1. Publishable summary

Project Context
TRANSFoRm aims to develop the technology that facilitates a learning healthcare system. Three carefully chosen clinical use cases will drive, evaluate and validate the approach to the ICT challenges of embedding diagnostic decision support and clinical trial workflow into the EHR and providing a secure infrastructure for large scale genotype-phenotype studies using primary care data. The project builds on existing work at international level in clinical trial information models (BRIDG and PCROM), service-based approaches to semantic interoperability and data standards (ISO11179 and controlled vocabulary), data discovery and machine learning. The approach to system design is modular and standards-based, providing services via a distributed architecture. The project is half way through four years of development and testing and will end with a fifth year dedicated to summative validation of the project deliverables in the Primary Care setting.

Figure 1 - Concept of TRANSFoRm

The TRANSFoRm project is based around the achievement of 12 core outputs that are essential to project impact. Progress towards these outputs is linked to deliverables over the 5 years of the project, some relating to individual work tasks, others to the result of a series of work tasks.
Principal project outputs

1. **SEMANTIC MEDIATOR** A web-service for terminology mapping available for this and similar projects (WT 7.2). This is an essential component of the system for semantic mediation of data at the point of care. TRANSFoRm will NOT be aiming to create and manage a mapping of minimum datasets for interoperability but will be working with the extension of already maintained reference terminology (via UMLS), presented as a service throughout the project infrastructure.

2. **PRIVACY MODEL** A generalizable model for privacy based on EU data protection laws (WT 3.1, 3.2). This model will underpin the operation of the security framework and implementation as well as the flow of data and authorization of access to data in the system.

3. **PROVENANCE** A service for managing provenance of EHR data obtained for research purposes (WT 5.4) is essential for validating data quality and auditing compliance with the privacy framework.

4. **DATA QUALITY** A model for assessing data quality in EHR systems and repositories with a tool for applying it (WT 5.1) is an essential part of validating the re-use of clinical data for research purposes.

5. **SQA AND INTEGRATION** Satisfactory Quality Assurance and software integration and testing procedures to enable use in research settings (WT3.5).

6. **EXPLOITATION** A technical exploitation and business model for the further development of the DSS proof-of-concept and research systems into use within European EHR systems (WT 9.1)

7. **CLINICAL PREDICTION RULE WEB SERVICE** A web service for clinical prediction rules (CPR), based on an ontological representation of clinical cues and differential diagnoses arising from a presenting clinical problem (WT 4.4).

8. **RESEARCH DATA INFORMATION MODEL** A standard for a computable representation of the operational elements of a clinical study protocol (WT 6.5, 6.6). This enables an xml document to be authored using a semantic research workbench that binds selected terms provided by the terminology service to a data model. The document will contain all the elements necessary to transact a study (eligibility criteria, data elements, timelines and interventions).

9. **ELECTRONIC CASE REPORT FORM (eCRF)** An interface for integrating clinical prediction rule data capture and research data element capture (via a functional eCRF) into the EHR. This is a common process and consists of both a functional prototype and a set of specifications for implementing in an existing EHR framework (WT 5.2, 5.3, 7.4).

10. **DATA FEDERATION** Middleware for transacting research workflow in distributed heterogeneous EHR systems and data repositories (WT 7.2).

11. **RESEARCH EVALUATIONS** Research papers in major journals describing well-designed and adequately powered evaluations of the use of the software tools (WT 1.4,1.5)
12. DECISION SUPPORT PROTOTYPE  
Research papers describing well-designed experiments to design and evaluate a pilot decision support service for diagnosis that integrates with clinical cognitive workflow (WT 2.2, 2.3, 2.5).

Description of work since the beginning of the project

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Figure 2: Projected progress of deliverables towards project outcomes

Figure 2 details the projected progress of deliverables towards project outcomes. During the first year of the project, initial contacts and a survey of capacity to conduct the research evaluations were carried out (D1.1, D6.1). A review of EU data protection was used to develop a privacy framework (D3.2) and subsequent security framework (D3.3). A Provenance model was developed and adopted (D3.1).

During year two the Milestone 4, which had been resubmitted after year one as a deliverable (Software Quality Assurance Plan), was used to develop a draft software integration plan (D3.4). An exploitation strategy (D9.1) has been developed and will be maintained throughout the project. A Clinical Research Integration Model (D6.2) has been developed and used along with the Clinical Data Integration Model (Milestone 6), to drive a data search and query workbench (D5.3) that integrates the project terminology service developed in year one. A provenance tool (D5.2) has been developed that uses the framework from year one. Project overall outcomes 2: SQA and Integration Plans, 10: Provenance Tool and 11: Research Data Model have been achieved this year (see Figure 2 above).

During year three work progressed towards the three use cases. For the phenotype-genotype study, D6.3 (clinical data integration model) has developed an ontology.
(Milestone 8), used by the workbench to enable data extraction from clinical data warehouses. This is supported by D5.1 (Data quality assessment tool) (Milestone 7), enabling the selection of practice sites within the data warehouse with appropriate quality. The GPRD RCT has now been agreed in five EHR systems in five member states, and work is progressing to implement embedded eCRFs in these systems, along with mobile Patient Related Outcome Measures, using CDIM as part of the semantic integration approach. A plan for the evaluations of both these use cases has been developed. Finally D2.1 has shown that in the UK, suggesting possible diagnoses leads to an improvement in diagnostic accuracy, whilst in Greece, both suggesting and a later alert can improve diagnosis (Milestone 10). Work is now progressing with one vendor to develop a prototype decision support system using the ontology of clinical prediction rules (Milestone 9).

During year 4, we completed the technical work of the project, consisting of three configurations to serve the Learning Healthcare System 1. The infrastructure for genotype-phenotype studies using linked genetic and routine GP data, 2. The integrated eCRF (D5.4a) and PROM (D5.5) system for the GORD RCT. (Milestone 12). 3 The functional prototype DSS integrated with the InPS EHR system (D5.4b) and Milestone 11. All three software configurations, and the underlying infrastructure (D7.1, 7.2, 7.3) were deployed for validation with the pilot vendor/site (NIVEL, MicroHis, InPS). The DSS was integrated with its underlying ontology service (D4.1). An evaluation of the ‘database’ configuration for the purposes of finding subjects for a clinical trial has been carried out by Quintiles using a Bristol-Myers-Squibb diabetes study and the NIVEL dataset. (D8.1)

During year 5 we completed the deployments and moved to full scale evaluation with four more sites for the genotype-phenotype study (Belgium-String of pearls, UK-CPRD, Greece-UoC, Scotland-GoDarts) and four more GORD sites (UK-TPP, Poland-Asseco, Greece- UoC, Belgium-Crossuite). Ethical and data agreements were completed. Regarding the genotype-phenotype study, we did not deploy the system in Greece as every clinic in the UoC system had a different configuration. In the UK one EHR vendor was very delayed on account of differences between test and deployed systems, so although we completed deployment, there was no longer time to recruit subjects. Crosssuite did not have any running EHR systems by year 5, so we substituted another UK vendor (InPS). Evaluations of the genotype-phenotype and GORD configurations were competed as planned (D1.2 and D1.3). Quintiles completed a successful demonstration of export of CDISC standardized data from TRANSFoRm to a commercial electronic remote data capture system (D8.2). Evaluation of the prototype DSS system was completed using General Practitioners and actors as simulated patients (D2.2). Final reports on exploitation (D9.2) and dissemination (D9.3) have been completed.

**Description of the main results achieved**

**Deliverables:**

D1.1 RCT and Genotype-phenotype use cases (M6)
D1.2 Final validation of the feasibility of TRANSFoRm to deliver the genotype-phenotype study (M66)
D1.3 Final validation of the feasibility of TRANSFoRm to deliver the GORD RCT (M69)
D2.1 Most promising type of support for diagnosis (M39)
D2.2 Final validation of prototype DSS (M66)
D3.1 Provenance Model (M12)
D3.2 Report on regulatory requirements, confidentiality and data privacy issues (M12)

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The aim of TRANSFoRm is to develop a ‘rapid learning healthcare system’ driven by advanced computational infrastructure that can improve both patient safety and the conduct and volume of clinical research in Europe. The EU policy framework for information society and media, i2010, identifies eHealth as one of the principal areas where advances in ICT can create better quality of life for Europe’s citizens. ICT has important roles in communication, decision-making, monitoring and learning in the healthcare setting. Providing interoperability between different clinical systems, across national boundaries, and integration of clinical systems and research systems lies at the heart of the eHealth Action Plan, 2004. This is however, a two-way street, just as clinical data are needed for research (for participant identification and evaluation of outcomes), research data is needed to support clinical care. Furthermore, advances in the understanding of clinical judgment and decision making, and the possible ways of supporting them via ICT can inform the design of more ‘intelligent’ electronic health record systems. The TRANSFoRm project will achieve its impact via exploitation of the principal study outputs listed above. Work Package 9: Dissemination and Exploitation will lead the engagement of exploitation partners throughout the project and be responsible for the creation and maintenance of an exploitation strategy, which was delivered in the 2nd year.

**Expected final results and their potential impact and use**

The aim of TRANSFoRm is to develop a ‘rapid learning healthcare system’ driven by advanced computational infrastructure that can improve both patient safety and the conduct and volume of clinical research in Europe. The EU policy framework for information society and media, i2010, identifies eHealth as one of the principal areas where advances in ICT can create better quality of life for Europe’s citizens. ICT has important roles in communication, decision-making, monitoring and learning in the healthcare setting. Providing interoperability between different clinical systems, across national boundaries, and integration of clinical systems and research systems lies at the heart of the eHealth Action Plan, 2004. This is however, a two-way street, just as clinical data are needed for research (for participant identification and evaluation of outcomes), research data is needed to support clinical care. Furthermore, advances in the understanding of clinical judgment and decision making, and the possible ways of supporting them via ICT can inform the design of more ‘intelligent’ electronic health record systems. The TRANSFoRm project will achieve its impact via exploitation of the principal study outputs listed above. Work Package 9: Dissemination and Exploitation will lead the engagement of exploitation partners throughout the project and be responsible for the creation and maintenance of an exploitation strategy, which was delivered in the 2nd year.

**Project logo**

TRANSFoRm

**Project public website**

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