area that requires both debate and piloting before its extensive use to feed clinical decision support systems (CDSS) embedded into integrated care clinical processes. It is our understanding that patient-based risk assessment and stratification in the clinical area constitutes a high priority clinical research area that will foster the way toward predictive and personalized medicine.

The current document serves to two purposes. The principal goal is to perform an initial systematic analysis of the population-based risk assessment tools used in the 5 ACT regions that is displayed in this Annex. It should be the basis for further joint actions with the **B3 group of EIP-AHA** to propose standardization of the approach at European level within the lifetime of these initiatives: ACT and EIP-AHA. A secondary purpose is the identification of areas for further refinement of the current state of the art tools to be developed beyond the ongoing project. Part I of this document sequentially describes: (i) the method followed to perform the systematic comparison among the 5 ACT regions; (ii) the results of the comparisons; (iii) conclusions on the study; and, (iv) recommendations for actions within ACT.

Part II of Annex D describes areas for further developments beyond ACT considering an "ideal" integrated care scenario.

2. Part I – ACT project lifespan

A.1.1 Population-based risk assessment: method

The analysis of the main predictive tools currently used in the ACT regions is being carried out **jointly with the B3 group of the EIP-AHA (European Innovation Partnerships for Active and Healthy Ageing)**. The study has been undertaken following the systematic approach proposed by OPIMEC (http://www.opimec.org/).
The survey proposed by OPIMEC was administered to the current responsible persons for the predictive risk modelling tools in each of the 5 regions. The main categories assessed by the survey are described below. The analysis carried out aimed to cover the following items:

- Identify the usefulness of the OPIMEC survey to properly characterize the nature and potential of the predictive risk models analyzed
- Compare the approaches adopted in the 5 ACT regions. Identify commonalities and ongoing developments
- Generate recommendations to achieve specific outcomes within ACT lifetime
- Generate recommendations for further developments beyond ACT (Part II of the Annex)

The results of the current report will be the basis for debate in the General Assembly on September 2014. The consensus achieved in the General Assembly will conform the joint working program with the B3 group of the EIP-AHA to be formalized within 2014 and completed by Spring 2015.
Main dimensions of the predictive risk models assessed using the OPIMEC survey:

- Information of the person answering the survey and his/her institution
- General information on the model for risk assessment (name of the model, population-based or individual-based, etc …)
- Statistics of the predictive risk model: (i) statistical approach (logistic regression, linear regression, etc…); (ii) dependent variable (mortality, hospitalization, etc...); (iii) covariates (age, sex, previous history of hospitalization, location, etc...); (iv) statistics of adjustment (R, odds ratio, sensitivy and specificity, etc…)
- Characteristics of the population used to develop the predictive risk model
- Other sources of information to generate the model
- Characteristics of the target population and usefulness for the model application (periodicity of update, applicability in a given patient, etc.)

A.1.2 Results of the comparisons among the 5 ACT regions

Table 1 summarizes the main results of the comparison among the 5 ACT regions and **Table 2** indicates the stratification of the population in four risk categories for each ACT regions using the corresponding predictive risk model. Briefly, the description of main results is as follows:

- Formal population–based predictive risk models estimating risk of mortality and acute events that may generate emergency room admissions and unplanned hospitalizations are only provided by Basque Country [1] and Scotland [2] The statistics generated by the predictive risk models provide quantitative estimation of sensitivity and specificity. The outcomes of the two models are connected with the electronic health record for case finding purposes.
- Catalunya has a similar, but statistically less sophisticated, approach. The interplay with the clinical setting for case finding is fully operational. The Catalan setting (explicative model) is rapidly evolving toward a true predictive risk model showing some highly remarkable traits, namely: (i) It will be open source based which implies fully access to internal algorithms and low-cost maintenance; (ii) the approach is shared by the Spanish government and it will be likely extended to most of the regions; and, (iii) the future, short-term, interoperability setting (see Part II of the document) offers an appropriate scenario for dynamic update of predictive risk modelling and for synergistic interactions between population-based and subject-specific risk assessment and stratification.
- Groningen provided information on a promising evolving setting based on interoperability with electronic health records, but the region does not have predictive risk modelling in place
- Lombardia indicates that the program relies on stratification tools essentially built-up on healthcare cost categories; but, no detailed information was made available to properly assess the approach. In any case, it deserves further analyses but it does not seem transferrable to other European regions.
- The different regional approaches are based on past-use of healthcare resources and are focused on identification of subjects with high risk of presenting undesirable health events (case finding). A common problem is that dynamic update of the predictive risk models is not in place and strategies for its development seem not mature.

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Table 1. – Comparison of main characteristics of predictive risk tools among the 5 ACT regions

	Basque country (i)	Catalonia (ii)	Groningen (iii, iv, v)	Lombardy (vi)	Scotland (vii)
Model Aim	Predictive	Explanatory	Real life primary care database	Classification System	Predictive
Main dependent variables	Unplanned hospital days, Pharmascy expenditure, Health costs, Health resource consumption.	Unscheduled admission, Unscheduled re-admission, Length of unplanned Hospital stay, Death, Functional impairment Cognitive Disabilities , Pharmacy expenditure, Expenditure on labs Transport cost, Health cost consumption.	-	Hospital discharges codes and co-payment exemptions.	Unplanned hospital admission, Unplanned hospital readmission, Unplanned hospital days, Functional decline, Cognitive decline.
Independent variables	Age, Sex, Location, Diagnosis, Visits annual average, Urgent visits, dispensed drugs, Hospital stay, Number of hospitalizations, Number of outpatient visits, Co morbidity, polypharmacy.	Age, Sex, Location, Diagnosis, urgent visits, number of hospitalizations, co morbidity.	Stage of the disease, exacerbations, health status and asthma control	-	Age, Sex, Diagnosis, Dispensed drugs, Hospital stay, Number of hospitalizations, Number of outpatient visits, polypharmacy.
Sample size for building up the model	2'100.000	7'500.000	12.000	10'000.000	500.000
Mathematical model	Linear Regression and Logistic Regression models	Poisson regression model	McNemar test and paired t tests	This is a classification model	Logistic Regression model
Statistics to assess the model (viii)	RR, probability percentage, R^2, PPV, AUC	Probability percentage, IC	Probability percentage, CI	-	Odds ratio, PPV, NPV, Sensitivity, Specificity, AUC
Periodicity of updates	Annual	Semester	Daily	Once only	Monthly

	Basque country (i)	Catalonia (ii)	Groningen (iii, iv, v)	Lombardy (vi)	Scotland (vii)
Targeted population	2100000	7500000	1738	10'000.000	5'300.000
Population-based use	Selection of population for intervention	Informative and selection of population for intervention	Informative and education data collectors	Selection of population for intervention	Selection of population for intervention
Clinical use	All levels of care can see the same information	Used for clinical criteria of the end user, validation of patients by clinicians. All levels of care can see the same information	Only Pulmonologist can use for clinical criteria of the end user	Clinicians have the possibility to assess and validate the patients. All levels of care can see the same information. Used for Clinical criteria of the end user	Clinicians have the possibility to assess and validate the patients. All levels of care can see the same information

(i) Basque Country uses ACG-Predictive Modelling based on ACG (Adjusted Clinical Groups), which identifies self-exclusive patient categories, predicting Health Cost, Pharmacy Cost, and Hospital Admission Risk. (ii) Catalonia uses the CRG algorithm, measuring comorbidity populations: (a) Healthcare management (clinical efficiency) (b) economic management (payment adjustment based on territory). (iii) Groningen, in the COPD-Telehealth program, population is stratified using GOLD stratification. (iv) Groningen, in the Embrace program, INTERMED-Elderly Self-Assessment and Groningen Frailty Indicator, participants will be stratified into one of three strata: (A) robust; (B) frail; and (C) complex care needs. (v) Groningen, in the Effective-cardio program the tool used for stratifications the NYHA (where people in the II or more --> high risk). (vi) Lombardy, CReG Classification (Based on: drug exemption, hospital-based diagnosis and procedures, economic data, outpatient), primary care HER and drug prescription. (vii) Scotland, the regional tool used for stratification is Case finding tool for anticipatory care planning and case management, the SPARRA model. (viii) RR Relative risk, OR.- Odds ratio, R2.- coefficient of determination, PPV.- positive predictive value, NPV.- negative predictive value, IC.- interval of confidence, AUC.- area under the curve.

Table 2. – Stratification by health risk in the 5 ACT regions

	Basque Country		Catalonia		Groningen						Lombardy		Scotland	
	Region (i)		Region (ii)		Program (iii) (COPD TeleHealth)		Program (iv) (Embrace)		Program (v) (Effective-cardio)		Org. Unit (vi)		Region (vii)	
	N	%	N	%	n	%	N	%	n	%	n	%	n	%
Total population	1 915 938	100	7 803 747	100	2004	100	1 468	100	13 000	100	12 707	100	4 257 390	100
Number of patients Level I (high risk)	28 341	1,5	’	-	480	24	858	58,4	9 100	70	801	6,3	31 300	0,7
N - Level II (High-moderate risk)	135 750	7,0	‘	-	155	7,7	241	16,4	not applicable	-	6 886	54,2	83 650	2
N - Level III (Low-moderate risk)	541 974	28,3	‘	-	797	39,7	not applicable	-	not applicable	-	5 020	39,5	284 800	6,7
N. Level IV (Low risk)	120 9873	63,2	2 340 558	30	572	28,5	369	25,1	3900	30	3 124	24,6	3 857 640	90,6

[i] Basque Country uses ACG-Predictive Modelling based on ACG (Adjusted Clinical Groups), which identifies self-exclusive patient categories, predicting Health Cost, Pharmacy Cost, and Hospital Admission Risk, [ii] Catalonia uses the CRG algorithm, measuring comorbidity populations: (i) Healthcare management (clinical efficiency) (ii) economic management (payment adjustment based on territory), [iii] Groningen, in the COPD-Telehealth program, population is stratified using GOLD stratification, [iv] Groningen, in the Embrace program, INTERMED-Elderly Self-Assessment and Groningen Frailty Indicator, participants will be stratified into one of three strata: (A) robust; (B) frail; and (C) complex care needs, [v] Groningen, in the Effective-cardio program the tool used for stratifications the NYHA (where people in the II or more --> high risk), [vi] Lombardy, CReG Classification (Based on: drug exemption, hospital-based diagnosis and procedures, economic data, outpatient), primary care HER and drug prescription, [vii] Scotland, the regional tool used for stratification is Case finding tool for anticipatory care planning and case management

A.1.3 Conclusions

Both concept and roles of population-based stratification show a high degree of maturity. Appropriate statistical tools and current challenges of this type of risk assessment were identified. In summary, it seems timely to generate recommendations, within the ACT lifespan, aiming to standardize population-based risk assessment at European level.

A.1.4 Recommendations

Generate a consensus document within 2014 producing: (i) recommendations for standardization of predictive risk modelling; and, (ii) piloting selected risk assessment tools at European level.

Actions:
1. Debate of the topic in the General Assembly
2. Define short-term joint actions with the B3 group of EIP-AHA
3. Produce the draft consensus document within 2014 for external review
4. Generate a final document within Spring 2015

3. Part II – Beyond ACT

A.1.5 Recommendations for future programs

Two important future challenges, beyond the project life span, are: (i) to implement dynamic population-based stratification; and, (ii) to foster synergies between population-based and patient-based stratification.

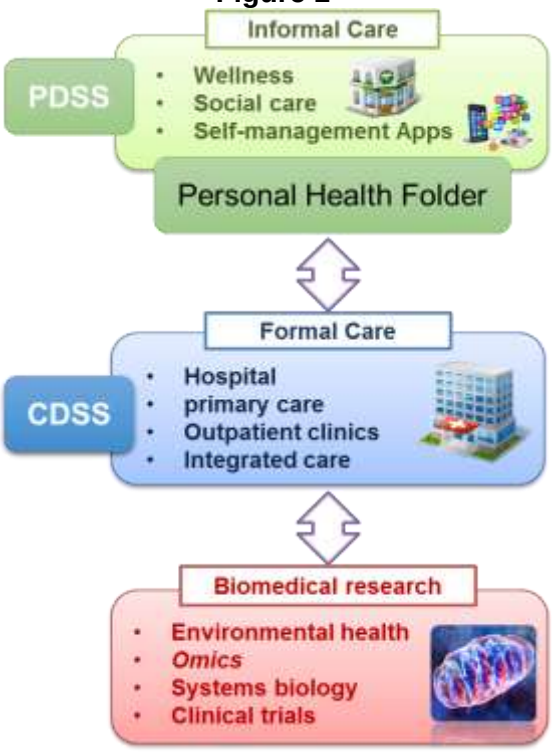
Dynamic articulation between subject-specific risk assessment and stratification and population-based stratification is needed. The hypothesis is that by addressing both approaches (subject-specific and population-based) in a coordinated manner, we will be generating synergies and prevent some of the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

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) [3] should be taken into account to facilitate continuous assessment as part of the novel healthcare model.

The concept of Digital Health Framework (DHF) (Figure 1) emerged from the Synergy-COPD project (2011-14) to foster adoption of predictive medicine that can be applied to the individual patient. The DHF consists of the articulation of open and modular ICT-platforms supporting organizational interoperability, and appropriate functionalities, among three main areas, namely: i) informal care, ii) formal care, and, iii) biomedical research. Briefly, informal care includes any aspect with impact on health (e.g. life style, environmental and behavioral aspects, etc.) occurring in the community, whereas formal care refers to any interaction with health professionals at any level of the healthcare system. Biomedical research refers to all research levels from bench to clinical and to public health. Our vision with the DHF is therefore to devise computer-based methods to bring research to clinical applicability at the individual patient level, both in the general community and when patients see healthcare professionals. To materialize such an ambitious vision, a building block approach is considered necessary. The progress from the initial proof-of-concept to pilot implementation and to extensive deployment shall be planned following a stepwise strategy.

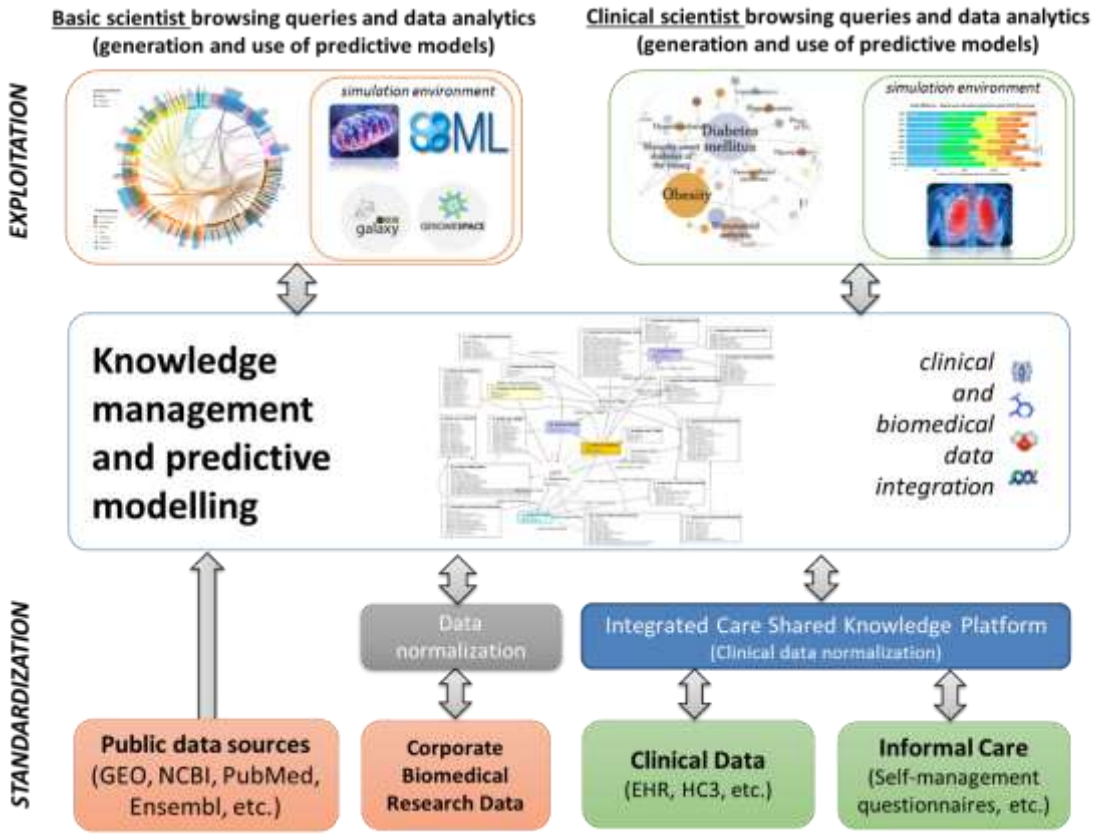
The first building-block was the design and initial deployment of an Integrated Care Shared Knowledge Platform supporting Integrated Care Services (ICS) for chronic patients [4], as part of the EU project NEXES, from 2008 to 2013. During the life span of NEXES, a Personal Health Folder (PHF) was successfully piloted [5], as a supporting tool to achieve long-term sustainability of training-induced effects and promote active life styles in COPD patients. The PHF constitutes the second building block as a tool to integrate informal and formal care in community-based ICS for frail chronic patients. Moreover, the Clinical Decision Support Systems (CDSS) generated during the Synergy-COPD lifetime has been integrated into the platform supporting ICS. Consequently, the interplay between the first two building blocks (informal and formal care) is operational in a controlled deployment scenario and is currently evolving toward maturity. We shall keep in mind, however, that active citizens/patients together with a prepared multidisciplinary health workforce will be the real key drivers of the transition from current healthcare practice to full deployment of predictive medicine for chronic patients. The current report focuses on the third building block of the DHF, tackling biomedical research (DHF-research), as pictured in Figure 2.

Figure 1



The concept of Digital Health Framework covers the different areas wherein information can be obtained and actions are taken: i) informal care, ii) formal care, and, iii) biomedical research. In this scenario, a personal health folder incorporating patient decision support systems (PDSS) might facilitate the incorporation of data coming from informal care into formal healthcare. In addition, biomedical research, referring to all research levels from clinical to basic research, should be shaped to provide user-profiled functionalities such that research professionals with different profiles can make use of clinical and biomedical knowledge from formal healthcare and heterogeneous biomedical research data sources, ultimately leading to the generation of novel rules that should feed in-place clinical decision support systems (CDSS).

Figure 2



DHF-research components and functionalities include semi-automatic data standardization approaches, data integration and knowledge management, profile-specific visual data mining portals and user-profiled simulation environments (see Cano I et al Journal of Translational Research Sept 2014 for further details) (currently in press – the full text can be made available).

4. References

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