# Project Publishable Summary

**Grant Agreement number: 305930**

**Project acronym: SENATOR**

**Project title: Development and clinical trials of a new Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons**

**Funding Scheme: Collaborative Project (small-or medium-scale focused research project)**

**Date of latest version of Annex I against which the assessment will be made: 02.07.2016**

**Periodic report: 1st ☐ 2nd ☐ 3rd ☒ 4th ☐**

**Period covered: from 1 October 2015 to 31 March 2017**

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# Section 1 - Publishable summary

## SENATOR

**Logo:** 


**Project title: Development and clinical trials of a new Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons**

**Website:** http://www.senator-project.eu/home/

**Contractors involved (SENATOR consortium):**

The project is coordinated by Prof. Denis O´Mahony [CR01] UCC (SENATOR) University College Cork, Ireland, Address of the Coordinator: UCC Medical School, Cork University Hospital, Wilton, Cork, Ireland, T12DC4A.

**Other partners and team leaders:**

| Beneficiary number | Beneficiary Name | Acronym | Team leader |
|---|---|---|---|
| 03 | Ghent University Hospital | UGENT | Prof. Mirko Petrovic |
| 04 | Clanwilliam Health® Health Limited (formerly Helix Health Ltd®), Dublin | Clanwilliam Health® | Mr. Joseph McMullin |
| 05 | Hospital Universitario Ramōn y Cajal, Madrid | SERMAS | Dr. Alfonso Cruz-Jentoft |
| 06 | Instituto Nazionale di Riposo e Cura per Anziani, Ancona | INRCA | Prof. Antonio Cherubini |
| 07 | Health Economics Consulting, Norwich Medical School, University of East Anglia | UEA | Prof. Richard Fordham |
| 08 | Landspitali University Hospital, Reykjavik | LUH | Prof. A. Gudmundsson |
| 11 | ClinInfo® S.A., Lyon | CLIN | Mr. Philippe Foerster |
| 12 | Grampian Health Board, Aberdeen | NHSG | Dr. Roy Louis Soiza |
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## 1.1 Summary description of project context and objectives

Multi-morbidity, i.e. multiple simultaneous medical conditions, increases steadily in prevalence beyond the age of 70 years. Multi-morbidity is a strong predictor of multiple medications, so-called polypharmacy (PP), which is recognised as the single greatest risk factor for adverse drug reactions (ADRs) and prescribing of potentially inappropriate medications (PIMs) in older people. The rising incidence of serious ADRs is now a recognised serious public health problem, with very serious implications for morbidity, mortality and health budgets in ageing societies. ADRs are particularly problematic in hospital for older people, where approximately 1/4 have ADRs at admission, 6% of acute admissions result directly from ADRs, and a further 6% - 21% suffer new ADRs during hospitalization. Together with the high rates of over-use and inappropriate use of drug therapy in these older patients, under-use of non-drug therapies (physiotherapy, occupational therapy, speech & language therapy, nutritional therapy etc.) is increasingly recognised. Despite these problems, there are no widely used methodologies for optimising drug and non-drug therapy in hospitalised older people. Valid and effective interventions are needed for assisting clinicians who are not specialised in Geriatric Medicine & Rehabilitation to optimise drug and non-drug therapies in the expanding multi-morbid older population. The central aims of this study are to:

- Develop a highly-powered and efficient software engine (SENATOR) capable of individually screening the

clinical status and pharmacological and non- pharmacological therapy of older people with multi-morbidity in order to define optimal drug therapy, highlight ADR risk, indicate best value drug brand for selection and provide advice on appropriate non-pharmacological therapy.

- Perform a multi-centre randomised controlled clinical trial (RCT) in older people with multi-morbidity admitted to hospital with acute unselected illness under the care of specialists other than geriatricians and clinical pharmacologists to examine the efficacy of SENATOR in reducing ADRs, inappropriate prescribing and healthcare costs in this age group. The RCT will also examine, as a proof-of-concept exercise, whether SENATOR's non-pharmacological therapy optimisation advice prompts the clinician to refer patients in the intervention arm for appropriate non-pharmacological therapies compared to control patients receiving standard care.
- Assess the cost-effectiveness of SENATOR-guided optimisation of drug and non-drug therapy compared to standard care in older hospitalised people.
- Assess the impact of the SENATOR intervention on the quality of life of older people after they are discharged from hospital following acute illness.
- Develop SENATOR as a commercial software product for the healthcare software market, if the previous work can show that SENATOR (a) improves clinical outcomes in older people and (b) reduces overall healthcare costs.
- The main objectives of the project are:
- To devise and validate a new ADR Risk scale in Older People (ADRROP) to help identify older people at higher risk from ADRs.
- To devise a database compendium of Optimal evidence-based Non-pharmacological Therapies in Older People (ONTOP) to complement pharmacological therapy.
- To design and validate a Software ENgine for the Assessment and optimisation of pharmacological and non-pharmacological Therapy in Older peRsons with multi-morbidity (SENATOR).
- To assess the clinical value of SENATOR in a population of hospitalised older people with chronic multi-morbid illness compared to current standard clinical care delivered by clinical staff who are not specialized in Geriatric Medicine. For proper assessment of SENATOR, a multi-centre randomized controlled clinical trial is clearly required.
- To assess the economic value of SENATOR deployment compared to current standard clinical care.
- To develop the SENATOR electronic tool as a commercial software product.

## 1.2 Work performed since the beginning of the project and the main results achieved so far

**WP01** (Adverse Drug Reaction Risk in Older People: ADRROP): The revision of ADRROP awaits the completion of Phase II of the SENATOR trial. The first iteration of the ADRROP scale indicates modest ADR prediction. The hope is that with high precision ADR definition in Phase II in approximately 1800 patients, the ADR predictive capability of a revised, updated ADRROP will be improved.

**WP02** (Definition of Optimal Evidence-Based Non-drug Therapies in Older People (ONTOP)):

The ONTOP work has progressed significantly, such that the ONTOP non-pharmacological treatment recommendations for 11 conditions have now been completed. There are now 9 full publications in peer reviewed international journals arising from the ONTOP work to date.

**WP03** (SENATOR Single Drug File): The SENATOR Drug File was completed at the time of the previous periodic report (36 months). The Drug File remains under ongoing review and updated versions of the Drug File are provided promptly to Clanwilliam Health® for rapid integration into the SENATOR software when required. So far, no major problems have emerged with the Drug File.

**WP04** (SENATOR software): Prior to the start of SENATOR Phase II (randomisation phase) in July 2016, all software testing and validation was completed satisfactorily i.e. June 2016.

**WP05** (SENATOR software validation): SENATOR software has been validated successfully as per work package description; the level of agreement between SENATOR software and a pair of clinicians with expertise in geriatric

pharmacotherapy (Gold Standard) was very high (kappa value = 0.823). Software validation was completed in July 2016.

**WP06** (SENATOR translation): This WP was completed in September 2015.

**WP07** (Trial Organisation & Governance): This WP was completed in July 2016.

**WP08** (SENATOR clinical trial): SENATOR Phase II commenced in Cork on July 28, 2016. The other 5 clinical sites initiated randomisation in a phased basis such that all sites were actively recruiting by the end of 2016 (delays were incurred in 2 sites because of recruitment staffing issues). By 31st March 2017 (month 54), 722 patients had been randomised out of a total of 6954 patients screened for possible study entry. The total number of SENATOR intervention patients was 355, the total number of control patients was 367.

**WP09** (Ethics & Safety Monitoring): During this period, the ESRG has reviewed site initiation checklists, site monitoring visits and deleterious event forms from all the study sites for the duration to date of Phase II of SENATOR. Source data verification identified minor errors in data entry. The third ESRG report to the Scientific Advisory Board (i.e. Deliverable 9.4) has been submitted the EC (May 2017).

**WP10** (Data Management): The adapted on-line electronic case report form (eCRF) for Phase II went 'live' in June 2016, some weeks in advance of randomisation of the first patient in Phase II in Cork. The intervening weeks were spent dealing with technical issues relating to the ICT interface between SENATOR software and the eCRF, and checking that test SENATOR advice reports being generated were accurate and appropriate. Testing and verification of transfer of data from the eCRF to the data storage facility in the UCC Clinical Research Facility was also finalised during this reporting period.

**WP11** (Economic Analysis): The model for calculating the economic impact of SENATOR software within the context of randomisation Phase II has been finalised and tested in the patients randomised in the first 3 months of Phase II i.e. July to October 2016. Overall, the economic analysis model is working satisfactorily. Moreover, this preliminary analysis has provided very important insights into the sensitivity analysis of the completed data set that is planned after data collection is completed.

**WP12** (Project Management, Communication & Dissemination): All work package data sets as they are completed are being presented at mainstream international scientific meetings and subsequently prepared in manuscript format for submission to relevant peer-reviewed international journals with a view to publication.

## 1.3 The expected final results and their potential impact and use (including the socio-economic impact and the wider societal implications of the project so far)

In the original FP7 HEALTH 2012: 2.2.2.2-2 research call, there were three main expected impacts from funded projects i.e.

(i) treatments better suited to the needs of older people,

(ii) a capacity for lowering health care costs and

(iii) engagement in the pre-normative setting of geriatric medicines.

In relation to these expected impacts, the SENATOR project now embarked on the randomization Phase II of the SENATOR trial which will determine the efficacy of the planned intervention (the SENATOR software-driven medication review). Significant project outputs at 54 months with potential impact and practical use include:

(A). Further ONTOP publications

Further peer-reviewed ONTOP publications have been achieved in this reporting period, adding to the compendium of up-to-date evidence-based non-pharmacological therapies of the core important conditions most commonly experienced by older people. Published papers between month 36 and month 54 include:

1. Abraha I, Rimland JM, Trotta FM, Dell'Aquila G, Cruz-Jentoft A, Petrovic M, Gudmundsson A, Soiza R, O'Mahony D, Guaita A, Cherubini A. Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia. The SENATOR-OnTop series. BMJ Open. 2017 Mar 16;7(3):e012759. doi: 10.1136/bmjopen-2016-012759. PubMed PMID: 28302633; PubMed Central PMCID: PMC5372076.
2. Abraha I, Rimland JM, Trotta F, Pierini V, Cruz-Jentoft A, Soiza R, O'Mahony D, Cherubini A. Non-

Pharmacological Interventions to Prevent or Treat Delirium in Older Patients: Clinical Practice Recommendations The SENATOR-ONTOP Series. J Nutr Health Aging. 2016;20(9):927-936. PubMed PMID: 27791223.

3. Rimland JM, Abraha I, Dell'Aquila G, Cruz-Jentoft A, Soiza R, Gudmusson A, Petrovic M, O'Mahony D, Todd C, Cherubini A. Effectiveness of Non-Pharmacological Interventions to Prevent Falls in Older People: A Systematic Overview. The SENATOR Project ONTOP Series. PLoS One. 2016 Aug 25;11(8):e0161579. doi: 10.1371/journal.pone.0161579. eCollection 2016. PubMed PMID: 27559744; PubMed Central PMCID: PMC4999091.
4. Lozano-Montoya I, Vélez-Díaz-Pallarés M, Abraha I, Cherubini A, Soiza RL, O'Mahony D, Montero-Errasquín B, Correa-Pérez A, Cruz-Jentoft AJ. Nonpharmacologic Interventions to Prevent Pressure Ulcers in Older Patients: An Overview of Systematic Reviews (The Software ENgine for the Assessment and optimization of drug and non-drug Therapy in Older peRsons [SENATOR] Definition of Optimal Evidence-Based Non-drug Therapies in Older People [ONTOP] Series). J Am Med Dir Assoc. 2016 Apr 1;17(4):370.e1-10. doi: 10.1016/j.jamda.2015.12.091.Epub 2016 Feb 5. Review. PubMed PMID: 26857298.

(B). Completed Drug File

The Drug File represents the up-to-date collection of all available pharmaceutical products available in all 6 participating countries. The Drug File is being monitored and amended regularly to ensure that it encompasses all new mainstream drug products entering the market in any of the 6 clinical sites.

(C). SENATOR software completed, translated, functioning and validated

The SENATOR software development has been completed, translated into Spanish, Italian, Dutch and Icelandic, and fully validated against a Gold Standard of clinical case assessment by a pair of trained clinicians with expertise in geriatric pharmacotherapy. The level of agreement between SENATOR software and the pair of expert clinicians was highly satisfactory, such that the SENATOR software was deployable at all clinical sites for commencement of Phase II of SENATOR.

(D). SENATOR Phase II (randomisation phase) in progress

SENATOR Phase II has commenced during this reporting period and at the time of submitting the present report is approaching the halfway stage of the target number of 1800 patients. The SENATOR software is working well in all clinical sites in that SENATOR prescription advice reports are being generated quickly and efficiently, and presented without delay to the attending doctors of the patients in the intervention arm of the trial. In this sense, the drug prescription optimisation system based on the SENATOR-driven medication review is working very efficiently.