FP7-ICT-611140 CARRE

Project co-funded by the European Commission
under the Information and Communication Technologies
(ICT) 7th Framework Programme

D.2.2. Functional Requirements & CARRE Information Model

DUTH, VULSK, OU

June 2014

October 2015

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Disclaimer

CARRE is a Specific Targeted Research Project partially funded by the European Union, under FP7-ICT-2013-10, Theme 5.1. “Personalized health, active ageing & independent living”.

Document Control Page

Project

Contract No.:	611140
Acronym:	CARRE
Title:	Personalized Patient Empowerment and Shared Decision Support for Cardiorenal Disease and Comorbidities
Type:	STREP
Start:	1 November 2013
End:	31 October 2016
Programme:	FP7-ICT-2013.5.1
Website:	http://www.carre-project.eu/

Deliverable

Deliverable No.:	D.2.2
Deliverable Title:	Functional Requirements & CARRE information model
Responsible Partner:	DUTH – Eleni Kaldoudi
Authors:	E. Kaldoudi, A. Third, G. Gotsis, S. Roumeliotis, N. Karvelyte N., L. Rimsevicius, K. Pafili., D. Papazoglou, G Juozalenaite., E. Semertzidou, Z. Visockiene, K. Zigeridou
Input from:	All partners
Peer Reviewers:	E. Liu (BED), D. Stundys (VULSK), J. Piwinski (PIAP), A. Third (OU)
Task:	T.2.2. Functional Requirements & CARRE information model
Task duration:	5 months: 1 Feb 2014 to 30 Jun 2014
Work Package:	WP2: Domain analysis, requirements and design
Work Package Leader:	DUTH – Eleni Kaldoudi
Due Date:	30 June 2014
Actual Delivery Date:	9 July 2014
Dissemination Level:	PU
Nature:	R & Web Demonstrator
Files and format:	Deliverable report: 1 pdf file Software: CARRE Risk Model Semantic Data Entry System http://entry.carre-project.eu
Version:	05 – update #2 (31 Oct 2015) on the submitted version 03 (9 July 2014).
Status:	☐ Draft ☒ Consortium reviewed ☒ WP leader accepted ☒ Coordinator accepted ☒ EC accepted

Document Revision History

Version	Date	Modifications	Contributors
v01.1	07 May 2014	new content – outline	Eleni Semertzidou Eleni Kaldoudi
v01.2	10 Jun 2014	Introduction Functional units Comorbidities conceptual model	Eleni Kaldoudi Eleni Semertzidou input from Technical meeting in London 6-7 May 2014
v02	24 Jun 1204	editing, figures Appendices	Eleni Kaldoudi Koula Zigeridou all authors
v03	09 Jul 2014	revised version based on reviews	Eleni Kaldoudi
v04	31 Oct 2014	Annex 2 updated	all DUTH and VULSK deliverable authors
v05	31 Oct 2015	Annex 2 updated	all DUTH and VULSK deliverable authors

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Executive Summary

The deliverable will contain a report on functional requirements and the corresponding CARRE information model. The deliverable also includes major risk factor associations and their descriptions, including descriptions on respective risk elements, observables, and evidence sources.

About CARRE

CARRE is an EU FP7-ICT funded project with the goal to provide innovative means for the management of comorbidities (multiple co-occurring medical conditions), especially in the case of chronic cardiac and renal disease patients or persons with increased risk of such conditions.

Sources of medical and other knowledge will be semantically linked with sensor outputs to provide clinical information personalised to the individual patient, so as to be able to track the progression and interactions of comorbid conditions. Visual analytics will be employed so that patients and clinicians will be able to visualise, understand and interact with this linked knowledge and also take advantage of personalised empowerment services supported by a dedicated decision support system.

The ultimate goal is to provide the means for patients with comorbidities to take an active role in care processes, including self-care and shared decision-making, and also to support medical professionals in understanding and treating comorbidities via an integrative approach.

Terms and Definitions

The following are definitions of terms, abbreviations and acronyms used in this document.

Term	Definition
API	Application programming interface
BMI	Body mass index
DOI	Digital Object Identifier: a unique alphanumeric string assigned by a registration agency (the International DOI Foundation) to identify content and provide a persistent link to its location on the Internet.
DoW	Description of Work
HR	Hazard ratio
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision, http://www.who.int/classifications/icd/en/
ID	Identification number
ISO/IEC/IEEE 29148:2011	International Standard: Systems and software engineering – Life cycle processes – Requirements engineering. First edition, 01-12-2011 - contains provisions for the processes and products related to the engineering of requirements for systems and software products and services throughout the life cycle
LOD	Linked Open Data cloud
MedLinePlus	The National Institutes of Health's Web site for patients and their families and friends, http://medlineplus.gov
MeSH	Medical Subject Headings, http://www.ncbi.nlm.nih.gov/mesh
OCEBM	Oxford Centre for Evidence-Based Medicine, http://www.cebm.net/ocebm-levels-of-evidence
OR	Odds ratio
PMID	PubMed identification number
PubMed	A service of the US National Library of Medicine that provides free access to MEDLINE, the NLM database of indexed citations and abstracts to medical, nursing, dental, veterinary, health care, and preclinical sciences journal articles. Accessible at http://www.ncbi.nlm.nih.gov/pubmed/
RR	Relative ratio
SNOMED CT	Systematized Nomenclature of Medicine Clinical Terms
UMLS	Unified Medical Language System: a compilation of many controlled vocabularies in the biomedical sciences which integrates and distributes key terminology, classification and coding standards, and associated resources to promote creation of more effective and interoperable biomedical information systems and services, including electronic health records
XML	Extensible Markup Language (XML) is a markup language that defines a set of rules for encoding documents in a format that is both human-readable and machine-readable.

1. Introduction

This report presents the CARRE conceptual model for comorbidities and the functional requirements for the proposed environment.

1.1. Functional Requirements and Conceptual Modelling

A requirement is a statement that defines a function of a system or its component. A function is described as a set of inputs, the behaviour, and outputs. Generally, functional requirements are expressed in the form "system must/shall do <requirement>".

According to the ISO/IEC/IEEE 29148:2011(E) International Standard on Requirements Engineering[1], a well formed requirement is a statement that can be verified, has to be possessed by a system to solve a stakeholder problem, is qualified by measurable conditions, and defines the performance of a system (not the performance of a user). According to the same standard, major characteristics of individual requirements include the following:

- necessary: it defines an essential function;
- implementation free: it states what is required, not how this will be implemented;
- unambiguous: stated in a way so that it can be interpreted only in one way;
- consistent: it is free of conflict with other requirements;
- complete: it is measurable and sufficiently describes the functionality;
- singular: it includes only one requirement;
- feasible: it is technically achievable;
- traceable: it is directly connected to a documented stakeholder need;
- verifiable: it has the means to prove that the system satisfies it.

The formulations of the functional requirements have been carried out by trying to follow, as much as possible, to the above-mentioned characteristics. It must however be mentioned that this work is positioned within the scope of a research project. As such, while the scope of this work to set the project execution on a well-defined direction, it is also deemed appropriate to allow the necessary flexibility for research and innovation.

An information model is “a representation of concepts and the relationships, constraints, rules, and operations to specify data semantics for a chosen domain of discourse. Typically it specifies relations between kinds of things, but may also include relations with individual things. It can provide sharable, stable, and organized structure of information requirements or knowledge for the domain context.”[2]

Information model is an abstract, formal representation of entity types that may include:

- entity properties
- relationships
- operations that can be performed on them

An information model provides formalism to the description of a problem domain without constraining how that description is mapped to an actual implementation.

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[1] ISO/IEC/IEEE 29148:2011(E) International Standard: Systems and software engineering – Life cycle processes – Requirements engineering. First edition, 01-12-2011

[2] http://en.wikipedia.org/wiki/Information_model

1.2. Methodology

The procedure used for drafting up this deliverable is summarized in Figure 1. CARRE functional requirements and conceptual model are directly based on and derived from the following:

- contractual obligations as stated in DoW;
- medical domain analysis and patient empowerment literature survey as presented in deliverable D.2.1;
- CARRE use cases as described in Deliverable D.2.1.

At a first stage, each use case was used to identify major functional units of the system, presented in Section 3. Then, functional requirements of each functional unit are presented in Section 5.1, and these were consolidated to a set of CARRE functional requirements, presented in Section 5.2.

Medical domain analysis and use cases were also used to identify basic CARRE concepts and draft the CARRE conceptual model, described in Section 4. The consolidated functional requirements and the conceptual model will then drive the design of system architecture and the elicitation of non-functional requirements in the forthcoming Deliverable D.2.5.

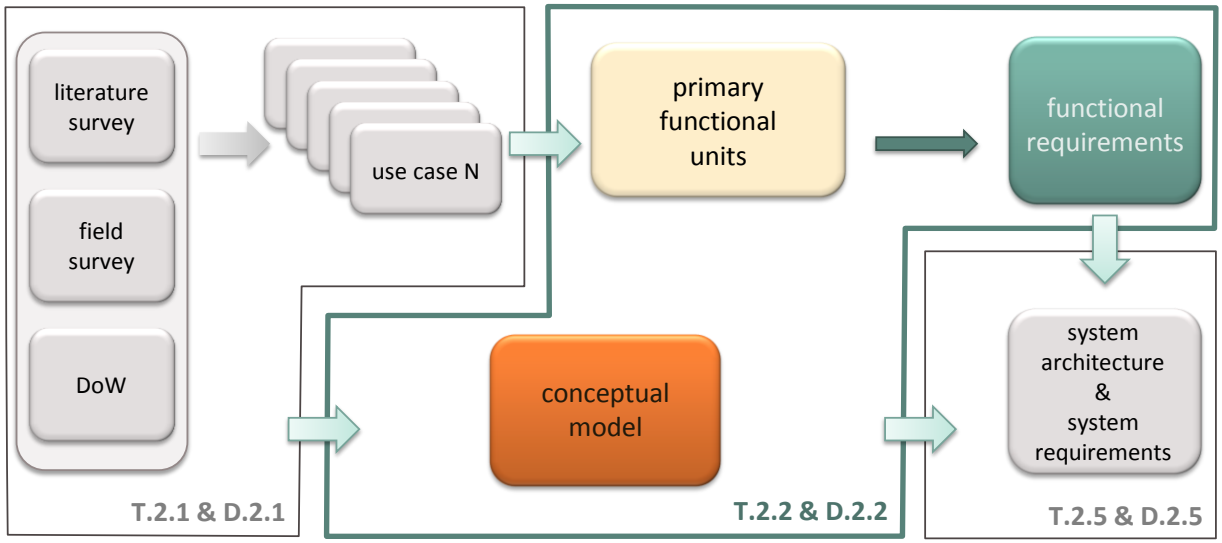

Figure 1. Process for deriving CARRE functional requirements and conceptual model.

Section 2 of this document presents briefly the concept of the project. Section 3 identifies the main functional units of the system as mandated by the DoW prerequisites, the medical domain analysis and the use cases described in Deliverable D.2.1. Section 4 presents the CARRE conceptual model of risk associations in comorbidities. Section 5 gives a list of functional requirements for the main functional units of the system.

Annex 1 presents a web-based system developed for semantic data entry of the risk association descriptions. Annex 2 presents major risk factor associations and their description, together with the respective risk elements, observables and evidence sources. The list presented here is indicative and will be continually updated and amended; the up-to-date version at any time is available via the on-line system described in Annex 1.

2. Prerequisites

2.1. CARRE Concept

CARRE **goal** is to provide the means for patients with comorbidities to take an active role in care processes, including self-care and shared decision-making, and also to support medical professionals in understanding and treating comorbidities via an integrative approach.

One common case of comorbidities is chronic cardiorenal disease, which is the condition characterized by simultaneous kidney and heart disease while the primarily failing organ may be either the heart or the kidney. Very often the dysfunction occurs when the failing organ precipitates the failure of the other. The cardiorenal patient (or the person at risk of this condition) presents an interesting example for addressing and demonstrating novel patient empowerment services for personalized disease & comorbidities management and prevention for a number of reasons, as chronic cardiorenal disease has an increasing incidence and a number of serious (and of increasing incidence) comorbidities.

The current medical evidence on the comorbidities involved in cardiorenal syndrome (prior, during and as a result of) have been presented extensively in CARRE D.2.1. and are summarized in Figure 2 therein.

CARRE research aims to create technology in order to:

– foster understanding of the complex interdependent nature of the comorbid condition in general and as specialized for the specific patient,

– calculate informed estimations for disease progression and transition,

– compile a variety of personalized alerting, planning and educational services so that patients (and professionals) are empowered.

In particular, the CARRE project plans research and technological development that will lead to a technological infrastructure for visual and quantitative understanding of disease progression and transition pathways and comorbidities trajectories and their dynamics, enriched with up-to-date medical evidence and personalized for the individual patient. Based on this, CARRE will develop personalized shared decision support services for the patient and the medical professional.

2.2. CARRE Objectives

CARRE aims to innovate towards a service environment for providing personalized empowerment and shared decision support services for cardiorenal disease comorbidities.

The overall technological goal of CARRE is to show the potential of semantic interlinking of heterogeneous data to construct dynamic personalized models of complex comorbid medical conditions with disease progression pathways and comorbidity trajectories. Also, to show that visual analytics based on such models can support patient understanding of personal complex conditions (projected against ground knowledge and statistical views of similar patient population) and be the basis for shared decision support services for the management of comorbidities.

The project **objectives** include:

– provide visual and quantitative understanding of disease progression pathways and comorbidities trajectories, as enriched with up-to-date medical evidence and personalized for the individual patient;

– provide personalized risk calculations and analytics for comparison of personal state with the current medical evidence and the overall statistical views of ‘similar’ patients;

– use the personalized model of comorbidities for building shared decision support services targeting personalized education, complex risk calculation for disease progression and comorbidity trajectories, alerts for adverse events of multiple co-existing treatments and personalized planning for comorbidity monitoring and treatment.

Major **expected technological breakthroughs** include:

- an ontology and schema for the description of comorbidities management (in the case of cardiorenal disease and comorbidities);
- data aggregators for integration of heterogeneous sources of information, such as medical evidence, personal data (including dynamic sensor data), medical information and personal disposition & lifestyle;
- text analysis tools to semantically annotate and extract relevant metadata from unstructured sources (medical evidence, social media);
- generic aggregator technology to harvest semantic information from structured data sources as listed above (e.g. personal sensors, educational content items);
- Linked Data technologies for semantic data interlinking, and enrichment;
- tools and infrastructure for large scale processing of aggregated data for visual analytics mentioned above;
- data/model driven decision support systems to build shared decision support services for the patient and the medical professional based on the personalized comorbidities model of the patient.

2.3. CARRE Predefined Framework

An overview of the envisaged CARRE **service environment is described in the DoW** and is reproduced in Figure 2.

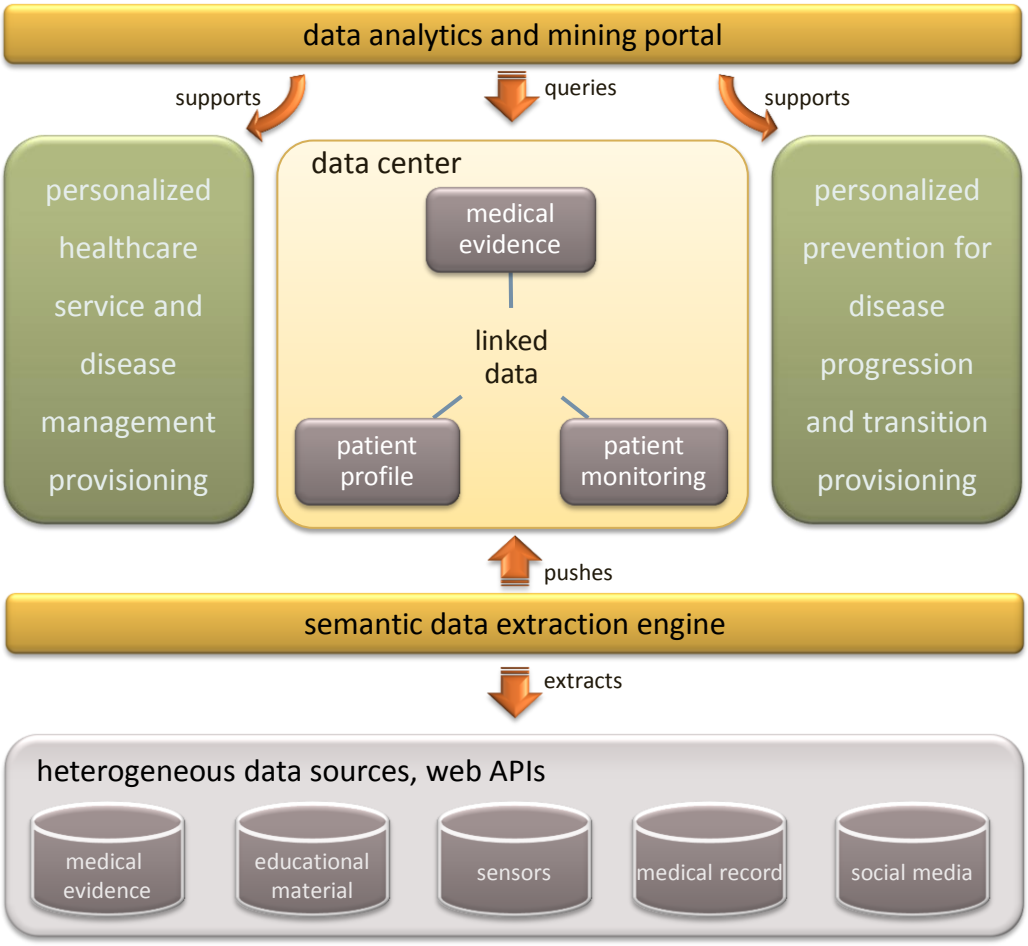

Figure 2. Overview of CARRE service environment as described in the DoW.

The overall environment includes six major components:

1. **Heterogeneous data resources** indicate all different kinds of data related to the personalised health care such as patient basic health caring environment, history record and social relationships/activities. These data should be the key factors for personalised care service selection and defining treatment plan. The data may be accessible from different types of resources with structured data formats (e.g. Web API outputs or database tables) or unstructured data formats (Web pages) and using heterogeneous presentation schema.
2. **Semantic data extraction engine** aims to enable crawling data harvested from heterogeneous data resources and extracting them with Linked Data principles into the Linked Data based repository (Data-centre). The extraction engine should follow the defined CARRE scheme to lift or transform all different crawled data into a unified data space.
3. **Linked Data based Data-centre** can efficiently integrate all different types of data, adding internal semantic links among them as well as external semantic links to Linked Open Data knowledge. In addition, the data centre will support the query endpoints for semantically retrieving the data.
4. **Data analytics and mining portal** supports the data analytics and mining tools and their accessing APIs to both patient self-caring applications at home and professional applications used in the health centres. The analytics and mining tools should enable the consumption of the Linked Data from the data centre for providing disease/treatment pattern recognition, prediction of patient health status and useful knowledge/information related to the particular patient.
5. **Personalised service for disease management** is a decision support services module that will suggest treatment guidance, alerts and education that are suitable to a particular patient's needs based on their personal data and supported by information from data analytics and mining. It can also provide personalised guidance for management of co-morbidities and integrated care to both the patient and professional organisation.
6. **Personalised prevention for disease progression and transition** is another decision support services module that will provide personalised information and life-style guidance to the patient in order to manage risks for comorbidities or progression of disease to more severe stages.

3. Primary Functional Units

Based on the above contractual commitments, on the medical domain analysis and use cases as presented in Deliverable D.2.1, we have identified the following major functional CARRE components (also shown in Figure 3):

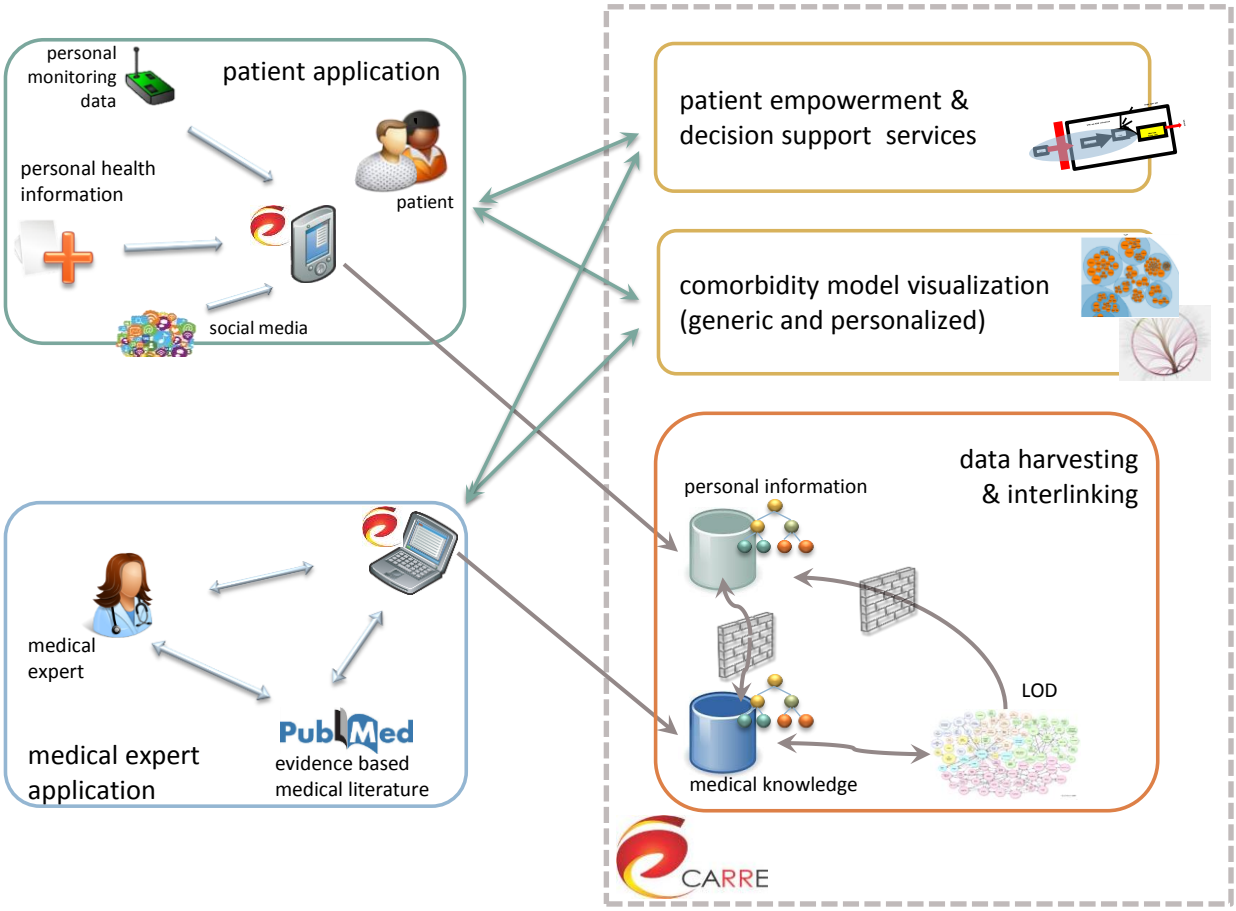

Figure 3. CARRE primary functional units.

Patient application: This application integrates patient related personal information and forwards this to the CARRE personal repository. The main types of information this application will integrate are the following:

- monitoring data from personal monitoring devices
- health related data from a personal health record
- other personal information from social media

The patient application is also supports interaction with the CARRE system, including visualisation of and interaction with the generic and personalized comorbidity model, and access to the personalized patient empowerment and decision support services.

Medical expert application: This application allows the medical expert to insert, review, and update medical evidence based knowledge required for the development of the generic comorbidity model. It also supports interaction with the CARRE system, including visualization of and interaction with the generic and

personalized comorbidity model, and input, review and update of medical knowledge required for creation of medical alerts and planning.

Data harvesting and interlinking: This includes the CARRE repository, consisting of public medical evidence data and metadata and private personal health related data. Medical evidence data refers to evidence based medicine knowledge, is enriched via medical controlled vocabularies and is public. Personal health related data is also enriched via controlled vocabularies and related information on the web, but remains private and secured.

Comorbidity model visualization: This module creates and presents the generic comorbidity model as constructed based on public medical knowledge. Also, this functional unit creates personalized versions of the model using the private patient data. The generic model visualization is public, while the personalized model is private and secured.

Patient empowerment and decision support unit: This functional unit generates and delivers personalized services, including: education, alert, planning, and social support.

4. Conceptual Model of Comorbidities

The core of CARRE functionality revolves around the concept of comorbidity, and in particular comorbidities in the case of cardiorenal syndrome. From the overview of the medical domain presented in the CARRE Deliverable D.2.1, it is evident that cardiorenal disease and comorbidities is a complex domain. Related conditions do not have a single cause, but medical evidence suggests that there are multiple causal chains. In order to capture this, the CARRE conceptual model is presented as a complex network of risk factors, that is pairs of conditions related to one another via a (apparently) causal associations.

4.1. Core Concepts and Concepts Relationships

The core concept in the CARRE model is the risk association, directly related to the medical risk factor as this was described in CARRE Deliverable D.2.1, Section 2.4.1. Based on this description, primary concepts and their relationships are identified in the paragraphs below and shown schematically in Figure 4.

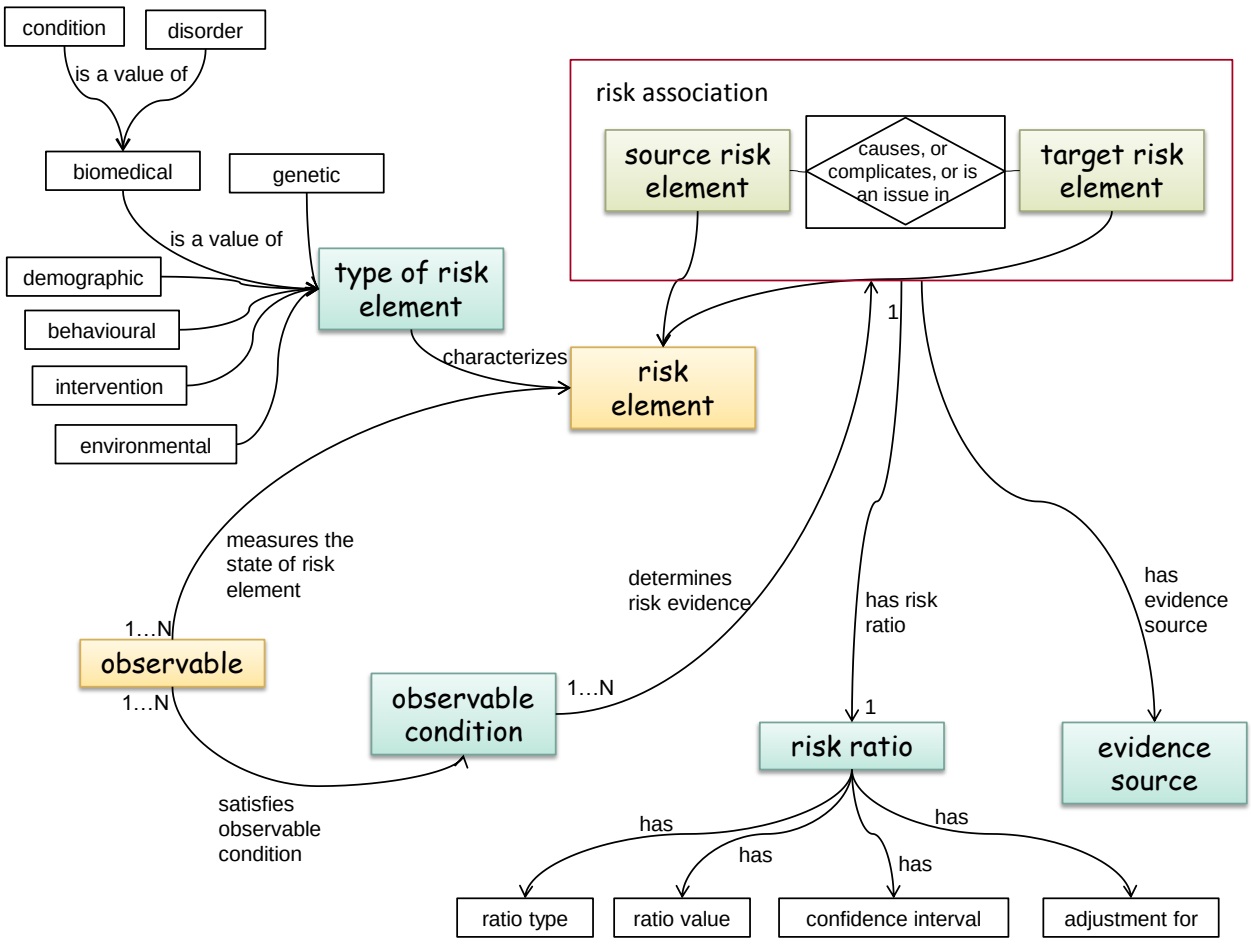

Figure 4. CARRE basic concepts and their relationships.

Risk Element: A risk association defines the (often causal) association of an agent (*source risk element*) to a health outcome (*target risk element*). This outcome is in most cases negative, but can also be positive (as shown in examples in Appendix 2). In cardiorenal disease and comorbidities, most often the (causal) agent is in itself a negative health outcome. In this sense, risk agents and their outcomes can be seen as instances of the same entity, called here '*risk element*'. Risk elements include all the disorders/diseases involved in the

comorbidity under discussion as well as any other risk causing agent, e.g. demographic (e.g. age, sex, race), genetic (gene polymorphisms), behavioural (e.g. smoking, physical exercise), environmental (e.g. air pollution, allergens) or even an intervention (e.g. pharmaceutical substances, contrast agents).

Risk Association: The association of one risk element as the risk source with another risk element which is the negative outcome under certain conditions is a '*risk association'*. This association is a rather complex one and is characterized by a number of other concepts:

- ***Association Type***: The association can be of a certain '*association type'*; most often, it is of type '*causes*', but it can also be '*complicates*', otherwise '*affects*' or in the general case (and when there is no knowledge of a specific effect), '*is_an_issue_in'*. There are also cases where an agent can have a positive effect, that is "*reduces*" the risk of a negative outcome. Generally, a number of other semantic relationships as described in UMLS could be encountered here.
- ***Risk Ratio***: The association is always accompanied by the likelihood of the negative outcome to occur. This likelihood is expressed as a '*risk ratio'*, that is the ratio of the probability of the negative outcome when the person is exposed to the risk agent over the probability of the negative outcome when the person is not exposed to the risk agent.
- ***Observables Condition***: For the association to occur, certain circumstances should exist. These prerequisite circumstances relate directly to the existence of the risk agent (source risk target) and/or its severity, and/or any other specific conditions. These are reported via certain '***observables***', that is, physical variables that can be measured or otherwise ascertained (e.g. biomarkers, biometric variables, biological signals and other non-biological factors e.g. environmental). The circumstances thus are ascertained via an explicit logical expression that involves observables; this logical expression is termed '*observables condition'*.
- ***Evidence Source***: Risk associations in medicine are determined from clinical studies as reported in evidence based medical literature. Thus each association is directly related to an '*evidence source*' which is a specific scientific publication.

Finally, a source risk element can be associated to a target risk element with more than one risk association.

4.2. Concept Attributes Tables

The basic concepts in modelling comorbidity are:

- risk factor;
- risk association;
- risk element;
- observable; and
- evidence source.

Based on the previous analysis, the draft description tables presented in CARRE Deliverable 2.1, Section 2.4.5 are revised and extended as in Table 1-Table 5.

Table 1. Risk Association (RA) Attributes

Attribute	Description	Multiplicity	Example
Risk Factor ID	Unique identifier of the particular risk factor	1	RF1
Risk Source	Risk agent	1 to N	obesity
Risk Target	Negative outcome	1	diabetes type 2
Risk Association ID	Risk association unique identifier (see Risk association attributes table)	1 to N	RA1

Table 2. Risk Association Evidence (RAE) Attributes			
Attribute	**Description**	**Multiplicity**	**Example**
RA ID:	Unique identifier of the particular association	1	RA1
Observables:	Name of observables included in the logical condition that has to be satisfied for the reported risk ratio	1 to N	BMI (= Body Mass Index)
Biomarker Condition:	What is the condition under which the following risk ratio is valid	1	23 < BMI < 34
Ratio Type:	The type of statistical ratio, reflecting the statistical method used for its calculation; most common values include: – relative ratio (RR) – hazard ratio (HR) – odds ratio (OR)	1	relative ratio
Ratio Value:	Value of risk ratio	1	1.61
Confidence Interval	Interval of values corresponding to the 95% confidence interval of ratio value	0 to 1	1.40 – 1.84
Adjusted for	Other parameters for which the ratio is statistically adjusted for	1 to N	sex, age
Evidence Source ID	Unique identifier of the scientific publication reporting this evidence	1 to N	ESID 1

Table 3. Risk Element (RE) Attributes			
Attribute	**Description**	**Multiplicity**	**Example**
Risk Element ID	Unique identifier of the particular risk element	1	RE1
Name	Name of the risk element	1	Diabetes
Classifier	Classifier corresponding to this element based on standardized medical controlled vocabularies; include vocabulary name followed by classifier. Major classification systems to be considered depend on the type of risk element. Common to all types are classification systems such as SNOMED CT, MeSH and MedLinePlus. For disorders and diseases ICD 9/10 classification is also appropriate.	0 to N	ICD10: E66 SNOMEDCT: 414916001 MSH: D009765 MEDLINEPLUS: C0028754
Description	Full name and short description of the element.	0 to 1	
Type	Risk elements can be of the following types: – biomedical (including condition, disorder and/or disease); – demographic (e.g. age, sex, race, occupation, education); – genetic (genetic polymorphism); – behavioural (e.g. physical activity, diet, smoking); – intervention (e.g. drugs); and	1	biomedical

	– environmental (e.g. air pollution, allergens).		
Modifiable:	If the risk element can be modified by human intervention (yes or no). For example, age and diabetes are not modifiable, while weight and smoking are modifiable.		yes
Observables ID	Unique identifiers of the observables that can be used to determine the status of the specific risk element.	1 to N	O1, O2

Table 4. Observable Attributes			
Attribute	**Description**	**Multiplicity**	**Example**
Observable ID	Unique identifier of the particular observable	1	O1
Name	Name of the observable	1	BMI
Classifier	Classifier corresponding to this observable based on standardized medical controlled vocabularies; include vocabulary name followed by classifier. Major classification systems to be considered depend on the nature of the observable, a common on to a majority of health related observables being SNOMED CT.	0 to N	
Description	Full name and short description of the element.	0 to 1	Body mass index, defined as the ratio of the mass (Kg) over the square of the height (m)
Type	Personal, clinical, other (e.g. third party measurement) – This reflects how this observable is measured, by the patient, the doctor or another party (e.g. air pollution as provided by certain bodies).	1 to N	
Data type	Type of the measurement, for example, real number, integer, value range, 2D signal, etc.	0 to 1	real
Unit	Unit of measurement	0 to 1	kg/m^2
Value ranges	Different expected value ranges of the observable and their classification if this exists as ground medical knowledge (i.e. normal, abnormal or other).	0 to N	BMI<18.5 underweight 25<BMI<30 overweight 30<BMI<40 obese BMI>40 morbid obese

Table 5. Evidence Source (ES) Attributes			
Attribute	**Description**	**Multiplicity**	**Example**
Evidence Source ID	Unique identifier of the particular risk element	1	ES1
Classifier	Classifier corresponding to this evidence source based on a standardized scientific classification system. For CARRE purposes this identifier will the PubMed identification	0 to N	PMID: 23766260 doi: 10.1161/ATVBAHA.113.301236

	number (PMID). However, other commonly used classifiers can also be included, e.g. DOI.		
Citation	Full citation. This may include a standardized publication XML format.	1	....
Publication Type	Type of the study producing the evidence, e.g. systematic review with meta-analysis,	1	meta-analysis
OCEBM level	Level of evidence according to the OCEBM system	1	1

4.3. Class Diagram

An overview of a class diagram is given in

Figure 5.

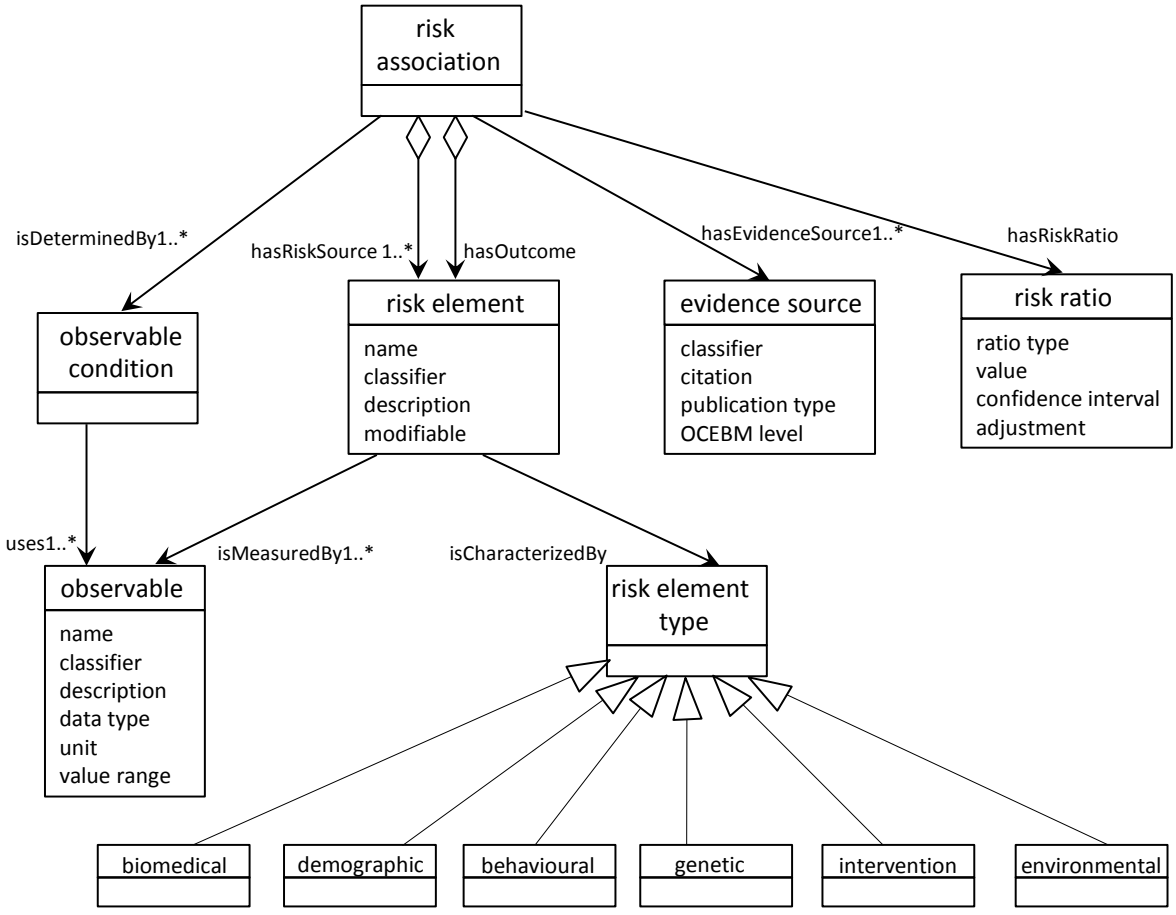

Figure 5. Risk factor class diagram.

4.4. Medical Controlled Vocabularies

As presented above, the model incorporates standardised classifiers as attributes for the basic concepts. This is to facilitate semantic integration based on commonly used domain specific controlled vocabularies and ontologies.

A list of relevant controlled vocabularies and ontologies with a short description are given in Table 6.

Table 6. Related medical controlled vocabularies and ontologies

No	Ontology	Description of Ontology
1	SNOMED CT	SNOMED CT is a systematically organized computer processable collection of medical terms providing codes, terms, synonyms and definitions used in clinical documentation and reporting. As a clinical terminology, SNOMED CT is inherently more suitable than other terminologies/classifications for clinical documentation in the EHR (electronic health record). http://www.ihtsdo.org/snomed-ct/
2	ICD-10	The ICD-10 is designed as a health care classification system, providing a system of diagnostic codes for classifying diseases, including nuanced classifications of a wide variety of signs, symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or disease. This system is designed to map health conditions to corresponding generic categories together with specific variations. Major categories are designed to include a set of similar diseases. http://www.who.int/classifications/icd/en/
3	MeSH - Medical Subject Headings	The MeSH Browser is an online vocabulary look-up aid available for use with MeSH (Medical Subject Headings). It is designed to help quickly locate descriptors of possible interest and to show the hierarchy in which descriptors of interest appear. Virtually complete MeSH records are available, including the scope notes, annotations, entry vocabulary, history notes, allowable qualifiers, etc. Pubmed translates common terms to MeSH terms. http://www.nlm.nih.gov/mesh/meshhome.html
4	MEDLINEPLUS - MedlinePlus Health Topics	MedlinePlus is the National Institutes of Health's Web site for patients and their families and friends. Produced by the National Library of Medicine, it brings information about diseases, conditions, and wellness issues in language that patient can understand. MedlinePlus offers reliable, up-to-date health information, anytime, anywhere for free. The MedLinePlus terminology contains terms meant for consumers. The topics are meant to cover a wide range of health interests, so topics may relate to more than one MeSH terms (956 MedLinePlus terms in 2013 as compared to more than 27,000 in MeSH) http://www.nlm.nih.gov/medlineplus/healthtopics.html
5	Online Mendelian Inheritance in Man (OMIM)	OMIM is a database that catalogues all the known diseases with a genetic component. http://www.ncbi.nlm.nih.gov/omim/
6	Environment Ontology	Ontology of environmental features and habitats produced by EnvO, community ontology for the concise, controlled description of environments. http://environmentontology.org/
7	Quantity, Unit, Dimension and Type, QUDT	The QUDT, or 'Quantity, Unit, Dimension and Type' collection of ontologies define the base classes properties, and restrictions used for modelling physical quantities, units of measure, and their dimensions in various measurement systems. The goal of the QUDT ontology is to provide a unified model of, measurable quantities, units for measuring different kinds of quantities, the numerical values of quantities in different units of measure and the data structures and data types used to store and manipulate these objects in

		software. This OWL schema is a foundation for a basic treatment of units. http://qudt.org/
8	Units of Measurement Ontology, UO	Metrical units for use in conjunction with PATO. http://code.google.com/p/unit-ontology/
9	ChEBI	Chemical Entities of Biological Interest (ChEBI) is a freely available dictionary of molecular entities focused on 'small' chemical compounds. The term 'molecular entity' refers to any constitutionally or isotopically distinct atom, molecule, ion, ion pair, radical, radical ion, complex, conformer, etc., identifiable as a separately distinguishable entity. The molecular entities in question are either products of nature or synthetic products used to intervene in the processes of living organisms. www.ebi.ac.uk/chebi/
10	ChEMBL	ChEMBL or ChEMBLdb is a manually curated chemical database of bioactive molecules with drug-like properties.[1] It is maintained by the European Bioinformatics Institute (EBI), of the European Molecular Biology Laboratory (EMBL), based on the Wellcome Trust Genome Campus, Hinxton, UK. https://www.ebi.ac.uk/chembldb/
11	RxNorm	RxNorm is a name of a US-specific terminology in medicine that contains all medications available on US market.[1] It can also be used in personal health records applications. It is part of UMLS terminology and is maintained by National Library of Medicine. http://www.nlm.nih.gov/research/umls/rxnorm/
11	UMLS	The Unified Medical Language System (UMLS) is a collection of many controlled vocabularies in the biomedical sciences. It provides a mapping structure among these vocabularies and thus allows one to translate among the various terminology systems. Each concept is assigned one or more semantic types (135 in total), which are linked with one another through semantic relationships (54 relationships in total). http://www.nlm.nih.gov/research/umls/

Based on the above suggested terminology classifiers for the CARRE concepts are listed in Table 7.

Table 7. Suggested controlled vocabularies as classifiers for CARRE primary and secondary concepts

Primary Concepts	
Concept	**Controlled Vocabulary as Classifier**
Risk element	1. of type biomedical: SNOMED, ICD-10, MeSH, Medlineplus 2. of type demographic: SNOMED 3. of type genetic: SNOMED, OMIM, MeSH, Medlineplus 4. of type behavioural: SNOMED, MeSH, Medlineplus 5. of type intervention: SNOMED, MeSH, Medlineplus, , ChEBI, ChEMBL, RxNorm 6. of type environmental: SNOMED, Environmental Ontology, MeSH, Medlineplus
Observable	SNOMED
Evidence source	PMID, DOI

Secondary Concepts	
Concept	**Controlled Vocabulary as Classifier**
Association type	UMLS
Observable unit	SNOMED, QUDT, UO
Observable value ranges	SNOMED, ICD-10

5. Functional Requirements

The system shall have the functional components:

1) patient application
2) medical expert application
3) data harvesting and interlinking
4) comorbidity model visualization
5) decision support and patient empowerment services

5.1. Functional Requirements of System Functional Units

5.1.1. Patient Application

Table 8. Patient application functional requirements	
Requirement ID	**Requirement Description**
FR_PA_01	The system must support user authentication.
FR_PA_02	The user must be able to register new monitoring devices (from the list supported by the system) with the system.
FR_PA_03	The system must retrieve monitoring data from personal monitoring devices.
FR_PA_04	In the case of external devices that do not support wireless communication, the system must support cable connection.
FR_PA_05	The system must accept manual observable data from end-users.
FR_PA_06	The user must be able to register new personal health record systems.
FR_PA_07	The system must retrieve health information from the personal health record system.
FR_PA_08	The user must be able to register new on-line social media accounts.
FR_PA_09	The system must retrieve personal information from the personal social media accounts.
FR_PA_10	The user must be able to review recorded/retrieved data.
FR_PA_11	The system must be able to transmit recorded/collected data to the data harvesting and interlinking module.
FR_PA_12	The system must use data anonymization prior to data transmission.
FR_PA_13	The system must be able to display the output of the model visualization module.
FR_PA_14	The system must support user interaction (i.e. various views) with the model visualization.
FR_PA_15	The system must be able to display the output of the patient empowerment and decision support services module.
FR_PA_16	The system must support interaction with the output of the patient empowerment and decision support services module.
FR_PA_17	Upon prompt for access to personal accounts, CARRE system must provide statement on privacy and legal issues.
FR_PA_18	The system must provide online user manual.

5.1.2. Medical Expert Application

Table 9. Medical expert application functional requirements	
Requirement ID	**Requirement Definition**
FR_ME_01	The system must support user authentication.
FR_ME_02	The system must allow the user to add descriptions of risk associations, risk elements, observables, and evidence based sources.
FR_ME_03	The system must allow the user to view existing descriptions of risk associations, risk elements, observables, and evidence based sources.
FR_ME_04	The system must allow the user to select and assign appropriate medical controlled vocabulary terms to descriptions of concepts.
FR_ME_05	The system must give access to medical evidence based sources (PubMed) available on the web, and allow the automatic retrieval of their metadata
FR_ME_06	The user must be able to select and assign appropriate medical controlled vocabulary terms to descriptions of concepts of risk associations, risk elements, observables, and evidence based sources.
FR_ME_07	The user must be able to edit existing descriptions of risk associations, risk elements, observables, and evidence based sources.
FR_ME_08	The system must search on-line medical literature to identify and suggest potential new risk associations.
FR_ME_09	The user must be able to interact with suggested data (outcome of FR_ME_08) for final judgement of new evidence on risk association.
FR_ME_10	The system must be able to display the output of data harvesting and interlinking.
FR_ME_11	The user must be able to interact with data harvesting and interlinking for concept disambiguation.
FR_ME_12	The system must be able to display the output of the model visualization module.
FR_ME_13	The system must support user interaction with the output of the model visualization.
FR_ME_14	The system must support user input to the patient empowerment and decision support services module.
FR_ME_15	The system must support interaction with the output of the patient empowerment and decision support services module.
FR_ME_16	The system must provide online user manual.

5.1.3. Data Harvesting and Interlinking

Table 10. Data harvesting & interlinking functional requirements	
Requirement ID	**Requirement Definition**
FR_DHI_01	The system must harvest data sent from the user (patient/physician) application.
FR_DHI_02	The system must harvest data from medical evidence sources.
FR_DHI_03	The system must harvest data from online patient education sources.
FR_DHI_04	The system must harvest data from Linked Data Cloud and semantic web sources.
FR_DHI_05	The system must harvest data only from authenticated user applications.
FR_DHI_06	The system must store personal data on a private secure semantic repository.
FR_DHI_07	The system must store public data on an open linked data repository.

FR_DHI_08	The system must provide interfaces for secure access of personal data.
FR_DHI_09	The system must provide public interfaces for open access of public data.
FR_DHI_10	The system must access and analyse schemas and ontologies used for CARRE data representation.
FR_DHI_11	The system must access additional datasets, such as common vocabularies, to enrich harvested data.
FR_DHI_12	The system must semantically enrich harvested data.
FR_DHI_13	The system must allow users (medical experts) to assess the 'noise' of data enrichment.

5.1.4. Comorbidities model visualization

Table 11. Comorbidities model functional requirements	
Requirement ID	**Requirement Definition**
FR_VIS_01	The system must display the generic comorbidities model constructed based on medical evidence.
FR_VIS_02	The system must give individual views of risk factor associations, risk element, observables and evidence sources.
FR_VIS_03	The system must allow user interaction with the generic risk association model.
FR_VIS_04	The system must display comorbidities model personalized to specific patient.
FR_VIS_05	The system must display personalized recorded data.
FR_VIS_06	The system must display personal potential disease progression and transition.
FR_VIS_07	The system must display actual personal disease progression and transition.
FR_VIS_08	The system must display comparison of personal state with current medical evidence
FR_VIS_09	The system must display comparison of personal state with overall statistical views of 'similar' patients.
FR_VIS_10	The system must display simulated personalized views of virtual patients (for treatment planning and medical education)
FR_VIS_11	The system must display overall statistical views of CARRE patients, in terms of health status, risk for progression, disease management

5.1.5. Patient Empowerment and Decision Support Services

Table 12. Patient empowerment & decision support services functional requirements	
Requirement ID	**Requirement Definition**
FR_DSS_01	The system must present educational material based on current state and risks
FR_DSS_02	The system must present new medical evidence related to current state and risks
FR_DSS_03	The system must support patients to create a personal plan for their diet.
FR_DSS_04	The system must support patients to create a personal plan for their physical activities.
FR_DSS_05	The system must allow comparison of plans with implied lifestyle, intentions, preferences (as deduced from social media).
FR_DSS_06	The system must alert patients for medical check-ups.
FR_DSS_07	The system must alert patients for monitoring.

FR_DSS_08	The system must alert patients for increased risk of disease progression and transition.
FR_DSS_09	The system must alert patients for increased risk of acute health episodes.
FR_DSS_10	The system must alert patients for the need to change diet.
FR_DSS_11	The system must alert patients for the need to change monitoring.

5.2. Consolidated Functional Requirements

Table 13. Consolidated functional requirements

Category	Requirement per Category
Data	CARRE systems must accept data from: ✓ end users ✓ social media ✓ PUBMED ✓ monitor devices ✓ CARRE database
Search	CARRE systems must search: ✓ PUBMED medical database ✓ CARRE database ✓ other medical databases
Visualize	CARRE systems must visualize: ✓ disease progression ✓ comparison between end-users health-status with similar patient ✓ comparison between end-users health-status with current medical evidence ✓ virtual patient ✓ pro & cons of different disease management
Export	CARRE system must export: ✓ data ✓ text ✓ visualization ✓ alert
Create	CARRE system must create: ✓ diet plan ✓ physical activity plan ✓ comparison ✓ alert
Alert	CARRE system must create an alert for: ✓ medical check-ups ✓ monitoring ✓ increased risk of acute episodes ✓ increased risk of comorbidities ✓ need to change diet ✓ need to change monitoring ✓ overall changes of condition

5.3. CARRE Security Requirements

Table 14. Security requirements	
Requirement ID	**Security Requirement**
FR_SEC_01	Secure computations in distributed programming frameworks
FR_SEC_02	Secure best practice for non-relational data stores
FR_SEC_03	Secure data storage and transactions logs.
FR_SEC_04	End point input validation/filtering.
FR_SEC_05	Real-time security/compliance monitoring.
FR_SEC_06	Scalable and composable privacy-preserving data mining and analytics.
FR_SEC_07	Granular access control.
FR_SEC_08	Granular audits
FR_SEC_09	Data provenance

Annex 1
CARRE Risk Model Semantic Data Entry System

The model presented in this deliverable enables the clinical experts in the CARRE project to encode the risk associations between biological, demographic, lifestyle and environmental elements and clinical outcomes in accordance with evidence from the clinical literature. The CARRE system is based fundamentally on Linked Data principles[3], and so in order to make the best use of these encoded associations, they must be available as Linked Data, making use of the vocabularies and ontologies discussed earlier; specifically, they must be encoded in the (standard) Resource Description Framework[4] (RDF) format.

We have developed a web-based system for clinicians to use to enter this data. In order to add evidence sources from the clinical literature, the system provides a search interface to PubMed[5], enabling publications to be located and their unique PubMed identifiers to be inserted into the system easily and conveniently.

The first version of this system (http://carre.kmi.open.ac.uk) was developed using the Drupal content management system[6]. While this first prototype has managed to successfully capture the information for which it was designed, it also suffered from a few limitations (as described in CARRE D.3.4). The main limitation is that this system is not tightly connected to the overall CARRE architecture. This limitation stems from the decision to use Drupal, which is tightly coupled with a relational database as a backend (MySQL) and does not allow the seamless integration with the main CARRE repositories (or any other repository). This constraint requires from users to create two user accounts and requires switching between different environments (i.e. RMSDE and remaining of the upcoming CARRE platform). Moreover, the Drupal-powered RMSDE is introducing extra technical effort when considering its integration with the other Aggregators of Medical Evidence discussed in this deliverable.

Hence, a new version of the semantic risk factor data entry system was developed (http://entry.carre-project.eu). The new version has been designed based on the concept of microservices architecture[7] which enhances modularity and scalability. A SPA (Single Page Application) has been developed using native HTML5[8] and bleeding edge javascript libraries like AngularJS[9]. The user authentication is performed using OAuth-compatible token based request by an external authorization server. The application follows a graph data model and the data scheme is described by the CARRE risk ontology. The supported databases include Virtuoso RDF server[10], Jena RDF server[11] and Sesame triple store[12] that implement SPARQL 1.0 or greater in their endpoint. The application is deployed to a custom linux-nginx container by self-hosted Docker PaaS (Platform as a Service).

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3 http://www.w3.org/DesignIssues/LinkedData.html

4 http://www.w3.org/RDF/

5 http://www.ncbi.nlm.nih.gov/pubmed

6 https://www.drupal.org/

7 Namiot, Dmitry, and Manfred Sneps-Sneppe. "On micro-services architecture."International Journal of Open Information Technologies 2.9 (2014): 24-27

8 http://www.w3.org/TR/html5/

9 https://angularjs.org/

10 http://www.w3.org/wiki/VirtuosoUniversalServer

11 https://jena.apache.org/

12 http://rdf4j.org/

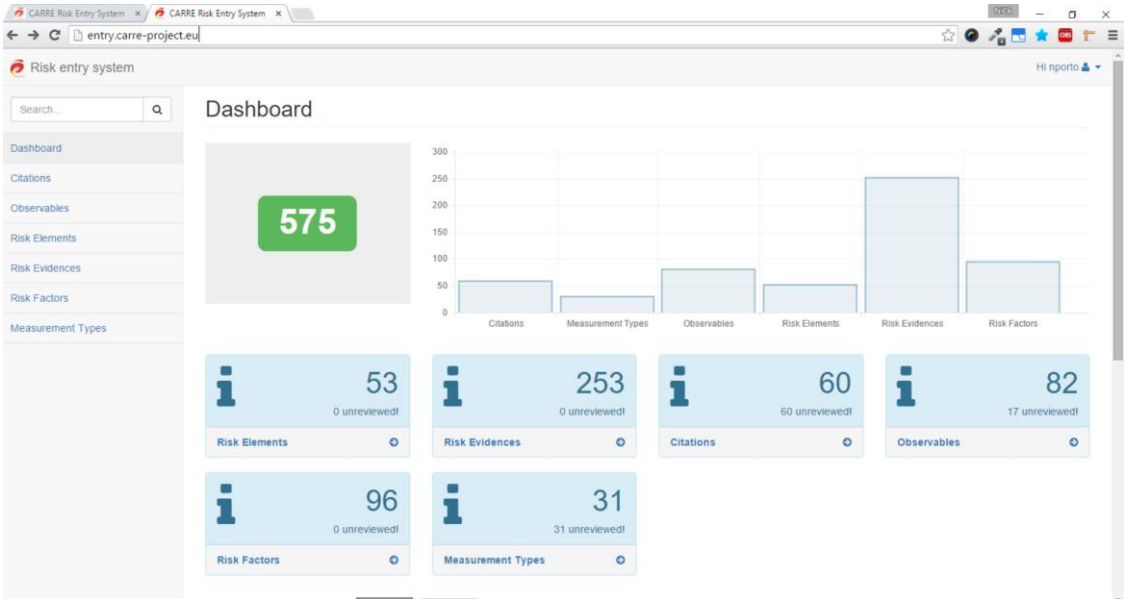

Figure 6. The system dashboard with collective statistics on the current content.

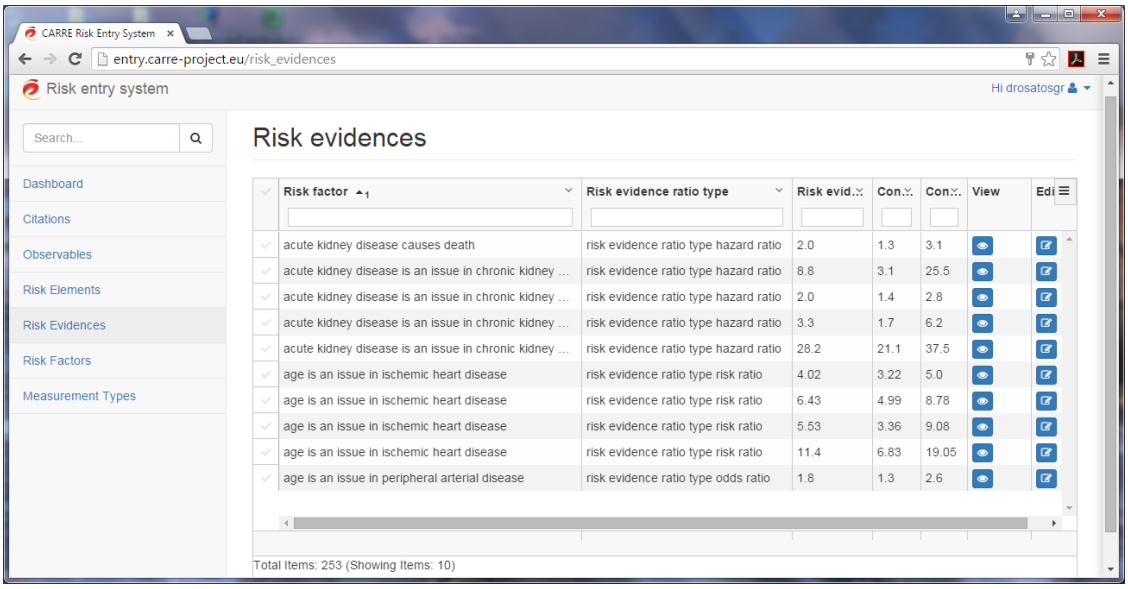

Figure 7. The list of risk factors with their different risk evidences.

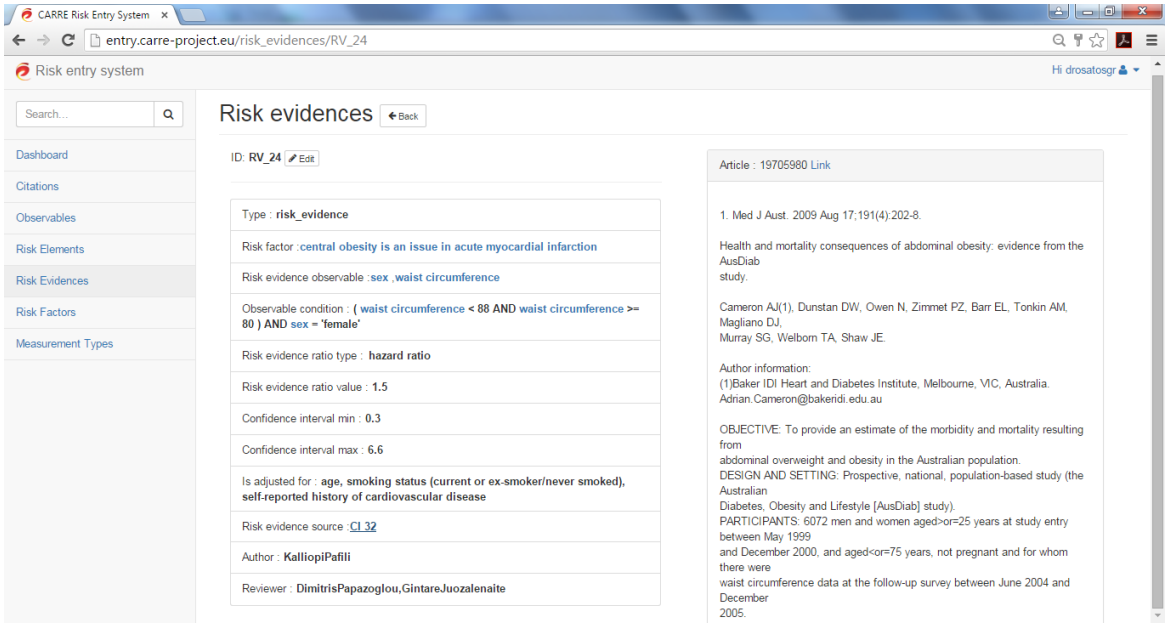

Figure 8. A particular risk evidence with all its information. On the right part of the screen the evidence source from PubMed is dynamically uploaded.

Annex 2
CARRE Risk Association Descriptions

1. Introduction

This Annex presents major risk factor associations and their description, together with the respective risk elements, observables and evidence sources.

This list is the updated list as on October 31, 2015.

The list presented here is indicative and will be continually updated and amended throughout the project. The list will be updated via manual medical expert entry and (semi)-automatically as a result of the work done in WP3, Task 3.4.

The up-to-date version at any time will be available via the on-line system described in Annex 1.

Section 2 of this Annex presents attributes tables for

- 98 risk factors
- 253 risk evidences
- 53 risk elements
- 63 observables
- 60 evidence sources.

Each risk factor has a variable number of different risk evidences, and the current frequency is presented in Figure 9.

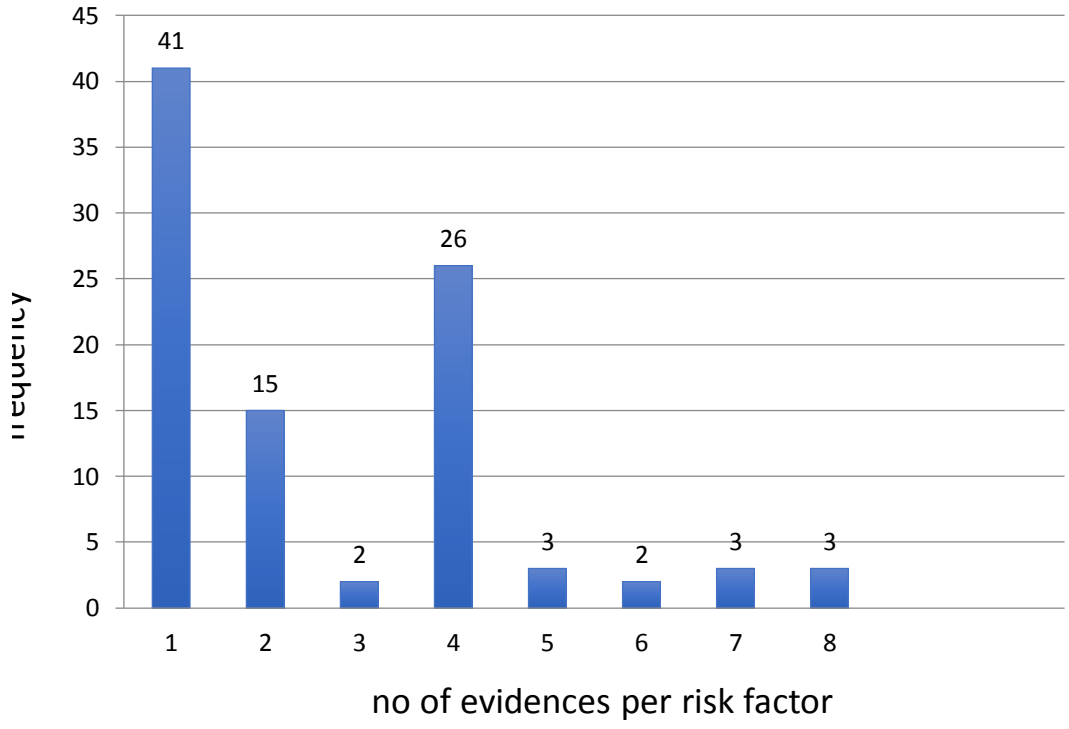

Figure 9. Histogram of the number of evidences per risk factor as in this current update #2.

1.1. Methodology

The aim is to create a first draft of a database (as a 'seed' risk factor database) to

a) showcase that the risk factor model and ontology works and

b) support CARRE DSS.

This initial database does not attempt to include all known and reported risk factors in the area of cardiorenal syndrome. It rather aims to create a first critical mass of such risk factor descriptions. This initial critical mass should contain

a) major risk factors as known from ground medical knowledge – these should be risk factors that have been reported in top level evidence sources (e.g. systematic reviews with meta-analysis). Only if no such source is found, and if the risk factor is considered within the group of major ones, values from lower level sources will be included (see table 12 in D.2.1 for major risk factors as identified from literature research)

b) certain risk factors that, although not considered major, may help to highlight interesting points considering the model and the concept of risk factor. For example,

- factors that are protective, i.e. they lower the risk instead of increasing it.
- risk factors that have a complex and/or uncommon observable condition (this would help to show and test the strength of the observable condition editor being developed in CARRE)
- Risk factors that refer to side effects of drugs which may help showcase that this ontology/model/database can be used to organize drug side effects.
- risk factors that are related with the progression or control of a condition, so that we can test how to treat the 'disease progression/control' concept in the model

We expect that this initial database will be updated and amended with new risk factors (and if needed with risk factors previously reported) as a crowdsourcing collaborative process during the project and beyond the project duration. This update is expected to be manual and collaborative, but also aided via semantic literature searching mechanisms as those developed in D.3.3.

Eventually the database can grow to include risk factors from other medical areas.

The basic methodology of creating this seed risk factor database is as follows:

> Investigators: certified physicians (cardiologists, nephrologists, endocrinologists, internists) and other medical professionals. 2 researchers did the same search independently in PubMed. The first to report a finding is included as 'author' in the database tables, the second as a 'reviewer'. If there was not an agreement at a particular entry, the 2 investigators discussed till they reached an agreement. If no agreement was possible a third investigator was called in.

1. Use common medical knowledge and literature research in D.2.1 and guidelines from KDIGO, KDOQI, ACC/AHA, NICE, ESC, EASD, ADA, IDF were identified and literature references were noted.
2. Construct a conceptual list of major risk factors as they are currently perceived in ground medical knowledge. The medical literature research of D.2.1 produced such a list (Table #12 in D.2.1)
3. Use the terms in this initial list to do a literature search in PubMed to find evidence sources. Search was done in PubMed, which comprises more than 24 million citations for biomedical literature from MEDLINE, life science journals, and online books. It also includes guidelines and systematic reviews and meta-analyses produced by commonly accepted independent evidence bodies such as Cochrane Collaboration.

   To do this, we searched for each term as follows:

   > condition A AND condition B limited to systematic reviews and meta-analyses
   >
   > if this yields results, we use the latest
   >
   > if no results, then

condition A AND condition B in the entire PubMed collection

if this yields results, we use the latest and the highest evidence level

if no results, then

drop this risk factor at this point – search again for next year's update

If the above search yields results that associate condition A with another condition X not included in the initial table of concepts, the investigators discuss this and decide whether or not to include this new risk association (based on the strength of the evidence source and the relevance to CARRE).

4. The aim is to include evidence from the most recent meta-analysis found. If a systematic review & meta-analysis (SR/MA) is found, all related risk associations are included (for example, risk associations for the general population and for specific age groups, sex, etc.)

   If a SR/MA is not found, then we include lower level evidence sources. Investigators have to review and agree on this, based on the size of the study, or whether it is part of a larger generally known and peer-accepted studies or epidemiological registries (e.g. Framingham, ARIC, UKPDS, KEEP, NHANES, etc.)

   For lower level evidence, only ratios for general population are included – unless investigators decide to include more associations for the specific reasons listed above (to test extreme/interesting cases of the risk factor model)

   For lower level evidence, if the 2 investigators find the same study, this is directly included. Otherwise, i.e. if they identify different studies, they discuss the results on the basis of the above mentioned criteria (study size, etc). If they agree on one of them, this one is included. If they cannot agree, associations from both studies are included (an example is diabetes → ischemic heart disease).

   Only full-text articles were considered. It was planned to contact authors of publications in case of no access to fulltext was granted. However, access to all related publications was available and no need to contact authors had arisen.

   Studies of special population cohorts are excluded. For example, only pediatric or only specific ethnicities or races are not included.

5. The database is updated at once a year. This is done by close manual monitoring of the literature and also with automatic help by tools that create literature alerts based on semantic literature searches.

   If a new evidence is found for an existing risk factor, it is included in the database along with the previous value. If a new risk factor is identified, it is also included.

   This process is done independently by all medical experts of the CARRE team. Once a new entry is identified by one of them, at least a second member of the team is asked to review it independently before inclusion in the database.

The following tables present discrepancies between the initial list (D.2.1) and final database. Also, some comments/findings on how to treat certain issues in risk factor descriptions are presented (e.g. drugs, disease progression/control, complex observable conditions, etc.)

1.2. Detailed analysis of risk factors in the current annex

TABLE 1			
Risk factors that are identified both in the initial concept Table 12 in D.2.1 and in the current risk factor database. Any discrepancy in terms is explained in the last column.			
No	**Cause**	**Effect**	**Comment**
1.	Age	Ischemic heart disease	In D.2.1 the effect was listed as 'coronary heart disease'. We decided to change this to 'chronic ischemic heart disease'. The correct term as in ICD10 is I25 (a group of terms)
2.	Age	Peripheral arterial disease	In D.2.1 the effect was listed as Peripheral vascular disease, which is a superset. Decided to change this to 'peripheral vascular disease', C0085096 and ICD10- I73.9
3.	Anemia AND Acute myocardial infarction	Death	While searching for anemia and the other mentioned conditions, risk factors as in D.2.1 were slightly modified according to evidence.
4.	Anemia AND Heart Failure	Death	While searching for anemia and the other mentioned conditions, risk factors as in D.2.1 were slightly modified according to evidence.
5.	AMI and CKD	death	While searching for anemia and the other mentioned conditions, risk factors as in D.2.1 were slightly modified according to evidence.
	Anaemia	cardiovascular disease	While searching for anemia and the other mentioned conditions, risk factors as in D.2.1 were slightly modified according to evidence.
7.	Anemia and CKD	CVD	While searching for anemia and the other mentioned conditions, risk factors as in D.2.1 were slightly modified according to evidence.
8.	Anemia and CKD	death	While searching for anemia and the other mentioned conditions, risk factors as in D.2.1 were slightly modified according to evidence.
9.	Chronic kidney disease	Ischemic heart disease OR Heart failure OR Ischemic stroke OR Peripheral arterial disease	a generalization of the risk factor just below should change this to peripheral vascular disease
10.	Chronic Kidney Disease	Peripheral arterial disease	'Peripheral arterial disease' should change to 'peripheral vascular disease'
11.	Chronic kidney disease AND (Hypertension OR Heart failure)	Hyperkalemia	
12.	Chronic obstructive pulmonary disease	Death: due to cardiovascular	D.2.1 includes the risk association of 'COPD → CVD' Literature search revealed this more specific association
13.	Depression	Ischemic stroke	D.2.1 includes the more general 'Depression → CVD'
14.	Depression	Ischemic heart disease	D.2.1 includes the more general 'Depression → CVD'
15.	Diabetes	Death: due to cardiovascular disease	
16.	Diabetes	Heart failure	
17.	Diabetes	Ischemic heart disease	D.2.1 includes the more general 'Diabetes → CVD'
18.	Diabetes	Ischemic heart disease OR Ischemic stroke	D.2.1 includes the more general 'Diabetes → CVD'
19.	Diabetes	Peripheral vascular	D.2.1 includes the more general 'Diabetes → CVD'

		disease	
20.	Diabetic nephropathy	Acute myocardial infarction OR Ischemic stroke	In D.2.1 the association was 'Diabetic nephropathy → CVD', now it is more specific based on the evidence found.
21.	Drugs: β-blockers	Diabetes	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
22.	Drugs: contrast agents: coronary angiography	Acute kidney injury	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
23.	Drugs: diuretics	Diabetes	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
24.	Drugs: renin-angiotensin system dual blockade (any)	Hyperkalemia	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
25.	Drugs: renin-angiotensin system dual blockade (any)	Hypotension	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
26.	Drugs: renin-angiotensin system dual blockade (any) AND Heart failure	Acute kidney injury	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
27.	Drugs: statins	Diabetes	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
28.	Drugs: statins AND Chronic kidney disease stage = 1 to 3	Chronic kidney disease = stage 5	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
29.	Drugs: statins AND Chronic kidney disease stage = 1 to 3	Death	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
30.	Drugs: statins AND Chronic kidney disease	Ischemic stroke	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
31.	Drugs: Statins AND Chronic kidney disease stage 1 to 3	Myocardial Infraction	In D.2.1 the risk source was the more general term 'Nephrotoxic drugs'
32.	Dyslipidemia	Peripheral arterial disease	In D.2.1 the effect was the more general term 'cardiovascular disease'. In next update, 'arterial' should change to 'vascular'.
33.	Hyperkalemia AND Chronic kidney disease	Death	
34.	Hypertension	Chronic kidney disease	
35.	Hypertension	Death: cardiovascular	
36.	Hypertension	Heart Failure	
37.	Hypertension	Peripheral arterial disease	In next update, 'arterial' should change to 'vascular'.
38.	Hyperuricemia	Heart failure	
39.	Hyperuricemia	Ischemic heart disease	
40.	Ischemic heart disease: family history	Ischemic heart disease	In D.2.1 cause was listed as the more general 'family history of CVD'. In next update, this will change to 'Family history: ischemic heart disease' – as 'family history' is considered the top category with a number of different possible types (e.g. ischemic heart disease, breast cancer, etc.).

41.	Ischemic heart disease: family history	Ischemic stroke	
42.	Ischemic heart disease: self history	Heart failure	
43.	Left ventricular hypertrophy	Acute myocardial infarction OR Ischemic stroke OR Heart Failure OR Death: cardiovascular	D.2.1. included only the effect 'cardiovascular disease', which based on literature was expanded to 5 more specific risk associations.
44.	Left ventricular hypertrophy	Death: cardiovascular	D.2.1. included only the effect 'cardiovascular disease', which based on literature was expanded to 5 more specific risk associations.
45.	Left ventricular hypertrophy	Heart failure	D.2.1. included only the effect 'cardiovascular disease', which based on literature was expanded to 5 more specific risk associations.
46.	Left ventricular hypertrophy	Hypertension	D.2.1. included only the effect 'cardiovascular disease', which based on literature was expanded to 5 more specific risk associations.
47.	Left ventricular hypertrophy	Ischemic stroke	D.2.1. included only the effect 'cardiovascular disease', which based on literature was expanded to 5 more specific risk associations.
48.	Obesity	Atrial fibrillation	
49.	Obesity	Diabetes	
50.	Obesity	Ischemic heart disease	In D.2.1 the effect was the more general term 'CVD'.
51.	Obesity	Ischemic stroke	In D.2.1 the effect was the more general term 'CVD'.
52.	Obesity: central	Acute myocardial infarction OR Old myocardial infarction	In D.2.1 cause was the term 'Central Obesity or obesity'.
53.	Obesity: central	Diabetes	In D.2.1 cause was the term 'Central Obesity or obesity'.
54.	Obesity: central	Dyslipidemia: HDL cholesterol serum concentration	In D.2.1 cause was the term 'Central Obesity or obesity'.
55.	Obesity: central	Dyslipidemia: Triclycerides serum concentration	In D.2.1 cause was the term 'Central Obesity or obesity'.
56.	Obesity: central	Hypertension	In D.2.1 cause was the term 'Central Obesity or obesity'.
57.	Obstructive sleep apnoea	Death: cardiovascular	in In D.2.1 the effect was the more general term 'CVD'.itially it was CVD, now it is more detailed
58.	Obstructive sleep apnoea	Diabetes	
59.	Obstructive sleep apnoea	Heart failure	In D.2.1 the effect was the more general term 'CVD'.
60.	Obstructive sleep apnoea	Hypertension	In D.2.1 the effect was the more general term 'CVD'.
61.	Obstructive sleep apnoea	Ischemic heart disease	In D.2.1 the effect was the more general term 'CVD'.
62.	Obstructive sleep apnoea	Ischemic stroke	In D.2.1 the effect was the more general term 'CVD'.
63.	Physical Activity	Diabetes	In D.2.1 'physical activity' was initially termed 'lack of physical activity' or physical exercise . The effect initially was the more general CVD.

64.	Physical Activity	Ischemic heart disease	In D.2.1 'physical activity' was initially termed 'lack of physical activity' or physical exercise . The effect initially was the more general CVD.
65.	Physical activity	Ischemic stroke	In D.2.1 'physical activity' was initially termed 'lack of physical activity' or physical exercise . The effect initially was the more general CVD.
66.	Smoking	Death: cardiovascular	In D.2.1 the effect was the more general term 'CVD'.
67.	Smoking	Chronic Kidney Disease	In D.2.1 the effect was 'renal disease' and 'progression of CKD'.
68.	Smoking	Heart failure	In D.2.1 the effect was the more general term 'CVD'.
69.	Smoking	Ischemic heart disease	In D.2.1 the effect was the more general term 'CVD'.
70.	Smoking	Ischemic stroke	In D.2.1 the effect was the more general term 'CVD'.
71.	Smoking	Peripheral Arterial Disease	In D.2.1 the effect was the more general term 'CVD'.

TABLE 2

Risk factors that were not initially mentioned in Table 12 in D.2.1. These factors were identified while searching for evidence for the risk factors listed in D.2.1. and added to the risk factor database.

No	Cause	Effect	Comments
1.	Acute kidney injury	Chronic kidney disease	
2.	Acute kidney injury	Death	
3.	Atrial fibrillation	Ischemic stroke	
4.	Atrial fibrillation	Heart failure	
5.	Chronic kidney disease	Death	
6.	Chronic kidney disease AND Heart failure	Death	
7.	Diabetes: disease control	Heart failure	In next update, this will be merged them with the respective risk factor 'diabetes→ heart failure'. Associations from both will be included as they come from 2 different cohort studies (Level 3).
8.	Diabetes: disease control	Ischemic heart disease	In next update, this will be merged them with the respective risk factor 'diabetes→ ischemic heart disease'.
9.	Diabetes: disease control	Ischemic heart disease OR Ischemic stroke	In next update, this will be merged them with the respective risk factor 'diabetes→ Ischemic heart disease OR Ischemic stroke'.
10.	Dyslipidemia	Heart Failure	
11.	Dyslipidemia	Ischemic heart disease	
12.	Dyslipidemia	Ischemic stroke	
13.	Heart failure	Ischemic stroke	
14.	Hypertension	Ischemic stroke	
15.	Hyperuricemia	Hypertension	
16.	Hyperuricemia	Ischemic stroke	

17.	Obesity	Asthma	
18.	Obesity	Cancer: colorectal cancer	This was found during literature search for obesity as a risk factor – although cancer is not within CARRE domain, investigators decided to include this both due to the severity and commonality of the end effect as well as to show that this database can lead to and is connected with other medical domains.
19.	Obesity	Cancer: gastric cardiac cancer	This was found during literature search for obesity as a risk factor – although cancer is not within CARRE domain, investigators decided to include this both due to the severity and commonality of the end effect as well as to show that this database can lead to and is connected with other medical domains.
20.	Obesity	Cancer: pancreatic cancer	This was found during literature search for obesity as a risk factor – although cancer is not within CARRE domain, investigators decided to include this both due to the severity and commonality of the end effect as well as to show that this database can lead to and is connected with other medical domains.
21.	Obesity	Death: cardiovascular	
22.	Obesity	Cholelithiasis	
23.	Obesity	Heart Failure	
24.	Ischemic heart disease	Death due to cardiovascular disease	
25.	Ischemic heart disease	Ischemic stroke	
26.	Ischemic heart disease AND Chronic kidney disease	Death	
27.	Ischemic heart disease OR Ischemic stroke	Peripheral vascular disease	
28.	Obesity	Osteoarthritis	
29.	Physical activity AND Chronic kidney disease	Death	
30.	Smoking	Albuminuria	

TABLE 3

Risk factors that were initially listed in Table 12 in D.2.1 but were not included in the current risk factor database. The last column shows the explanation for this discrepancy and plans (if any) to include these risk factors in the next update.

No	Cause	Effect	Comment
1.	Abnormalities of mineral metabolism (High serum levels of phosphorus, calcium and parathyroid hormone) in CKD	CVD	It is not CARRE's primary goal to include this, as it is related to end stage kidney disease (not our patient group) and is measured during hospitalization.
2.	Abnormalities of mineral metabolism (High serum levels of phosphorus, calcium and parathyroid	Cardiovascular mortality	It is not CARRE's primary goal to include this, as it is related to end stage kidney disease (not our patient group) and is measured during hospitalization.

	hormone) in CKD		
3.	Abnormalities of mineral metabolism (High serum levels of phosphorus, calcium and parathyroid hormone) in CKD	All cause mortality	It is not CARRE's primary goal to include this, as it is related to end stage kidney disease (not our patient group) and is measured during hospitalization.
4.	Abnormalities of mineral metabolism (High serum levels of phosphorus, calcium and parathyroid hormone) in CKD	Nonfatal cardiovascular events	It is not CARRE's primary goal to include this, as it is related to end stage kidney disease (not our patient group) and is measured during hospitalization.
5.	Acute myocardial infarction	Atrial Fibrillation	It is not CARRE's primary goal to include this, as this is not related to chronic cardio-renal, is more an acute heart disease issue.
6.	Age	cerebrovascular disease	Although initially listed (by mistake) it is not related to CARRE, so it was left out
7.	Alcohol abuse	hypertension	During first search, no strong evidence was found. A new study came out (PMID=25091872), so this will be included in the next update. 'Alcohol abuse' will change to 'alcohol consumption'.
8.	Alcohol abuse	renal disease	During first search, no strong evidence was found. A new study came out (PMID=25833405), so this will be included in the next update. 'Alcohol abuse' will change to 'alcohol consumption'.
9.	Alcohol abuse	cardiovascular disease	During first search, no strong evidence was found. Specifically, we found PMID=23845148, which was deemed as a very generic study about a lot of factors, so initially we thought it probably is too general to include. A new study came out (PMID=4533962), so this will be included in the next update. 'Alcohol abuse' will change to 'alcohol consumption'.
10.	Atherosclerosis	MI	Atherosclerosis leads to peripheral vascular disease and then to all the other conditions mentioned here – we decided to start with PVD (instead of atherosclerosis) as atherosclerosis is a process, not a condition, which leads to the condition of peripheral vascular disease (and ischemic heart disease, and cerebrovascular).
11.	Atherosclerosis	heart failure (HF)	Atherosclerosis leads to peripheral vascular disease and then to all the other conditions mentioned here – we decided to start with PVD (instead of atherosclerosis) as atherosclerosis is a process, not a condition, which leads to the condition of peripheral vascular disease (and ischemic heart disease, and cerebrovascular).
12.	Atherosclerosis	peripheral vascular disease	Atherosclerosis leads to peripheral vascular disease and then to all the other conditions mentioned here – we decided to start with PVD (instead of atherosclerosis) as atherosclerosis is a process, not a condition, which leads to the condition of peripheral vascular disease (and ischemic heart disease, and cerebrovascular).
13.	Atherosclerosis	sudden cardiac death	Atherosclerosis leads to peripheral vascular disease and then to all the other conditions mentioned here – we decided to start with PVD (instead of atherosclerosis) as atherosclerosis is a process, not a condition, which leads to the condition of peripheral vascular disease (and ischemic heart disease, and cerebrovascular).
14.	Cardiomyopahty	Ischemic heart disease	Cardiomyopathy is not very specific to be studied as a risk factor as such. Different types of cardiomyopathy would behave differently as risk factors. At this point we decided not to include any more detailed relevant terms.

			We chose to look into ischemic heart disease instead, as a relevant, more specific condition.
15.	Cardiomyopahty	HF	Cardiomyopathy is not very specific to be studied as a risk factor as such. Different types of cardiomyopathy would behave differently as risk factors. At this point we decided not to include any more detailed relevant terms. We chose to look into ischemic heart disease instead, as a relevant, more specific condition.
16.	CKD	AKI	Literature indicates evidence for this association only under very specific co-occurring conditions (e.g. contrast agent administration). So, we decided not to include this at this point. After submitting the deliverable, a meta-analysis came out (PMID=25975964), so now we will include this risk factor in the next version.
17.	CKD	anaemia	Anaemia is mentioned in the literature as a natural, very common complication, but no risk ratio values are reported from appropriate high level evidence studies (probably because it is considered common knowledge). There is only evidence from lower level studies (large cross sectional) is available.
18.	Chronic Kidney Disease and AF	end stage renal disease (ESRD)	No evidence was found at the time. A new study came out (PMID=25001152 and 25424480), so this will be included in the next update.
19.	Diabetes	renal disease	We just missed to report this by mistake. There is an appropriate meta-analysis (PMID=123013602) and we will include this in the next update.
20.	Dilatated cardiomyopahty	chronic heart failure	No high level evidence was found at the time.
21.	Dyslipidemia	diabetes	No high level evidence was found at the time.
22.	ESRD (end stage renal disease)	Infectious complications	As ESRD is end stage we decided that this is not that relevant to CARRE
23.	ESRD (end stage renal disease)	Sudden cardiac death	
24.	Excessive salt intake (diet) in CKD	high blood pressure	No high level evidence was found at the time. A systematic review (PMID=25691262) is now published (see below) with rather inconclusive results, so we decided not to include this risk factor at this point. PMID: 25691262 concludes that: We found a critical evidence gap in long-term effects of salt restriction in people with CKD that meant we were unable to determine the direct effects of sodium restriction on primary endpoints such as mortality and progression to end-stage kidney disease (ESKD). We found that salt reduction in people with CKD reduced blood pressure considerably and consistently reduced proteinuria. If such reductions could be maintained long-term, this effect may translate to clinically significant reductions in ESKD incidence and cardiovascular events. Research into the long-term effects of sodium-restricted diet for people with CKD is warranted, as is investigation into adherence to a low salt diet.
25.	Excessive salt intake (diet) in CKD	albuminuria	
26.	Excessive salt intake (diet) in CKD	progression of CKD	
27.	High protein intake (diet) in CKD	progression of CKD	No high level evidence was found at the time. In the next update, we will change the ‘high protein intake’ to ‘protein intake’ and use evidence from PMID= 19588328 which reports on the protective value of low protein uptake.
28.	Hypertension	diabetes	No high level evidence was found at the time. Investigators decided not to include this due to the complex nature of common comorbid conditions such as obesity.

29.	Hypertension	LVH	No high level evidence was found at the time. A new study came out (PMID= 254618808), so this will be included in the next update.
30.	Inappropriate dose adjustment of certain drugs (e.g antibiotics) in CKD	progression of CKD	The cause was not clearly phrased so that to correspond to published evidence.
31.	Inappropriate dose adjustment of certain drugs (e.g antibiotics) in CKD	AKI	The cause was not clearly phrased so that to correspond to published evidence.
32.	Insufficient glycemic control in diabetic CKD	progression of CKD	The cause 'issuficient glycemic control in diabetic CKD' was merged with 'diabetes'.
33.	Insufficient glycemic control in diabetic CKD	retinopathy	The cause 'issuficient glycemic control in diabetic CKD' was merged with 'diabetes'.
34.	Late referral to physician in CKD	hospitalization	Investigators decided not to include this at first draft as being too detailed. Next update will include this based on the PMID=24938824 Also, 'late referral' will change to 'referal' with possible values "early or late'.
35.	Late referral to physician in CKD	mortality	Investigators decided not to include this at first draft as being too detailed. Next update will include this based on the PMID=24938824 Also, 'late referral' will change to 'referal' with possible values "early or late'.
36.	Menopause	CVD	Investigators decided not to include this at first draft as being too detailed and not 'major' in the sense that refers to a certain part of the population. Next update will include it, based on evidence from PMID= 23633307, and its update PMID=25754617.
37.	Obesity in CKD	progression of CKD	Investigators decided not to include this at first draft as being too detailed.
38.	Obesity in CKD	mortality	Investigators decided not to include this at first draft as being too detailed. The effect should be substituted with 'death.
39.	Obesity in CKD	morbitity	Investigators decided not to include this at first draft as being too detailed. The effect should be substituted with 'death.
40.	Obesity in CKD	Reduction in life expectancy	Investigators decided not to include this at first draft as being too detailed. The effect should be substituted with 'death.
41.	Lack of physical activity in CKD	progression of CKD	Investigators decided not to include this at first draft as being too detailed. Next update will include the risk factor based on PMID=21975737.
42.	Physical exercise	hypertension	Omitted by mistake. Next update will include this factor with evidence based on PMID=24582191 and an earlier one PMID=24082054 'Physical exercise' is replaced by 'physical activity'.
43.	Physical exercise	dyslipidemia	Omitted by mistake. Next update will include this factor with evidence based on PMID=26116691 and an earlier one PMID=23116535.

			'Physical exercise' is replaced by 'physical activity'.
44.	Smoking	atherosclerosis	Evidence found reports directly the association to the end result of peripheral vascular disease and not the in-between of atherosclerosis. So this risk factor was replaced with the appropriate one.
45.	Atrial Fibrillation	Myocardial Infarction	?

1.3. Changes in the current update #2

- Source risk elements that were combinations of more than one (representing the concurrent existence of more than one risk elements – logical operator AND) were modified as follows: only the major risk element remains in the risk factor name, while the others remain as part of the observable condition. This resulted in merging risk evidences of certain risk factors
- Source and/or target risk elements that were groups of other risk elements (logical operator OR) were combined to form risk element groups which were then defined as new, collective risk elements. This introduces a new attribute for the risk element concept, that of '*includes risk elements*' which can have 0 to N multiplicity.
- All risk evidences were reviewed for correctness

2. Risk Associations

2.1. Acute kidney disease → Chronic kidney disease

Risk Association	
Risk Source:	Acute kidney disease
Risk Target:	Chronic kidney disease
Association Type:	Is an issue in
No. of risk evidences:	4
Author	Laurynas
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = yes
Ratio Type:	HR
Ratio Value:	8.8
Confidence Interval:	3.1 – 25.5
Adjusted for:	-
Evidence source PMID	22113526
Author	Laurynas
Reviewed	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = mild
Ratio Type:	HR
Ratio Value:	2.0
Confidence Interval:	1.4 – 2.8
Adjusted for:	-
Evidence source PMID	22113526
Author	Stefanos
Reviewed	Ploumis Laurynas

Risk Evidence ID3	
RiskID:	3

Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = moderate
Ratio Type:	HR
Ratio Value:	3.3
Confidence Interval:	1.7 – 6.2
Adjusted for:	-
Evidence source PMID	22113526
Author	Stefanos
Reviewed	Ploumis, Laurynas

Risk Evidence ID4	
RiskID:	4
Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = severe
Ratio Type:	HR
Ratio Value:	28.2
Confidence Interval:	21.1- 37.5
Adjusted for:	-
Evidence source PMID	22113526
Author	Stefanos
Reviewed	Ploumis, Laurynas

2.2. Acute kidney disease → Death

Risk Association	
Risk Source:	Acute kidney disease
Risk Target:	Death
Association Type:	Causes
No. of risk evidences:	1
Author	Laurynas
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = yes
Ratio Type:	HR

Ratio Value:	2.0
Confidence Interval:	1.3 – 3.1
Adjusted for:	-
Evidence source PMID	22113526
Author	Laurynas
Reviewed	Stefanos, Ploumis

2.3. Age → Ischemic heart disease

Risk Association	
Risk Source:	Age
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observables:	Age AND sex
Observable Condition:	50 ≤ age ≤ 59 AND sex=male
Ratio Type:	Risk ratio
Ratio Value:	4.02
Confidence Interval:	3.22 – 5.00
Adjusted for:	Age, study year, and area, smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Age Sex
Observable Condition:	60 ≤ age ≤ 64 AND

	sex = male
Ratio Type:	Risk ratio
Ratio Value:	6.43
Confidence Interval:	4.99 – 8.78
Adjusted for:	Age, study year, and area, smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Age AND sex
Observable Condition:	54 ≤ age ≤ 59 AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	5.53
Confidence Interval:	3.36 – 9.08
Adjusted for:	Age, study year, and area, smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Age AND Sex
Observable Condition:	60 ≤ age ≤ 64 AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	11.40
Confidence Interval:	6.83 – 19.05
Adjusted for:	Age, study year, and area, smoking, HDL/cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi

Reviewed	Stefanos, Ploumis, Gintare

2.4. Age → Peripheral arterial disease

Risk Association	
Risk Source:	Age
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
No. of risk evidences:	2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	age
Observable Condition:	55 ≤ age ≤ 64
Ratio Type:	Odds ratio
Ratio Value:	1.8
Confidence Interval:	1.3 – 2.6
Adjusted for:	sex
Evidence source PMID	11282794
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	age
Observable Condition:	65 ≤ age
Ratio Type:	Odds ratio
Ratio Value:	4.0
Confidence Interval:	2.8 – 5.9
Adjusted for:	sex
Evidence source PMID	11282794
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.5. Anemia → Acute myocardial infarction

Risk Association	
Risk Source:	Anemia
Risk Target:	Acute myocardial infarction
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	anemia diagnosis AND Acute myocardial infarction
Observable Condition:	anemia diagnosis = yes AND myocardial infarction self history = yes
Ratio Type:	Relative risk
Ratio Value:	1.25
Confidence Interval:	1.02 - 1.53
Adjusted for:	-
Evidence source PMID	23351816
Author	Gintare
Reviewed	Stefanos, Ploumis

2.6. Anemia → Death

Risk Association	
Risk Source:	Anemia
Risk Target:	Death
Association Type:	is an issue in
No. of risk evidences:	2
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	anemia diagnosis AND myocardial infarction self history

Observable Condition:	anemia diagnosis = yes AND myocardial infarction self history = yes
Ratio Type:	Relative risk
Ratio Value:	1.49
Confidence Interval:	1.23 - 1.81
Adjusted for:	Age, sex, history of type 2 diabetes mellitus, congestive heart failure, revascularization, treatment with thrombolysis, Killip class on presentation, and renal function
Evidence source PMID	23351816
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observable:	anemia diagnosis AND heart failure diagnosis
Observable Condition:	anemia diagnosis = yes AND heart failure diagnosis = yes
Ratio Type:	Hazard ratio
Ratio Value:	1.46
Confidence Interval:	1.26 – 1.69
Adjusted for:	Age, Gender, Renal Function, Severity of Heart Failure, Medical History, Medication
Evidence source PMID	18755344
Author	Dimitris
Reviewed	Kalliopi

2.7. Atrial fibrillation → Heart failure

Risk Association	
Risk Source:	Atrial fibrillation
Risk Target:	Heart failure
Association Type:	is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Atrial fibrillation diagnosis
Observable Condition:	Atrial fibrillation diagnosis = yes
Ratio Type:	Hazard ratio
Ratio Value:	1.89
Confidence Interval:	1.42 – 2.51
Adjusted for:	sex, hypertension, BMI, ischemic heart disease, diabetes mellitus, smoking, valvular heart disease, lower high-density lipoprotein cholesterol, atrial fibrillation, and the presence of LV hypertrophy or left bundle-branch block
Evidence source PMID	23271790
Author	Dimitris
Reviewed	Kalliopi

2.8. Atrial fibrillation → Ischemic stroke

Risk Association	
Risk Source:	Atrial fibrillation
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed by	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	Atrial fibrillation diagnosis = yes AND 50 <= age <= 59
Ratio Type:	Relative Risk
Ratio Value:	4.0
Confidence Interval:	...
Adjusted for:	Hypertension, Ischemic heart disease, Heart failure
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	atrial fibrillation diagnosis = yes AND 60 <= age <=69
Ratio Type:	Relative Risk
Ratio Value:	2.6
Confidence Interval:	...
Adjusted for:	hypertension, Ischemic heart disease, Heart failure
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	atrial fibrillation diagnosis = yes AND 70 <= age <= 79
Ratio Type:	Relative Risk
Ratio Value:	3.3
Confidence Interval:	...
Adjusted for:	Hypertension, Ischemic heart disease, Heart failure
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	Atrial fibrillation diagnosis = yes AND 80 ≤ age ≤ 89
Ratio Type:	Relative Risk
Ratio Value:	4.5

Confidence Interval:	...
Adjusted for:	Hypertension, Ischemic heart disease, Heart failure
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

2.9. Beta-blockers → Diabetes

Risk Association	
Risk Source:	Drugs: β-blockers
Risk Target:	Diabetes
Association Type:	issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	beta-blockers administration
Observable Condition:	beta-blockers administration = yes
Ratio Type:	Relative risk
Ratio Value:	1.32
Confidence Interval:	1.16 –1.49
Adjusted for:	-
Evidence source PMID	18490538
Author	Dimitris
Reviewed	Kalliopi

2.10. Cardiovascular events group 4 (Ischemic heart disease OR Ischemic stroke) → Peripheral vascular disease

Risk Association	
Risk Source:	Cardiovascular disease
Risk Target:	Peripheral vascular disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Ischemic heart disease diagnosis OR Ischemic stroke diagnosis
Observable Condition:	ischemic heart disease diagnosis = yes OR ischemic stroke diagnosis = yes
Ratio Type:	Odds ratio
Ratio Value:	2.27
Confidence Interval:	1.98–2.59
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.11. Central obesity → Acute myocardial infarction

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Acute myocardial infarction
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND sex
Observable Condition:	94 <= waist circumference < 102 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.1
Confidence Interval:	0.4 – 3.4
Adjusted for:	age, smoking status (current or ex-smoker/never smoked), self-reported history of cardiovascular disease
Evidence source PMID	19705980

Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference => 102 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	2.8
Confidence Interval:	1.1- 7.0
Adjusted for:	age, smoking status (current or ex-smoker/never smoked), self-reported history of cardiovascular disease
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 <= waist circumference < 88 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.5
Confidence Interval:	0.3- 6.6
Adjusted for:	age, smoking status (current or ex-smoker/never smoked), self-reported history of cardiovascular disease
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND sex
Observable Condition:	waist circumference ≥ 88

	AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.4
Confidence Interval	0.4- 5.5
Adjusted for:	age, smoking status (current or ex-smoker/never smoked), self-reported history of cardiovascular disease
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

2.12. Central obesity → Diabetes

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Diabetes
Association Type:	Causes
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	waist circumference (WC) AND sex
Observable Condition:	94 <= waist circumference < 102 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	1.7
Confidence Interval:	0.9 – 3.0
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC)

	AND Sex
Observable Condition:	waist circumference >= 102 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	3.5
Confidence Interval:	2.1 – 5.9
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 <= waist circumference < 88 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	0.9
Confidence Interval:	0.4 – 1.8
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND sex
Observable Condition:	waist circumference >= 88 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	3.8
Confidence Interval	2.3 – 6.3
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980

Author	Kalliopi
Reviewed	Dimitris Gintare

2.13. Central obesity → HDL cholesterol serum concentration

Risk Association	
Risk Source:	Obesity: central
Risk Target:	HDL cholesterol serum concentration
Association Type:	issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND sex
Observable Condition:	94 <= waist circumference < 102 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	1.7
Confidence Interval:	1.3 – 2.5
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference >= 102 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	2.0
Confidence Interval:	1.4 – 2.7
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)

Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 <= waist circumference < 88 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	1.8
Confidence Interval:	1.3 – 2.5
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND sex
Observable Condition:	waist circumference >= 88 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	2.6
Confidence Interval	1.9 – 3.6
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

2.14. Central obesity → Hypertension

Risk Association	
Risk Source:	Central obesity
Risk Target:	Hypertension

Association Type:	causes
No. of risk evidences:	8
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	88.2 <= waist circumference <= 94.2 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	1.5
Confidence Interval:	1.0 – 3.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	94.3 <= waist circumference <= 99.3 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	1.7
Confidence Interval:	1.0 – 3.5
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex

Observable Condition:	99.4 <= waist circumference <= 106.2 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	2.5
Confidence Interval:	1.5 – 4.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference > 106.2 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	3.5
Confidence Interval:	2.0 – 5.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	73.7 <= waist circumference <= 80.3 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	1
Confidence Interval:	0.5 -1.5
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Reviewed	Dimitris

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80.4 <= waist circumference <= 87 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	2
Confidence Interval:	1.0 – 3.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID7	
RiskID:	7
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	87.1 <= waist circumference <= 96.2 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	1.5 – 3.9
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID8	
RiskID:	8
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference > 96.2 AND sex = female

Ratio Type:	Odds ratio
Ratio Value:	5
Confidence Interval:	3.5 -7.5
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris

2.15. Central obesity → Triglycerides serum concentration

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Triclycerides serum concentratiion
Association Type:	elevates
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND sex
Observable Condition:	94 <=waist circumference < 102 AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	2.3
Confidence Interval:	1.7 – 3.1
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference >= 102

	AND sex = male
Ratio Type:	Odds ratio
Ratio Value:	2.1
Confidence Interval:	1.5 – 2.8
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 <= waist circumference < 88 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	2.2
Confidence Interval:	1.6 – 3.1
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND sex
Observable Condition:	waist circumference >= 88 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	4.0
Confidence Interval	3.0 – 5.4
Adjusted for:	age, smoking status (current or ex-smoker/never smoked)
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Dimitris Gintare

2.16. Chronic kidney disease → Cardiovascular events group 1 (Ischemic heart disease OR Heart failure OR Ischemic stroke OR Peripheral arterial disease)

Risk Association	
Risk Source:	Chronic Kidney Disease (CKD)
Risk Target:	Ischemic disease OR heart failure OR Ischemic stroke, OR peripheral arterial disease
Association Type:	causes
No. of risk evidences:	4
Author:	Stefanos
Reviewed	Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR estimated glomerular filtration rate
Observable Condition:	45 <= estimated glomerular filtration rate <= 59 OR chronic kidney disease diagnosis = stage3A
Ratio Type:	HR
Ratio Value:	1.4
Confidence Interval:	1.4 – 1.5
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	Chronic kidney disease diagnosis OR estimated glomerular filtration rate
Observable Condition:	30 <= estimated glomerular filtration rate <= 44 OR chronic kidney disease diagnosis = stage3B
Ratio Type:	HR
Ratio Value:	2.0
Confidence Interval:	1.9 – 2.1

Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID3	
RiskID:	3
Observable:	Chronic kidney disease diagnosis OR estimated glomerular filtration rate
Observable Condition:	15 <= estimated glomerular filtration rate <= 29 OR chronic kidney disease diagnosis = stage4
Ratio Type:	HR
Ratio Value:	2.8
Confidence Interval:	2.6 – 2.9
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID4	
RiskID:	4
Observable:	Chronic kidney disease diagnosis OR estimated glomerular filtration rate
Observable Condition:	estimated glomerular filtration rate < 15 OR chronic kidney disease diagnosis = stage5
Ratio Type:	HR
Ratio Value:	3.4
Confidence Interval:	3.1 – 3.8
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or

	less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

2.17. Chronic kidney disease → Death

Risk Association	
Risk Source:	Chronic kidney disease
Risk Target:	Death
Association Type:	causes
No. of risk evidences:	5
Author:	Stefanos
Reviewed	Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	chronic kidney disease diagnosis = stage3A OR 45 <= estimated glomerular filtration rate <= 59
Ratio Type:	HR
Ratio Value:	1.2
Confidence Interval:	1.1 – 1.2
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	chronic kidney disease diagnosis = stage3B

	OR 30 <= estimated glomerular filtration rate <= 44
Ratio Type:	HR
Ratio Value:	1.8
Confidence Interval:	1.7 – 1.9
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID3	
RiskID:	3
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	chronic kidney disease diagnosis = stage4 OR 15 <= estimated glomerular filtration rate <= 29
Ratio Type:	HR
Ratio Value:	3.2
Confidence Interval:	3.1 – 3.4
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID4	
RiskID:	4
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	chronic kidney disease diagnosis = stage5 OR estimated glomerular filtration rate < 15
Ratio Type:	HR

Ratio Value:	5.9
Confidence Interval:	5.4 – 6.5
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID5	
RiskID:	5
Observable:	[Chronic kidney disease diagnosis OR estimated glomerular filtration rate] AND Heart failure diagnosis
Observable Condition:	[estimated glomerular filtration rate < 90 OR chronic kidney disease diagnosis = stage2 OR chronic kidney disease diagnosis = stage3 OR chronic kidney disease diagnosis = stage4 OR chronic kidney disease diagnosis = stage 5] AND heart failure diagnosis = yes
Ratio Type:	Hazard ratio
Ratio Value:	1.56
Confidence Interval:	1.53 - 1.60
Adjusted for:	age, gender, race, comorbidities, medications, physical exam and symptoms, ejection fraction, electrocardiogram findings, laboratory values, and neurohormonal measures
Evidence source PMID	16697315
Author	Dimitris
Reviewed	Kalliopi

2.18. Chronic kidney disease → Hospitalization

Risk Association	
Risk Source:	Chronic Kidney Disease (CKD)

Risk Target:	Hospitalization
Association Type:	causes
No. of risk evidences:	4
Author:	Stefanos
Reviewed	Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	45 <= estimated glomerular filtration rate <= 59 OR chronic kidney disease diagnosis = stage3A
Ratio Type:	HR
Ratio Value:	1.1
Confidence Interval:	1.1-1.1
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	30 <= estimated glomerular filtration rate <= 44 OR chronic kidney disease diagnosis = stage3B
Ratio Type:	HR
Ratio Value:	1.5
Confidence Interval:	1.5-1.5
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.

Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID3	
RiskID:	3
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	15 <= estimated glomerular filtration rate <= 29 OR chronic kidney disease diagnosis = stage4
Ratio Type:	HR
Ratio Value:	2.1
Confidence Interval:	2.0-2.2
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Ploumis Laurynas

Risk Evidence ID4	
RiskID:	4
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	estimated glomerular filtration rate < 15 OR chronic kidney disease diagnosis = stage5
Ratio Type:	HR
Ratio Value:	3.1
Confidence Interval:	3.0-3.3
Adjusted for:	age, sex, income, education, use or nonuse of dialysis, the presence or absence of prior Ischemic heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos

Reviewed:	Ploumis Laurynas

2.19. Chronic kidney disease → Hyperkalemia

Risk Association	
Risk Source:	Chronic kidney disease
Risk Target:	Hyperkalemia
Association Type:	Issue in
No. of risk evidences:	1
Author	Neringa
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	(chronic kidney disease diagnosis OR estimated glomerular filtration rate) AND (hypertension OR heart failure)
Observable Condition:	(estimated glomerular filtration rate < 60 OR chronic kidney disease diagnosis = stage3 OR chronic kidney disease diagnosis = stage4 OR chronic kidney disease diagnosis = stage5) AND (hypertension diagnosis = yes OR heart failure diagnosis = yes)
Ratio Type:	Odds ratio
Ratio Value:	2.14
Confidence Interval:	2.02-2.28
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa
Reviewed	Stefanos, Ploumis

2.20. Chronic kidney disease → Peripheral arterial disease

Risk Association	
Risk Source:	Chronic kidney disease

Risk Target:	Peripheral Arterial Disease
Association Type:	causes
No. of risk evidences:	1
Author:	Stefanos
Reviewed	Dimitris, Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR estimated glomerular filtration rate
Observable Condition:	estimated glomerular filtration rate < 60 OR [chronic kidney disease diagnosis = stage3 OR chronic kidney disease diagnosis = stage4 OR chronic kidney disease diagnosis = stage5]
Ratio Type:	OR
Ratio Value:	2.5
Confidence Interval:	1.2-5.1
Adjusted for:	age, diabetes, hypertension, ischemic heart disease, stroke history, and hypercholesterolemia
Evidence source PMID	14732743
Author:	Stefanos
Reviewed:	Kalliopi, Dimitris Laurynas

2.21. Chronic obstructive pulmonary disease → Death due to cardiovascular disease

Risk Association	
Risk Source:	Chronic obstructive pulmonary disease
Risk Target:	Death: Cardiovascular
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1

Observable:	Chronic obstructive pulmonary disease diagnosis
Observable Condition:	chronic obstructive pulmonary disease diagnosis = yes
Ratio Type:	Hazard ratio
Ratio Value:	1.28
Confidence Interval:	1.01–1.57
Adjusted for:	age, gender, BMI, emergency procedure, prior myocardial infarction, congestive heart failure, stroke, peripheral artery disease, chronic atrial fibrillation, malignancy, hypertension, diabetes without insulin therapy, diabetes with insulin therapy, dialysis, chronic renal disease, anemia, current smoking status, left ventricular dysfunction, chronic total occlusion of the coronary artery, proximal left anterior descending ischemic heart disease, left main Ischemic heart disease, triple vessel disease
Evidence source PMID	19368979
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.22. Chronic obstructive pulmonary disease → Heart failure

Risk Association	
Risk Source:	Chronic obstructive pulmonary disease
Risk Target:	Heart failure
Association Type:	is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic obstructive pulmonary disease
Observable Condition:	chronic obstructive pulmonary disease diagnosis = yes
Ratio Type:	Odds ratio
Ratio Value:	3.84
Confidence Interval:	3.56–4.14
Adjusted for:	history of cardiovascular events, diabetes, hypertension, hypercholesterolemia
Evidence source PMID	16039877
Author	Dimitris
Reviewed	Gintare

2.23. Contrast agents → Acute kidney injury

Risk Association	
Risk Source:	Contrast agents: coronary angiography
Risk Target:	Acute kidney injury
Association Type:	causes
No. of risk evidences:	1
Author:	Dimitris
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	coronary angiography contrast agents administration
Observable Condition:	contrast agents administration = yes
Ratio Type:	RR
Ratio Value:	2.39
Confidence Interval:	1.98 – 2.90
Adjusted for:	baseline severity of illness variables
Evidence source PMID	23322741
Author:	Dimitris
Reviewed	Stefanos, Ploumis

2.24. Depression → Ischemic heart disease

Risk Association	
Risk Source:	Depression
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk evidence ID1	
RiskID:	1
Observable	Depression diagnosis
Observable Condition:	depression diagnosis = yes
Ratio Type:	Relative risk
Ratio Value:	1.90

Confidence Interval:	1.49–2.42
Adjusted for:	age, sex, marital status, smoking, alcohol, physical activity, cholesterol, blood pressure, BMI, diabetes, CHD severity—previous history, number of affected vessels, dyspnoea, left ventricular function
Evidence source PMID	17082208
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.25. Depression → Ischemic stroke

Risk Association	
Risk Source:	Depression
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Depression diagnosis
Observable Condition:	depression diagnosis = yes
Ratio Type:	Relative risk
Ratio Value:	1.34
Confidence Interval:	1.17–1.54
Adjusted for:	age, sex, body mass index, smoking, educational level, hypertension, diabetes, history of cardiac disease
Evidence source PMID	22020036
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.26. Diabetes → Cardiovascular events group 2 (acute myocardial infarction OR ischemic stroke OR ischemic heart disease)

Risk Association	
Risk Source:	Diabetes
Risk Target:	Myocardial infarction OR Ischemic heart disease OR Ischemic stroke

Association Type:	is an issue in
No. of risk evidences:	7
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable	Diabetes diagnosis
Observable Condition:	diabetes diagnosis = yes
Ratio Type:	Hazard ratio
Ratio Value:	1.96
Confidence Interval:	1.44-2.66
Adjusted for:	age, sex, systolic blood pressure, hypertension treatment, current smoking, total cholesterol, body mass index
Evidence source PMID	15562129
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND glycated haemoglobin < 6.0
Ratio Type:	Hazard ratio
Ratio Value:	1
Confidence Interval:	-
Adjusted for:	age at diagnosis, duration of diabetes, gender, ethnicity, socio-economic status, smoking status, systolic blood pressure, serum total cholesterol : HDL ratio, body mass index, urine albumin to creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID3	
RiskID:	3
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes

	AND 6.0 <= glycated haemoglobin < 7.0
Ratio Type:	Hazard ratio
Ratio Value:	1.08
Confidence Interval:	0.97 – 1.19
Adjusted for:	age at diagnosis, duration of diabetes, gender, ethnicity, socio-economic status, smoking status, systolic blood pressure, serum total cholesterol : HDL ratio, body mass index, urine albumin to creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID4	
RiskID:	4
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 7.0 <= glycated haemoglobin < 8.0
Ratio Type:	Hazard ratio
Ratio Value:	1.13
Confidence Interval:	1.02 – 1.25
Adjusted for:	age at diagnosis, duration of diabetes, gender, ethnicity, socio-economic status, smoking status, systolic blood pressure, serum total cholesterol : HDL ratio, body mass index, urine albumin to creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID5	
RiskID:	5
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 8.0 <= glycated haemoglobin < 9.0
Ratio Type:	Hazard ratio
Ratio Value:	1.26
Confidence Interval:	1.12 – 1.41
Adjusted for:	age at diagnosis, duration of diabetes, gender, ethnicity, socio-economic status, smoking status, systolic blood pressure, serum total cholesterol : HDL ratio, body mass index, urine albumin to creatinine ratio

Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID6	
RiskID:	6
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 9.0 <= glycated haemoglobin < 10.0
Ratio Type:	Hazard ratio
Ratio Value:	1.31
Confidence Interval:	1.15 – 1.50
Adjusted for:	age at diagnosis, duration of diabetes, gender, ethnicity, socio-economic status, smoking status, systolic blood pressure, serum total cholesterol : HDL ratio, body mass index, urine albumin to creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID7	
RiskID:	7
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND glycated haemoglobin >= 10.0
Ratio Type:	Hazard ratio
Ratio Value:	1.53
Confidence Interval:	1.34 – 1.73
Adjusted for:	age at diagnosis, duration of diabetes, gender, ethnicity, socio-economic status, smoking status, systolic blood pressure, serum total cholesterol : HDL ratio, body mass index, urine albumin to creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi

2.27. Diabetes → Death due to cardiovascular event

Risk Association	
Risk Source:	Diabetes
Risk Target:	Death: due to cardiovascular disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	diabetes diagnosis AND Sex
Observable Condition:	diabetes diagnosis = yes AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.93
Confidence Interval:	2.13 – 4.04
Adjusted for:	age, menopausal status, postmenopausal hormone use, prior report of ischemic heart disease, hypertension, smoking, hypercholesterolemia, parental history of myocardial infarction, BMI
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris Stefanos

2.28. Diabetes → Heart failure

Risk Association	
Risk Source:	Diabetes
Risk Target:	Heart failure
Association Type:	is an issue in
No. of risk evidences:	5
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	REID1

Observable:	Diabetes diagnosis
Observable Condition:	diabetes diagnosis =yes
Ratio Type:	Hazard ratio
Ratio Value:	2.50
Confidence Interval:	2.03–3.08
Adjusted for:	age, sex, hypertension, BMI, heart rate, CHD, valvular heart disease, lower high-density lipoprotein cholesterol, atrial fibrillation, presence of LV hypertrophy or left bundle-branch block
Evidence source PMID	23271790
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	diabetes diagnosis = yes AND 7.0 <= glycated haemoglobin < 8.0
Ratio Type:	Hazard ratio
Ratio Value:	1.15
Confidence Interval:	0.93–1.43
Adjusted for:	age, sex, blood pressure, lipid, smoking, BMI or WC, DM medication, DM duration
Evidence source PMID	11390335
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 8.0 <= glycated haemoglobin < 9.0
Ratio Type:	Hazard ratio
Ratio Value:	1.10
Confidence Interval:	0.88–1.38
Adjusted for:	Age, sex, BP, lipid, smoking, BMI or WC, DM medication, DM duration
Evidence source PMID	11390335
Author	Zydrune

Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 9.0 <= glycated haemoglobin < 10.0
Ratio Type:	Hazard ratio
Ratio Value:	1.39
Confidence Interval:	1.11–1.74
Adjusted for:	Age,sex, BP, lipid, smoking, BMI or WC, DM medication, DM duration
Evidence source PMID	11390335
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND glycated haemoglobin >= 10.0
Ratio Type:	Hazard ratio
Ratio Value:	1.56
Confidence Interval:	1.26–1.93
Adjusted for:	Age, sex, BP, lipid, smoking, BMI or WC, DM medication, DM duration
Evidence source PMID	11390335
Author	Zydrune
Reviewed	Kalliopi, Dimitris

2.29. Diabetes → Ischemic heart disease

Risk Association	
Risk Source:	Diabetes
Risk Target:	Ischemic heart disease
Association Type:	causes
No. of risk evidences:	7

Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID1:	1
Observables:	Diabetes diagnosis AND Sex
Observable Condition:	diabetes diagnosis = yes AND sex = female
Ratio Type:	RR
Ratio Value:	2.82
Confidence Interval:	2.35 – 3.38
Adjusted for:	age, blood pressure, cigarette smoking, BMI, lipids
Evidence source PMID	24859435
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Diabetes diagnosis AND Sex
Observable Condition:	diabetes diagnosis = yes AND sex = male
Ratio Type:	RR
Ratio Value:	2.16
Confidence Interval:	1.82 – 2.56
Adjusted for:	age, blood pressure, cigarette smoking, BMI, lipids
Evidence source PMID	24859435
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes

	AND glycated haemoglobin < 5.2
Ratio Type:	Hazard ratio
Ratio Value:	1
Confidence Interval:	-
Adjusted for:	age, sex, BP, lipids, smoking, BMI
Evidence source PMID	16157837
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID4	
RiskID:	4
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 5.2 <= glycated haemoglobin < 5.7
Ratio Type:	Hazard ratio
Ratio Value:	1.24
Confidence Interval:	0.77 – 1.98
Adjusted for:	Age, Sex, BP, Lipids, Smoking, BMI
Evidence source PMID	16157837
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID5	
RiskID:	5
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND 5.7 <= glycated haemoglobin < 6.5
Ratio Type:	Hazard ratio
Ratio Value:	1.57
Confidence Interval:	0.98 – 2.52
Adjusted for:	Age, Sex, BP, Lipids, Smoking, BMI
Evidence source PMID	16157837
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID6	
RiskID:	6
Observable:	diabetes diagnosis AND HbA1c
Observable Condition:	diabetes diagnosis = yes AND 6.5 <= glycated haemoglobin < 8.2
Ratio Type:	Hazard ratio
Ratio Value:	2.04
Confidence Interval:	1.30 – 3.19
Adjusted for:	Age, Sex, BP, Lipids, Smoking, BMI
Evidence source PMID	16157837
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID7	
RiskID:	7
Observable:	Diabetes diagnosis AND glycated haemoglobin
Observable Condition:	diabetes diagnosis = yes AND glycated haemoglobin >=8.2
Ratio Type:	Hazard ratio
Ratio Value:	2.37
Confidence Interval:	1.50 - 3.72
Adjusted for:	Age, Sex, BP, Lipids, Smoking, BMI
Evidence source PMID	16157837
Author	Dimitris
Reviewed	Kalliopi

2.30. Diabetes → Peripheral vascular disease

Risk Association	
Risk Source:	Diabetes
Risk Target:	Peripheral vascular disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare

Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes diagnosis
Observable Condition:	diabetes diagnosis = yes
Ratio Type:	Odds ratio
Ratio Value:	1.68
Confidence Interval:	1.53–1.84
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.31. Diuretics → Diabetes

Risk Association	
Risk Source:	Diuretics
Risk Target:	Diabetes
Association Type:	issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Diuretics administration
Observable Condition:	diuretics administration = yes
Ratio Type:	Relative risk
Ratio Value:	1.32
Confidence Interval:	0.18 –1.49
Adjusted for:	-
Evidence source PMID	18490538
Author	Dimitris
Reviewed	Kalliopi

2.32. Dyslipidemia → Heart Failure

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Heart failure
Association Type:	is an issue in
No. of risk evidences:	4
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	high-density lipoprotein cholesterol (mg/dL) AND Sex
Observable Condition:	40 <= high-density lipoprotein cholesterol <= 54 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	0.77
Confidence Interval:	0.65 – 0.91
Adjusted for:	age, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, smoking
Evidence source PMID	19933936
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observable:	high-density lipoprotein cholesterol (mg/dL) AND Sex
Observable Condition:	50 <= high-density lipoprotein cholesterol <= 64 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	0.77
Confidence Interval:	0.65 – 0.91
Adjusted for:	Age, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, and smoking
Evidence source PMID	19933936
Author	Gintare

Reviewed	Stefanos, Ploumis

Risk Evidence ID3	
RiskID:	3
Observable:	high-density lipoprotein cholesterol (mg/dL) AND Sex
Observable Condition:	high-density lipoprotein cholesterol >= 55 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	0.60
Confidence Interval:	0.48 – 0.74
Adjusted for:	Age, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, and smoking
Evidence source PMID	19933936
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID4	
RiskID:	4
Observable:	high-density lipoprotein cholesterol (mg/dL) AND Sex
Observable Condition:	high-density lipoprotein cholesterol >= 65 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	0.60
Confidence Interval:	0.48 – 0.74
Adjusted for:	Age, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, and smoking
Evidence source PMID	19933936
Author	Gintare
Reviewed	Stefanos, Ploumis

2.33. Dyslipidemia → Ischemic heart disease

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Ischemic heart disease

Association Type:	is an issue in
No. of risk evidences:	3
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	non high-density lipoprotein cholesterol (mg/dL)
Observable Condition:	non high-density lipoprotein cholesterol >= 169
Ratio Type:	Hazard ratio
Ratio Value:	1.56
Confidence Interval:	1.47-1.66
Adjusted for:	nonlipid risk factors
Evidence source PMID	19903920
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	high-density lipoprotein cholesterol (mg/dL)
Observable Condition:	high-density lipoprotein cholesterol <= 50
Ratio Type:	Hazard ratio
Ratio Value:	0.71
Confidence Interval:	0.68-0.75
Adjusted for:	nonlipid risk factors
Evidence source PMID	19903920
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID3	
RiskID:	3
Observable:	triglycerides (mg/dL)
Observable Condition:	triglycerides >= 150
Ratio Type:	Hazard ratio
Ratio Value:	1.37
Confidence Interval:	1.31-1.42
Adjusted for:	nonlipid risk factors
Evidence source PMID	19903920

Author	Dimitris
Reviewed	Kalliopi, Laurynas

2.34. Dyslipidemia → Ischemic stroke

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	3
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	non high-density lipoprotein cholesterol (mg/dL)
Observable Condition:	non high-density lipoprotein cholesterol >= 169
Ratio Type:	Hazard ratio
Ratio Value:	1.12
Confidence Interval:	1.04-1.20
Adjusted for:	nonlipid risk factors
Evidence source PMID	19903920
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	high-density lipoprotein cholesterol (mg/dL)
Observable Condition:	high-density lipoprotein cholesterol <= 50
Ratio Type:	Hazard ratio
Ratio Value:	0.93
Confidence Interval:	0.84-1.02
Adjusted for:	nonlipid risk factors
Evidence source PMID	19903920
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID3	
RiskID:	3
Observable:	triglycerides (mg/dL)
Observable Condition:	triglycerides >= 150
Ratio Type:	Hazard ratio
Ratio Value:	1.02
Confidence Interval:	0.94-1.11
Adjusted for:	nonlipid risk factors
Evidence source PMID	19903920
Author	Dimitris
Reviewed	Kalliopi, Laurynas

2.35. Dyslipidemia → Peripheral arterial disease

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
No. of risk evidences:	4
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	total cholesterol (mg/Dl)
Observable Condition:	total cholesterol > 200
Ratio Type:	Odds ratio
Ratio Value:	1.16
Confidence Interval:	1.08–1.25
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	low-density lipoprotein cholesterol (mg/dL)

Observable Condition:	low-density lipoprotein cholesterol > 130
Ratio Type:	Odds ratio
Ratio Value:	1.03
Confidence Interval:	0.94–1.13
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	high-density lipoprotein cholesterol (mg/dL)
Observable Condition:	high-density lipoprotein cholesterol < 40
Ratio Type:	Odds ratio
Ratio Value:	0.92
Confidence Interval:	0.83–1.01
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	triglycerides (mg/dL)
Observable Condition:	triglycerides >150
Ratio Type:	Odds ratio
Ratio Value:	1.22
Confidence Interval:	1.10–1.35
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

2.36. Heart failure → Ischemic stroke

Risk Association	
Risk Source:	Heart failure

Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed by	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	heart failure diagnosis AND Age
Observable Condition:	heart failure diagnosis = yes AND 50 <= age <= 59
Ratio Type:	Relative Risk
Ratio Value:	3.9
Confidence Interval:	...
Adjusted for:	Hypertension, Ischemic heart disease, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Heart failure diagnosis AND Age
Observable Condition:	heart failure diagnosis = yes AND 60 <= age <= 69
Ratio Type:	Relative Risk
Ratio Value:	2.4
Confidence Interval:	...
Adjusted for:	Hypertension, Ischemic heart disease, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Heart failure diagnosis

	AND Age
Observable Condition:	heart failure diagnosis = yes AND 70 <= age <= 79
Ratio Type:	Relative Risk
Ratio Value:	2.2
Confidence Interval:	...
Adjusted for:	Hypertension, Ischemic heart disease, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Heart failure diagnosis AND Age
Observable Condition:	heart failure diagnosis = yes AND 80 <= age <=89
Ratio Type:	Relative Risk
Ratio Value:	1.7
Confidence Interval:	...
Adjusted for:	hypertension, ischemic heart disease, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

2.37. Hyperkalemia → Death

Risk Association	
Risk Source:	Hyperkalemia
Risk Target:	death
Association Type:	cause
No. of risk evidences:	1
Author	Neringa
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1

Observable:	serum potassium (mEq/L) AND (chronic kidney disease diagnosis OR estimated glomerular filtration rate)
Observable Condition:	serum potassium > 5.0 AND (chronic kidney disease diagnosis = stage3 OR stage4 OR stage5 OR estimated glomerular filtration rate <= 44)
Ratio Type:	Odds ratio
Ratio Value:	1.63
Confidence Interval:	1.04-2.55
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa
Reviewed	Stefanos, Ploumis

2.38. Hypertension → Chronic kidney disease

Risk Association	
Risk Source:	Hypertension
Risk Target:	Chronic kidney disease (CKD)
Association Type:	Causes
No. of risk evidences:	1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Hypertension diagnosis
Observable Condition:	hypertension diagnosis = yes
Ratio Type:	Odds ratio
Ratio Value:	2.0
Confidence Interval:	1.8 - 2.2
Adjusted for:	age, sex, smoking status and eGFR
Evidence source PMID	21852664
Author	Dimitris
Reviewed	kalliopi, Stefanos

2.39. Hypertension → Death due to cardiovascular event

Risk Association	
Risk Source:	Hypertension
Risk Target:	Death: due to cardiovascular disease
Association Type:	Is an issue
No. of risk evidences:	2
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	diastolic blood pressure AND systolic blood pressure
Observable Condition:	120 <= systolic blood pressure <= 139mmHg, OR 80 <= diastolic blood pressure <= 89
Ratio Type:	Relative Risk
Ratio Value:	1.23
Confidence Interval:	0.85 - 1.79
Adjusted for:	age, gender, race/ethnicity, smoking status, leisure time physical activity, hypercholesterolemia, obesity, diabetes, chronic kidney disease, history of heart attack, congestive heart failure and stroke
Evidence source PMID	18261929
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	diastolic blood pressure AND systolic blood pressure
Observable Condition:	systolic blood pressure >= 140 OR diastolic blood pressure >= 90
Ratio Type:	Relative Risk
Ratio Value:	1.64
Confidence Interval:	1.11 - 2.41
Adjusted for:	age, gender, race/ethnicity, smoking status, leisure time physical activity, hypercholesterolemia, obesity, diabetes, chronic kidney disease, history of heart attack, congestive heart failure and stroke.
Evidence source PMID	18261929

Author	Dimitris
Reviewed	Kalliopi, Laurynas

2.40. Hypertension → Heart Failure

Risk Association	
Risk Source:	Hypertension
Risk Target:	Heart failure
Association Type:	Causes
No. of risk evidences:	1
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	systolic blood pressure AND diastolic blood pressure OR hypertension diagnosis
Observable Condition:	hypertension diagnosis = yes OR [systolic blood pressure >= 140 OR diastolic blood pressure >= 90]
Ratio Type:	Hazard ratio
Ratio Value:	1.58
Confidence Interval:	1.26–1.9
Adjusted for:	Multivariable-Adjusted
Evidence source PMID	23271790
Author	Gintare
Reviewed	Dimitris

2.41. Hypertension → Ischemic stroke

Risk Association	
Risk Source:	Hypertension
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	4

Author	Kalliopi
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observables:	hypertension diagnosis AND age
Observable Condition:	hypertension diagnosis = yes AND 50 <= age<= 59
Ratio Type:	Relative Risk
Ratio Value:	3.5
Confidence Interval:	...
Adjusted for:	Ischemic heart disease, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed	Stefanos, Ploumis Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Hypertension diagnosis AND Age
Observable Condition:	hypertension diagnosis = yes AND 60 <= age <= 69
Ratio Type:	Relative Risk
Ratio Value:	3.2
Confidence Interval:	...
Adjusted for:	Ischemic heart disease, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Hypertension diagnosis AND Age
Observable Condition:	hypertension diagnosis = yes AND

	70 <= age <= 79
Ratio Type:	Relative Risk
Ratio Value:	2.5
Confidence Interval:	...
Adjusted for:	Ischemic heart disease, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Hypertension diagnosis AND Age
Observable Condition:	hypertension diagnosis = yes AND 79 <= age <= 89
Ratio Type:	Relative Risk
Ratio Value:	1.7
Confidence Interval:	...
Adjusted for:	ischemic heart disease, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

2.42. Hypertension → Peripheral arterial disease

Risk Association	
Risk Source:	Hypertension
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure OR Hypertension diagnosis

Observable Condition:	hypertension diagnosis = yes OR [systolic blood pressure >=140 OR diastolic blood pressure >= 90]
Ratio Type:	Odds ratio
Ratio Value:	1.47
Confidence Interval:	1.37–1.57
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

2.43. Hyperuricemia → Death

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Death
Association Type:	is an issue in
No. of risk evidences:	1
Author	Larynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	uric acid serum concentration (mg/dL) OR uric acid serum concentration (mmol/L)
Observable Condition:	uric acid serum concentration (mg/dL) >6.7 OR uric acid serum concentration (mmol/L) >0.4
Ratio Type:	RR
Ratio Value:	1.33
Confidence Interval:	1.24 – 1.43
Adjusted for:	-
Evidence source PMID	24468137
Author	Larynas
Reviewed	Dimitris stefanos

2.44. Hyperuricemia → Heart failure

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Heart failure
Association Type:	is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration (mg/dL)
Observable Condition:	uric acid serum concentration (mg/dL) > 6.8
Ratio Type:	Hazard ratio
Ratio Value:	1.65
Confidence Interval:	1.41 – 1.94
Adjusted for:	-
Evidence source PMID	23933579
Author	Dimitris
Reviewed	Laurynas

2.45. Hyperuricemia → Hypertension

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Hypertension
Association Type:	is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	uric acid serum concentration (mg/dL)
Observable Condition:	uric acid serum concentration > 6.8
Ratio Type:	RR
Ratio Value:	1.41

Confidence Interval:	1.23 – 1.58
Adjusted for:	Multivariable adjusted
Evidence source PMID	20824805
Author	Dimitris
Reviewed	Laurynas

2.46. Hyperuricemia → Ischemic heart disease

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration (mg/dL)
Observable Condition:	uric acid serum concentration > 6.8
Ratio Type:	RR
Ratio Value:	1.09
Confidence Interval:	1.03 – 1.16
Adjusted for:	age, gender, hypertension, hypercholesterolemia and blodd glucose
Evidence source PMID	20191515
Author	Dimitris
Reviewed	Kalliopi Laurynas

2.47. Hyperuricemia → Ischemic stroke

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	2
Author	Larynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration (mg/dL) AND Sex
Observable Condition:	uric acid serum concentration > 6.7 AND sex = male
Ratio Type:	RR
Ratio Value:	1.08
Confidence Interval:	0.85 – 1.38
Adjusted for:	Multivariable adjusted to established cardiovascular risk factors
Evidence source PMID	24468137
Author	Larynas
Reviewed	Dimitris stefanos

Risk Evidence ID2	
RiskID:	2
Observables:	Uric acid serum concentration AND Sex
Observable Condition:	uric acid serum concentration > 6.7 AND sex = female
Ratio Type:	RR
Ratio Value:	1.25
Confidence Interval:	1.04–1.46
Adjusted for:	Multivariable adjusted to established cardiovascular risk factors
Evidence source PMID	24468137
Author	Larynas
Reviewed	Dimitris stefanos

2.48. Ischemic heart disease → Death

Risk Association	
Risk Source:	Ischemic heart disease AND Chronic kidney disease
Risk Target:	Death
Association Type:	cause
No. of risk evidences:	1

Author	Neringa
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Ischemic heart disease diagnosis AND (Chronic kidney disease diagnosis (5 levels) OR estimated glomerular filtration rate)
Observable Condition:	ischemic heart disease diagnosis = yes AND (chronic kidney disease diagnosis (5 levels) = stage3 OR Chronic kidney disease diagnosis (5 levels) = stage4 OR Chronic kidney disease diagnosis (5 levels) = stage5 OR estimated glomerular filtration rate <= 44)
Ratio Type:	Odds ratio
Ratio Value:	1.66
Confidence Interval:	1.05 – 2.63
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa
Reviewed	Stefanos, Ploumis

2.49. Ischemic heart disease → Death due to cardiovascular disease

Risk Association	
Risk Source:	Ischemic heart disease
Risk Target:	Death due to cardiovascular disease
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observables:	Ischemic heart disease diagnosis AND age

	AND sex
Observable Condition:	ischemic heart disease diagnosis = yes AND 50 <= age <= 59 AND sex = male
Ratio Type:	Risk ratio
Ratio Value:	6.79
Confidence Interval:	4.81 – 9.59
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Ischemic heart disease diagnosis AND age AND sex
Observable Condition:	ischemic heart disease diagnosis = yes AND 60 <= age <= 64 AND sex = male
Ratio Type:	Risk ratio
Ratio Value:	12.93
Confidence Interval:	8.91 – 18.77
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Ischemic heart disease diagnosis AND age AND sex
Observable Condition:	ischemic heart disease diagnosis = yes AND 54 <= age <= 59

	AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	7.84
Confidence Interval:	2.87 – 21.40
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Ischemic heart disease diagnosis AND age AND sex
Observable Condition:	ischemic heart disease diagnosis = yes AND 60 <= age <= 64 AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	40.38
Confidence Interval:	15.38 – 102.01
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis, Gintare

2.50. Ischemic heart disease → Ischemic stroke

Risk Association	
Risk Source:	Ischemic heart disease
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed by	Dimitris

Risk Evidence ID1

RiskID:	1
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	ischemic heart disease diagnosis = yes AND 50 <= age <= 59
Ratio Type:	Relative Risk
Ratio Value:	2.9
Confidence Interval:	...
Adjusted for:	Hypertension, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	ischemic heart disease diagnosis = yes AND 60 <= age <= 69
Ratio Type:	Relative Risk
Ratio Value:	2.0
Confidence Interval:	..
Adjusted for:	Hypertension, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Kalliopi, Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	ischemic heart disease diagnosis = yes AND 70 <= age <= 79
Ratio Type:	Relative Risk
Ratio Value:	1.7
Confidence Interval:	...

Adjusted for:	Hypertension, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi
Reviewed by	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	ischemic heart disease diagnosis = yes AND 80 <= age <= 89
Ratio Type:	Relative Risk
Ratio Value:	0.7
Confidence Interval:	...
Adjusted for:	Hypertension, heart failure, atrial fibrillation
Evidence source PMID	1866765
Author	Kalliopi,
Reviewed by	Dimitris, Gintare

2.51. Ischemic heart disease: Family history → Ischemic heart disease

Risk Association	
Risk Source:	Ischemic heart disease: family history
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	6
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = maternal AND sex = male
Ratio Type:	Relative risk
Ratio Value	2.14

Confidence Interval:	1.64–2.79
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease history = maternal AND sex = female
Ratio Type:	Relative risk
Ratio Value	1.76
Confidence Interval:	1.09–2.87
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease history = paternal AND sex = male
Ratio Type:	Relative risk
Ratio Value	1.58
Confidence Interval:	1.33–1.89
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199

Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease history = paternal AND sex = female
Ratio Type:	Relative risk
Ratio Value	0.93
Confidence Interval:	0.60–1.45
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease history = paternal AND ischemic heart disease history = paternal AND sex = male
Ratio Type:	Relative risk
Ratio Value	1.98
Confidence Interval:	1.41–2.78
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease history = paternal AND ischemic heart disease history = paternal AND sex = female
Ratio Type:	Relative risk
Ratio Value	2.49
Confidence Interval:	1.46–4.24
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.52. Ischemic heart disease: Family history → Ischemic stroke

Risk Association	
Risk Source:	Ischemic heart disease: family history
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	6
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = maternal AND sex = male
Ratio Type:	Relative risk
Ratio Value	1.26
Confidence Interval:	0.92–1.72

Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = maternal AND sex = female
Ratio Type:	Relative risk
Ratio Value	1.14
Confidence Interval:	0.69–1.90
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = paternal AND sex = male
Ratio Type:	Relative risk
Ratio Value	1.05
Confidence Interval:	0.87–1.27
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare

Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = paternal AND sex = female
Ratio Type:	Relative risk
Ratio Value	1.15
Confidence Interval:	0.81–1.63
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = paternal AND ischemic heart disease family history maternal AND sex = male
Ratio Type:	Relative risk
Ratio Value	1.03
Confidence Interval:	0.67–1.60
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID6

RiskID:	6
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	ischemic heart disease family history = paternal AND ischemic heart disease family history maternal AND sex = female
Ratio Type:	Relative risk
Ratio Value	1.45
Confidence Interval:	0.80–2.62
Adjusted for:	age, BMI, smoking status, exercise, and alcohol intake. Additional covariates in models for men included randomized aspirin and beta-carotene treatment; for women, randomized aspirin and vitamin E treatment, postmenopausal status, and postmenopausal hormone use
Evidence source PMID	11468199
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.53. Ischemic heart disease: Self history → Heart failure

Risk Association	
Risk Source:	Ischemic heart disease: self history
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Ischemic heart disease self history
Observable Condition:	ischemic heart disease self history = yes
Ratio Type:	Hazard ratio
Ratio Value	1.70
Confidence Interval:	1.37–2.12
Adjusted for:	age, sex, hypertension, BMI, heart rate, CHD, diabetes mellitus, valvular heart disease, lower high-density lipoprotein cholesterol, atrial fibrillation, presence of LV hypertrophy or left bundle-branch block
Evidence source PMID	23271790

Author	Dimitris
Reviewed	Laurynas

2.54. Left ventricular hypertrophy → Cardiovascular events group 5 (Acute myocardial infarction OR Ischemic stroke OR Heart Failure OR Death: cardiovascular)

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Acute myocardial infarction OR Ischemic stroke OR Heart Failure OR Death: cardiovascular
Association Type:	issue in
No. of risk evidences:	2
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk EvidenceID1	
RiskID:	1
Observables:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.39
Confidence Interval:	1.12 – 1.73
Adjusted for:	adjusted for age, race, SBP, diabetes, total cholesterol, smoking and QRS duration
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk EvidenceID2	
RiskID:	2
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes AND

	sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.37
Confidence Interval:	1.06 – 1.76
Adjusted for:	adjusted for age, race, SBP, diabetes, total cholesterol, smoking and QRS duration
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

2.55. Left ventricular hypertrophy → Death due to cardiovascular event

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Death: cardiovascular
Association Type:	issue in
No. of risk evidences:	1
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	2.37
Confidence Interval:	1.52 – 3.71
Adjusted for:	ECG-LVH, Insulin sensitivity index, proinsulin, LDL cholesterol, HDL cholesterol, Triglycerides, waist circumference, hypertension, smoking, previous ischemic heart disease
Evidence source PMID	11352882
Author	Neringa
Reviewed	Kalliopi, Dimitris

2.56. Left ventricular hypertrophy → Heart failure

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Heart failure
Association Type:	Issue in
No. of risk evidences:	2
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.96
Confidence Interval:	1.36-2.83
Adjusted for:	-
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	2.75
Confidence Interval:	1.94-3.91
Adjusted for:	-
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

2.57. Left ventricular hypertrophy → Hypertension

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Hypertension
Association Type:	Issue in
No. of risk evidences:	1
Author	Neringa
Reviewed	Dimitris, Kalliopi

Risk Evidence ID1	
RiskID:	REID1
Observable:	Left ventricular hypertrophy diagnosis
Observable Condition:	left ventricular hypertrophy diagnosis = yes
Ratio Type:	Odds ratio
Ratio Value:	1.2
Confidence Interval:	1.04 – 1.39
Adjusted for:	sex, baseline age, systolic and diastolic blood pressures, body mass index, alcohol consumption, and systolic blood pressure from 8 years before the index examination.
Evidence source PMID	08025994
Author	Neringa
Reviewed	Dimitris, Kalliopi

2.58. Left ventricular hypertrophy → Ischemic stroke

Risk Assocation	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Ischemic stroke
Association Type:	Issue in
No. of risk evidences:	2
Author	Neringa
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	REID1
Observable:	left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes

	AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.7
Confidence Interval:	1.01-1.84
Adjusted for:	-
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	REID2
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	left ventricular hypertrophy diagnosis = yes AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	2.77
Confidence Interval:	1.70 – 4.52
Adjusted for:	-
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

2.59. Obesity → Asthma

Risk Association	
Risk Source:	Obesity
Risk Target:	asthma
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk EvidenceID1	
RiskID1:	1
Observables:	body mass index AND Sex

Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.20
Confidence Interval:	1.08 – 1.33
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID2:	2
Observables:	BMI AND sex
Observable Condition:	body mass index >= 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.43
Confidence Interval:	1.14 – 1.79
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID3:	3
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.25
Confidence Interval:	1.05 – 1.49
Adjusted for:	-
Evidence source PMID	1932098
Author	Kalliopi

Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID4:	4
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.78
Confidence Interval:	1.36 – 2.32
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.60. Obesity → Atrial fibrillation

Risk Association	
Risk Source:	Obesity
Risk Target:	Atrial fibrillation
Association Type:	Is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	body mass index AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.10
Confidence Interval:	0.84 – 1.46
Adjusted for:	age, systolic blood pressure, use of antihypertensive therapy, diabetes mellitus, electrocardiographic left ventricular hypertrophy, prior myocardial infarction or congestive heart failure, regular use of cigarettes in the prior year, significant heart

	murmur, interim myocardial infarction and heart failure events
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID2:	2
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.13
Confidence Interval:	0.84 – 1.52
Adjusted for:	age, systolic blood pressure, use of antihypertensive therapy, diabetes mellitus, electrocardiographic left ventricular hypertrophy, prior myocardial infarction or congestive heart failure, regular use of cigarettes in the prior year, significant heart murmur, interim myocardial infarction and heart failure events
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.52
Confidence Interval:	1.09 – 2.13
Adjusted for:	age, systolic blood pressure, use of antihypertensive therapy, diabetes mellitus, electrocardiographic left ventricular hypertrophy, prior myocardial infarction or congestive heart failure, regular use of cigarettes in the prior year, significant heart murmur, interim myocardial infarction and heart failure events
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	body mass index AND Sex
Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.46
Confidence Interval:	1.03 – 2.07
Adjusted for:	age, systolic blood pressure, use of antihypertensive therapy, diabetes mellitus, electrocardiographic left ventricular hypertrophy, prior myocardial infarction or congestive heart failure, regular use of cigarettes in the prior year, significant heart murmur, interim myocardial infarction and heart failure events
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.61. Obesity → Cholelithiasis

Risk Association	
Risk Source:	Obesity
Risk Target:	Cholelithiasis
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.09
Confidence Interval:	0.87 – 1.37
Adjusted for:	-
Evidence source PMID	19320986

Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.43
Confidence Interval:	1.04 – 1.96
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.44
Confidence Interval:	1.05 – 1.98
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	BMI AND sex
Observable Condition:	body mass index >= 30 AND

	sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.32
Confidence Interval:	1.17 – 4.57
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.62. Obesity → Colorectal cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: colorectal cancer
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.47
Confidence Interval:	1.36–1.58
Adjusted for:	Multivariable-adjusted
Evidence source PMID	23349764
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex

Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.15
Confidence Interval:	1.08–1.23
Adjusted for:	Multivariable-adjusted
Evidence source PMID	23349764
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	waist circumference (WC) AND Sex
Observable Condition:	waist circumference >= 94 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.48
Confidence Interval:	1.30–1.68
Adjusted for:	Multivariable-adjusted
Evidence source PMID	23349764
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference >= 80 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.44
Confidence Interval:	1.30–1.60
Adjusted for:	Multivariable-adjusted
Evidence source PMID	23349764
Author	Kalliopi

Reviewed	Dimitris, Gintare

2.63. Obesity → Death due to cardiovascular event

Risk Association	
Risk Source:	Obesity
Risk Target:	Sudden cardiac death
Association Type:	is an issue in
No. of risk evidences:	2
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	BMI AND Sex
Observable Condition:	25 <= body mass index <= 29.9 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.26
Confidence Interval:	0.86-1.84
Adjusted for:	age, menopausal status, postmenopausal hormone use, and prior report of Ischemic heart disease, parental history myocardial infarction, Hypercholesterolemia, smoking, hypertension, diabetes
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris stefanos

Risk Evidence ID2	
RiskID:	2
Observable:	BMI
Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.65
Confidence Interval:	1.82-3.82
Adjusted for:	age, menopausal status, postmenopausal hormone use, and prior report of Ischemic heart disease, parental history myocardial infarction,

	Hypercholesterolemia, smoking, hypertension, diabetes
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris stefanos

2.64. Obesity → Diabetes

Risk Association	
Risk Source:	Obesity
Risk Target:	Diabetes
Association Type:	causes
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Waist to height ratio
Observable Condition:	0.49 <= waist to height ratio <= 0.65
Ratio Type:	RR
Ratio Value:	1.62
Confidence Interval:	1.48 – 1.78
Adjusted for:	Multivariable adjusted
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	23 <= body mass index <= 34
Ratio Type:	RR
Ratio Value:	1.55
Confidence Interval:	1.43 – 1.69
Adjusted for:	Multivariable adjusted
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observable:	Waist circumference
Observable Condition:	79.3 <= waist circumference <= 107.5
Ratio Type:	RR
Ratio Value:	1.63
Confidence Interval:	1.49 – 1.79
Adjusted for:	Multivariable adjusted
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observable:	Waist to hip ratio
Observable Condition:	0.81 <= waist to hip ratio <= 0.93
Ratio Type:	RR
Ratio Value:	1.52
Confidence Interval:	1.40 – 1.66
Adjusted for:	Multivariable adjusted
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.65. Obesity → Gastric cardia cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: gastric cardia cancer
Association Type:	is an issue in
No. of risk evidences:	2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID3:	1

Observables:	BMI
Observable Condition:	25 <= body mass index < 30
Ratio Type:	Relative Risk
Ratio Value:	1.21
Confidence Interval:	1.03 – 1.42
Adjusted for:	Multivariable adjusted
Evidence source PMID	23697611
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	body mass index >= 30
Ratio Type:	Relative Risk
Ratio Value:	1.82
Confidence Interval:	1.32 – 2.49
Adjusted for:	Multivariable adjusted
Evidence source PMID	23697611
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.66. Obesity → Gastric non-cardia cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: gastric non-cardia cancer
Association Type:	is an issue in
No. of risk evidences:	2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID3:	1
Observables:	BMI
Observable Condition:	25 <= body mass index < 30
Ratio Type:	Relative Risk

Ratio Value:	0.93
Confidence Interval:	0.82 – 1.05
Adjusted for:	Multivariable adjusted
Evidence source PMID	23697611
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	body mass index >= 30
Ratio Type:	Relative Risk
Ratio Value:	1.00
Confidence Interval:	0.87 – 1.15
Adjusted for:	Multivariable adjusted
Evidence source PMID	23697611
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.67. Obesity → Heart Failure

Risk Association	
Risk Source:	Obesity
Risk Target:	Heart failure
Association Type:	Is an issue in
No. of risk evidences:	7
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.5

Confidence Interval:	1.1 – 2.0
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	30 <= body mass index < 35 AND sex = female
Ratio Type:	hazard ratio
Ratio Value:	1.6
Confidence Interval:	1.1 – 2.4
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	BMI AND Sex
Observable Condition:	35 <= body mass index < 40 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	3.4
Confidence Interval:	2.1 – 5.7
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467

Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	BMI AND sex
Observable Condition:	body mass index >= 40 AND sex = female
Ratio Type:	Hazard ratio
Ratio Value:	5.6
Confidence Interval:	2.5 – 12.4
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID5	
RiskID5:	5
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.2
Confidence Interval:	0.9 – 1.6
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID6	
RiskID:	6

Observables:	BMI AND Sex
Observable Condition:	30 <= body mass index < 35 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.8
Confidence Interval:	1.2 – 2.7
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID7	
RiskID:	7
Observables:	BMI AND Sex
Observable Condition:	35 <= body mass index < 40 AND sex = male
Ratio Type:	Hazard ratio
Ratio Value:	2.8
Confidence Interval:	1.4 – 5.9
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.68. Obesity → Ischemic heart disease

Risk Association	
Risk Source:	Obesity
Risk Target:	Ischemic heart disease
Association Type:	Is an issue in
No. of risk evidences:	8

Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	risk ratio
Ratio Value:	1.29
Confidence Interval:	1.18 – 1.41
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	body mass index >30 AND sex = male
Ratio Type:	risk ratio
Ratio Value:	1.72
Confidence Interval:	1.51 – 1.96
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	94 <= waist circumference < 102 AND

	sex = male
Ratio Type:	risk ratio
Ratio Value:	1.41
Confidence Interval:	1.16 – 1.72
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference >= 102 AND sex = male
Ratio Type:	risk ratio
Ratio Value:	1.81
Confidence Interval:	1.45 – 2.25
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 <= waist circumference < 88 AND sex = female
Ratio Type:	risk ratio
Ratio Value:	1.82
Confidence Interval:	1.41 – 2.36
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	waist circumference >= 88 AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	2.69
Confidence Interval:	2.05 – 3.53
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID7	
RiskID:	7
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	risk ratio
Ratio Value:	1.80
Confidence Interval:	1.64 – 1.98
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID8	
RiskID8:	8
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	risk ratio

Ratio Value:	3.10
Confidence Interval:	2.81 – 3.43
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

2.69. Obesity → Ischemic stroke

Risk Association	
Risk Source:	Obesity
Risk Target:	Ischemic stroke
Association Type:	Is an issue in
No. of risk evidences:	2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	25 <= body mass index < 30
Ratio Type:	Risk ratio
Ratio Value:	1.22
Confidence Interval:	1.05 – 1.41
Adjusted for:	Multivariable adjusted
Evidence source PMID	20299666
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	body mass index >= 30
Ratio Type:	Risk ratio
Ratio Value:	1.64
Confidence Interval:	1.36 – 1.99
Adjusted for:	Multivariable adjusted

Evidence source PMID	20299666
Author	Kalliopi
Reviewed	Dimitris Gintare

2.70. Obesity → Osteoarthritis

Risk Association	
Risk Source:	Obesity
Risk Target:	Osteoarthritis
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	2.76
Confidence Interval:	2.05 – 3.70
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.80
Confidence Interval:	1.75 – 1.85

Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	4.20
Confidence Interval:	2.76–6.41
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.96
Confidence Interval:	1.88 – 2.04
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

2.71. Obesity → Pancreatic cancer

Risk Association	
Risk Source:	Obesity

Risk Target:	Cancer: pancreatic cancer
Association Type:	is an issue in
No. of risk evidences:	4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.28
Confidence Interval:	0.94 – 1.75
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris, Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	25 <= body mass index < 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.24
Confidence Interval:	0.98–1.56
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk EvidenceID3	
RiskID:	3
Observables:	BMI

	AND Sex
Observable Condition:	body mass index >= 30 AND sex = male
Ratio Type:	Relative Risk
Ratio Value:	2.29
Confidence Interval:	1.65 – 3.19
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

Risk EvidenceID4	
RiskID:	4
Observables:	BMI AND Sex
Observable Condition:	body mass index >= 30 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.60
Confidence Interval:	1.17–2.20
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris Gintare

2.72. Obstructive sleep apnoea → Death due to cardiovascular event

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Death due to Cardiovascular disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1

Observable:	AHI
Observable Condition:	apnoea-hypopnea index > 30
Ratio Type:	Hazard ratio
Ratio Value:	2.09
Confidence Interval:	1.20–3.65
Adjusted for:	Age, gender, race, BMI, smoking, alcohol consumption, glucose, lipid levels, lipid disorders, lipid-lowering medications, diabetes mellitus, blood pressure, use of antihypertensives, CV disease, CV drugs, left ventricular function, Ischemic intervention, lung disease, atrial fibrillation.
Evidence source PMID	22828826
Author	Gintare
Reviewed	Dimitris

2.73. Obstructive sleep apnoea → Diabetes

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Diabetes
Association Type:	is an issue in
No. of risk evidences:	2
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	AHI OR Obstructive sleep apnea diagnosis
Observable Condition:	5 <= apnoea-hypopnea index < 15 OR obstructive sleep apnea diagnosis = mild
Ratio Type:	Hazard ratio
Ratio Value:	1.22
Confidence Interval:	0.91–1.6
Adjusted for:	multivariate
Evidence source PMID	22988888
Author	Gintare
Reviewed	Kalliopi, Dimitris stefanos

Risk Evidence ID2

RiskID:	2
Observable:	AHI OR Obstructive sleep apnea diagnosis
Observable Condition:	apnoea-hypopnea index >= 15 OR obstructive sleep apnea diagnosis = moderate OR obstructive sleep apnea diagnosis = severe
Ratio Type:	Hazard ratio
Ratio Value:	1.63
Confidence Interval:	1.09–2.45
Adjusted for:	multivariate
Evidence source PMID	22988888
Author	Gintare
Reviewed	Kalliopi, Dimitris stefanos

2.74. Obstructive sleep apnoea → Hypertension

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Hypertension
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	AHI
Observable Condition:	1.5 <= apnoea-hypopnea index
Ratio Type:	Odds ratio
Ratio Value:	1.37
Confidence Interval:	1.03-1.83
Adjusted for:	Adjusted for demographics-anthropometric, BMI, neck circumference, waist-to-hip ratio, alcohol intake, smoking
Evidence source PMID	10770144
Author	Gintare
Reviewed	Kalliopi, Dimitris, Stefanos

2.75. Obstructive sleep apnoea → Ischemic heart disease

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Obstructive sleep apnea diagnosis
Observable Condition:	obstructive sleep apnea diagnosis = yes
Ratio Type:	Hazard ratio
Ratio Value:	1.92
Confidence Interval:	1.06–3.48
Adjusted for:	Age, gender, race, BMI, smoking, alcohol consumption, glucose, lipid levels, lipid disorders, lipid-lowering medications, diabetes mellitus, blood pressure, use of antihypertensives, CV disease, CV drugs, left ventricular function, coronary intervention, lung disease, atrial fibrillation.
Evidence source PMID	22828826
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.76. Obstructive sleep apnoea → Ischemic stroke

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Obstructive sleep apnea diagnosis
Observable Condition:	obstructive sleep apnea diagnosis = yes

Ratio Type:	Hazard ratio
Ratio Value:	2.24
Confidence Interval:	1.57–3.19
Adjusted for:	Age, gender, race, BMI, smoking, alcohol consumption, glucose, lipid levels, lipid disorders, lipid-lowering medications, diabetes mellitus, blood pressure, use of antihypertensives, CV disease, CV drugs, left ventricular function, coronary intervention, lung disease, atrial fibrillation.
Evidence source PMID	22828826
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.77. Physical activity→ Chronic Kidney Disease

Risk Association	
Risk Source:	Physical activity
Risk Target:	CKD
Association Type:	is an issue in
No. of risk evidences:	1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Physical activity
Observable Condition:	physical activity = low
Ratio Type:	Relative risk
Ratio Value:	2.2
Confidence Interval:	1.3-3.8
Adjusted for:	age, sex, race, BMI
Evidence source PMID	12843775
Author	stefanos
Reviewed	Dimitris

2.78. Physical activity→ Diabetes

Risk Association	
Risk Source:	Physical activity
Risk Target:	Diabetes type 2

Association Type:	is an issue in
No. of risk evidences:	2
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Physical activity
Observable Condition:	Physical activity = moderate
Ratio Type:	RR
Ratio Value:	0.83
Confidence Interval:	0.76 – 0.90
Adjusted for:	BMI
Evidence source PMID	17327354
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Physical activity
Observable Condition:	Physical activity = high
Ratio Type:	RR
Ratio Value:	0.83
Confidence Interval:	0.75 – 0.91
Adjusted for:	BMI
Evidence source PMID	17327354
Author	Dimitris
Reviewed	Kalliopi, Gintare

2.79. Physical activity → Ischemic heart disease

Risk Association	
Risk Source:	Physical activity
Risk Target:	Ischemic heart disease
Association Type:	Is an issue in
No. of risk evidences:	4
Author	Dimitris

Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = moderate AND sex = male
Ratio Type:	RR
Ratio Value:	0.85
Confidence Interval:	0.77-0.93
Adjusted for:	Multivariable adjusted
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = moderate AND sex = female
Ratio Type:	RR
Ratio Value:	0.78
Confidence Interval:	0.72-0.85
Adjusted for:	Multivariable adjusted
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID3	
RiskID:	3
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = high AND sex = male

Ratio Type:	RR
Ratio Value:	0.79
Confidence Interval:	0.73-0.85
Adjusted for:	Multivariable adjusted
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID4	
RiskID:	4
Observable:	Physical activity AND sex
Observable Condition:	physical activity = high AND sex = female
Ratio Type:	RR
Ratio Value:	0.71
Confidence Interval:	0.65-0.77
Adjusted for:	Multivariable adjusted
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Gintare

2.80. Physical activity → Ischemic stroke

Risk Association	
Risk Source:	Physical activity
Risk Target:	Ischemic stroke
Association Type:	Is an issue in
No. of risk evidences:	4
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = moderate

	AND sex = male
Ratio Type:	RR
Ratio Value:	0.73
Confidence Interval:	0.62-0.85
Adjusted for:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = moderate AND sex = female
Ratio Type:	RR
Ratio Value:	0.89
Confidence Interval:	0.79-1.00
Adjusted for:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID3	
RiskID:	3
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = high AND sex = male
Ratio Type:	RR
Ratio Value:	0.71
Confidence Interval:	0.60-0.84
Adjusted for:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID4	
RiskID:	4
Observable:	Physical activity AND Sex
Observable Condition:	physical activity = high AND sex = female
Ratio Type:	RR
Ratio Value:	0.78
Confidence Interval:	0.66-0.92
Adjusted for:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi

2.81. Renin-angiotensin system dual blockade → Acute kidney disease

Risk Association	
Risk Source:	Dual blockade of the renin-angiotensin system AND Heart failure
Risk Target:	Acute kidney disease
Association Type:	Causes
No. of risk evidences:	1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Heart failure AND Drugs: Renin-angiotensin system dual blockade (any) administration
Observable Condition:	heart failure diagnosis = yes AND renin-angiotensin system dual blockade administration = yes
Ratio Type:	RR
Ratio Value:	2.19
Confidence Interval:	1.82 - 2.65
Adjusted for:	-
Evidence source PMID	23358488

Author	Laurynas
Reviewed	Dimitris Stefanos

2.82. Renin-angiotensin system dual blockade → Hyperkalemia

Risk Association	
Risk Source:	Drugs: renin-angiotensin system dual blockade (any)
Risk Target:	Hyperkalemia
Association Type:	Causes
No. of risk evidences:	1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	renin-angiotensin system dual blockade administration
Observable Condition:	renin-angiotensin system dual blockade administration = yes
Ratio Type:	RR
Ratio Value:	1.55
Confidence Interval:	1.32-1.82
Adjusted for:	-
Evidence source PMID	23358488
Author	Laurynas
Reviewed	Dimitris Stefanos

2.83. Renin-angiotensin system dual blockade → Hypotension

Risk Association	
Risk Source:	Dual blockade of the renin-angiotensin system (any)
Risk Target:	Hypotension
Association Type:	Causes
No. of risk evidences:	1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1

Observable:	Drugs: Renin-angiotensin system dual blockade (any) administration
Observable Condition:	renin-angiotensin system dual blockade administration = yes
Ratio Type:	RR
Ratio Value:	1.66
Confidence Interval:	1.38 - 1.98
Adjusted for:	-
Evidence source PMID	23358488
Author	Laurynas
Reviewed	Dimitris Stefanos

2.84. Smoking → Albuminuria

Risk Association	
Risk Source:	Smoking
Risk Target:	Albuminuria
Association Type:	Causes
No. of risk evidences:	2
Author:	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	smoking status = smoker
Ratio Type:	Relative Risk
Ratio Value:	3.26
Confidence Interval:	1.66 - 6.80
Adjusted for:	no
Evidence source PMID	10972692
Author:	Stefanos
Reviewed:	Dimitris Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status
Observable Condition:	smoking status = ex-smoker
Ratio Type:	Relative Risk

Ratio Value:	2.69
Confidence Interval:	1.24 – 5.99
Adjusted for:	no
Evidence source PMID	10972692
Author:	Stefanos
Reviewed:	Dimitris Laurynas

2.85. Smoking → Chronic Kidney Disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Chronic kidney disease
Association Type:	Is an issue in
No. of risk evidences:	1
Author	Dimitris
Reviewed	Stefanos

Risk Evidence ID1	
RiskID:	1
Observables:	Smoking status AND Sex
Observables Condition:	smoking status = smoker AND sex = male
Ratio Type:	Relative risk
Ratio Value:	2.4
Confidence Interval:	1.2-4.5
Adjusted for:	-
Evidence source PMID	17541263
Author	Dimitris
Reviewed	Gintare

2.86. Smoking → Death due to cardiovascular event

Risk Factor	
Risk Source:	Smoking status
Risk Target:	Death: cardiovascular
Association Type:	is an issue in

No. of risk evidences:	4
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	Smoking status AND Sex
Observable Condition:	smoking status = ex-smoker AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.49
Confidence Interval:	1.08-2.06
Adjusted for:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status AND tobaco consumption (cigs. per day) AND sex
Observable Condition:	status = smoker AND 1 <= tobaco consumption (cigs. per day) <= 14 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.83
Confidence Interval:	1.80-4.45
Adjusted for:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3

Observable:	Smoking status AND tobaco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND 15 <= tobaco consumption (cigs. per day) <= 24 AND sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.40
Confidence Interval:	1.55-3.72
Adjusted for:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	Smoking status AND tobaco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND tobaco consumption (cigs. per day) >= 25 AND sex=female
Ratio Type:	Relative Risk
Ratio Value:	4.13
Confidence Interval:	2.69- 6.33
Adjusted for:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.87. Smoking → Heart failure

Risk Association	
Risk Source:	Smoking
Risk Target:	Heart failure
Association Type:	is an issue in

No. of risk evidences:	1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	smoking status = smoker
Ratio Type:	Hazard ratio
Ratio Value:	1.64
Confidence Interval:	1.28 – 2.01
Adjusted for:	age, sex, hypertension, BMI, heart rate, CHD, diabetes mellitus, valvular heart disease, lower high-density lipoprotein cholesterol, atrial fibrillation, presence of LV hypertrophy or left bundle-branch block
Evidence source PMID	23271790
Author	Dimitris
Reviewed	Gintare

2.88. Smoking → Ischemic heart disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
No. of risk evidences:	8
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status AND Sex
Observable Condition:	smoking status = ex-smoker AND sex = male
Ratio Type:	Relative risk
Ratio Value:	1.11
Confidence Interval:	0.86 - 1.42
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood

	pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status AND tobaco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND 1 <= tobacco consumption (cigs. per day) <= 14 AND sex = male
Ratio Type:	Relative risk
Ratio Value:	1.60
Confidence Interval:	1.24 - 2.07
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID3	
RiskID:	3
Observable:	Smoking status AND Tobacco consumption AND Sex
Observable Condition:	smoking status = smoker AND 15 <= tobacco consumption (cigs. per day) <= 24 AND sex = male
Ratio Type:	Relative risk
Ratio Value:	1.75
Confidence Interval:	1.37 - 2.23
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood

	pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID4	
RiskID:	4
Observable:	Smoking status AND tobacco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND tobacco consumption (cigs. per day) > 24 AND sex = male
Ratio Type:	Relative risk
Ratio Value:	2.09
Confidence Interval:	1.58 to 2.77
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID5	
RiskID:	5
Observable:	smoking status AND Sex
Observable Condition:	smoking status = ex-smoker AND sex = female
Ratio Type:	Relative risk
Ratio Value:	1.05
Confidence Interval:	0.74 - 1.50
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris

Reviewed	Kalliopi, Gintare

Risk Evidence ID6	
RiskID:	6
Observable:	Smoking status AND tobacco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND 1 <= tobacco consumption (cigs. per day) <= 14 AND sex = female
Ratio Type:	Relative risk
Ratio Value:	2.76
Confidence Interval:	2.08 - 3.68
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID7	
RiskID:	7
Observable:	Smoking status AND tobacco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND 15 <= tobacco consumption (cigs. per day) <= 24 AND sex = female
Ratio Type:	Relative risk
Ratio Value:	3.27
Confidence Interval:	2.42 - 4.42
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris

Reviewed	Kalliopi, Gintare

Risk Evidence ID8	
RiskID:	8
Observable:	Smoking status AND tobacco consumption (cigs. per day) AND Sex
Observable Condition:	smoking status = smoker AND tobacco consumption (cigs. per day) > 24 AND sex = female
Ratio Type:	Relative risk
Ratio Value:	2.82
Confidence Interval:	1.45 - 5.46
Adjusted for:	age, cohort of origin, smoking status, sex, systolic blood pressure, diastolic blood pressure, cholesterol, triglyceride, body mass index, education, alcohol, diabetes, physical activity, height
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Gintare

2.89. Smoking → Ischemic stroke

Risk Association	
Risk Source:	Smoking
Risk Target:	Ischemic stroke
Association Type:	is an issue in
No. of risk evidences:	4
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status Number of cigarettes smoked
Observable Condition:	smoking status = smoker tobaco consumption (cigs. per day) < 10
Ratio Type:	Relative risk

Ratio Value:	1.37
Confidence Interval:	1.24 – 1.52
Adjusted for:	Age
Evidence source PMID	2496858
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status tobaco consumption (cigs. per day)
Observable Condition:	smoking status = smoker 10 <= tobaco consumption (cigs. per day) < 20
Ratio Type:	Relative risk
Ratio Value:	1.45
Confidence Interval:	1.33 – 1.57
Adjusted for:	Age
Evidence source PMID	2496858
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID3	
RiskID:	3
Observable:	Smoking status tobacco consumption (cigs. per day)
Observable Condition:	smoking status = smoker tobacco consumption (cigs. per day) >= 20
Ratio Type:	Relative risk
Ratio Value:	1.82
Confidence Interval:	1.70 – 1.96
Adjusted for:	Age
Evidence source PMID	2496858
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID4	
RiskID:	4
Observable:	Smoking status

Observable Condition:	smoking status = ex-smoker
Ratio Type:	Relative risk
Ratio Value:	1.17
Confidence Interval:	1.05 - 1.30
Adjusted for:	Age
Evidence source PMID	2496858
Author	Dimitris
Reviewed	Kalliopi, Gintare

2.90. Smoking → Peripheral Arterial Disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
No. of risk evidences:	2
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	smoking status = smoker
Ratio Type:	Odds ratio
Ratio Value:	2.71
Confidence Interval:	2.28 - 3.21
Adjusted for:	-
Evidence source PMID	23922053
Author	Dimitris
Reviewed	Kalliopi, Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status
Observable Condition:	smoking status = ex-smoker
Ratio Type:	Odds ratio
Ratio Value:	1.67

Confidence Interval:	1.54 - 1.81
Adjusted for:	-
Evidence source PMID	23922053
Author	Dimitris
Reviewed	Kalliopi, Gintare

2.91. Statins → Acute myocardial infarction

Risk Association	
Risk Source:	statins
Risk Target:	acute myocardial infarction
Association Type:	Is an issue in
No. of risk evidences:	1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Statin administration AND Chronic kidney disease diagnosis
Observable Condition:	(chronic kidney disease diagnosis = stage1 OR chronic kidney disease diagnosis = stage2 OR chronic kidney disease diagnosis = stage3 OR 30 <= estimated glomerular filtration rate <= 90) AND statin administration = yes
Ratio Type:	RR
Ratio Value:	0.73
Confidence Interval:	0.54-0.98
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos
Reviewed	Dimitris Laurynas

2.92. Statins → Chronic kidney disease stage 5

Risk Association	
Risk Source:	Statins
Risk Target:	Chronic kidney disease = stage 5
Association Type:	Is an issue in
No. of risk evidences:	1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	(Chronic kidney disease diagnosis OR eGFR) AND Statins administration
Observable Condition:	statins administration = yes AND (chronic kidney disease diagnosis = stage1 OR chronic kidney disease diagnosis = stage2 OR chronic kidney disease diagnosis = stage3 OR 30 <= estimated glomerular filtration rate <= 90)
Ratio Type:	RR
Ratio Value:	0.98
Confidence Interval:	0.62-1.56
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos
Reviewed	Dimitris Laurynas

2.93. Statins → Death

Risk Association	
Risk Source:	Use of statins
Risk Target:	Death
Association Type:	Is an issue in
No. of risk evidences:	1
Author	Stefanos

Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Statin administration AND Chronic kidney disease diagnosis
Observable Condition:	(chronic kidney disease diagnosis = stage1 OR chronic kidney disease diagnosis = stage2 OR chronic kidney disease diagnosis = stage3 OR 30 <= estimated glomerular filtration rate <= 90) AND statin administration = yes
Ratio Type:	RR
Ratio Value:	0.81
Confidence Interval:	0.71-0.94
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos
Reviewed	Dimitris Laurynas

2.94. Statins → Diabetes

Risk Association	
Risk Source:	Drug therapy: statins
Risk Target:	Diabetes
Association Type:	issue in
No. of risk evidences:	5
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Statin administration
Observable Condition:	statin administration = atorvastatin
Ratio Type:	Relative risk

Ratio Value:	1.14
Confidence Interval:	0.89 –1.46
Adjusted for:	-
Evidence source PMID	20167359
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID2	
RiskID:	2
Observable:	Statin administration
Observable Condition:	statin administration = simvastatin
Ratio Type:	Relative risk
Ratio Value:	1.11
Confidence Interval:	0.97 –1.26
Adjusted for:	-
Evidence source PMID	20167359
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID3	
RiskID:	3
Observable:	Statin administration
Observable Condition:	statin administration = rosuvastatin
Ratio Type:	Relative risk
Ratio Value:	1.18
Confidence Interval:	1.04 –1.33
Adjusted for:	-
Evidence source PMID	20167359
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID4	
RiskID:	4
Observable:	Statin administration
Observable Condition:	statin administration = pravastatin
Ratio Type:	Relative risk
Ratio Value:	1.03
Confidence Interval:	0.90 –1.19

Adjusted for:	-
Evidence source PMID	20167359
Author	Dimitris
Reviewed	Kalliopi, Laurynas

Risk Evidence ID5	
RiskID:	5
Observable:	Statin administration
Observable Condition:	statin administration = lovastatin
Ratio Type:	Relative risk
Ratio Value:	0.98
Confidence Interval:	0.70 –1.38
Adjusted for:	-
Evidence source PMID	20167359
Author	Dimitris
Reviewed	Kalliopi, Laurynas

2.95. Statins → Ischemic stroke

Risk Association	
Risk Source:	statins
Risk Target:	Ischemic stroke
Association Type:	Is an issue in
No. of risk evidences:	1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Statin administration AND Chronic kidney disease diagnosis OR estimated glomerular filtration rate
Observable Condition:	(chronic kidney disease diagnosis = stage1 OR chronic kidney disease diagnosis = stage2 OR chronic kidney disease diagnosis = stage3 OR

	30 <= estimated glomerular filtration rate <= 90) AND Statin administration = yes
Ratio Type:	RR
Ratio Value:	0.61
Confidence Interval:	0.41-0.91
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos
Reviewed	Dimitris Laurynas

3. Risk Elements

3.1. Acute kidney disease

Risk Element	
Name	Acute Kidney Injury
Code	http://purl.bioontology.org/ontology/ICD9CM/584 C0022660
Synonyms	
Type	biomedical
Modifiable	yes
Observables	serum creatinine urine output diagnosis
Diagnosis Condition	[(serum creatine = personal baseline+0.3 OR personal baseline +150% ≤ serum creatine ≤ personal baseline +200%) AND <0.5 ml/kg/h urine output for more than 6 hours] OR acute kidney injury diagnosis = mild
	[serum creatine +200-300% of baseline AND <0.5 ml/kg/h urine output for more than 12 hours] OR acute kidney injury diagnosis = moderate
	[(serum creatine +>300% of baseline OR serum creatine >0.4mg/dl) AND (urine output <0.3 ml/kg/h for more than 24 hours OR urine output < 100 ml/24 hours for 12 hours)] OR acute kidney injury diagnosis = severe
Author	Stefanos
Reviewed	Ploumis

3.2. Acute myocardial infarction

Risk Element	
Name	Acute myocardial infarction

Code	http://purl.bioontology.org/ontology/ICD9CM/410 C0155626
Synonyms	Cardiac infarction; infarction of heart, myocardium, ventricle
Type	Biomedical
Modifiable	No
Observables	Acute myocardial infarction
Diagnosis Condition	Acute myocardial infarction = diagnosed
Author	Kalliopi, Dimitris
Reviewed	Gintare,,Kostas

3.3. Age

Risk Element	
Name	Age
Code	http://purl.bioontology.org/ontology/SNOMEDCT/71395006 C0001783
Synonyms	
Type	Demographic
Modifiable	No
Observables	Age
Diagnosis condition	N/A
Author	Kalliopi
Reviewed	Gintare

3.4. Albuminuria

Risk Element	
Name	Albuminuria
Code	http://purl.bioontology.org/ontology/SNOMEDCT/274769005 C0001925
Synonyms	
Type	biomedical
Modifiable	yes
Observables	albuminuria
Diagnosis condition	Albuminuria ≥ 30 mg/24h
Author	Stefanos
Reviewed	Dimitris

3.5. Anemia

Risk Element	
Name	Anemia
Code	http://purl.bioontology.org/ontology/SNOMEDCT/271737000 C0002871 C1510654
Synonyms	
Type	Biomedical
Modifiable	Yes
Observables	Hemoglobin level
Diagnosis condition	IF Sex = male, Hb <13 g/dL IF Sex = female, Hb <12g/dL
Author	Gintare
Reviewed	Kalliopi, Stefanos

3.6. Asthma

Risk Element	
Name	Asthma
Code	http://purl.bioontology.org/ontology/ICD9CM/493 C0004096
Synonyms	Bronchial asthma
Type	Biomedical
Modifiable	Yes
Observables	Asthma
Diagnosis condition	Asthma = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.7. Atrial fibrillation

Risk Element	
Name	Atrial fibrillation
Code	http://purl.bioontology.org/ontology/ICD10/I48 C0155709
Synonyms	Atrial fibrillation and flutter
Type	Biomedical
Modifiable	No

Observables	Atrial fibrillation diagnosis
Diagnosis condition	Atrial fibrillation = diagnosed
Author	Neringa
Reviewed	Kalliopi, Kostas

3.8. Beta-blockers

Risk Element	
Name	Drugs: β-blockers
Code	http://purl.bioontology.org/ontology/LNC/LP18062-7 C0001645
Synonyms	
Type	Intervention
Modifiable	Yes
Observables	β-blockers administration
Diagnosis condition	β-blockers administration = yes
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.9. Cardiovascular events group 1

Risk Element	
Name	cardiovascular events group
Code	http://purl.bioontology.org/ontology/SNOMEDCT/405617006 C1320716
Synonyms	
Includes risk elements	Ischemic heart disease Heart failure Ischemic stroke Peripheral arterial disease
Type	biomedical
Modifiable	No
Observables	Acute myocardial infarction diagnosis Heart failure diagnosis Ischemic stroke diagnosis Peripheral arterial disease diagnosis
Diagnosis condition	Acute myocardial infarction diagnosis = yes OR Heart failure diagnosis = yes OR

	Ischemic stroke diagnosis = yes OR Peripheral arterial disease diagnosis = yes
Author	Stefanos
Reviewed	Dimitris

3.10. Cardiovascular events group 2

Risk Element	
Name	cardiovascular events group
Code	http://purl.bioontology.org/ontology/SNOMEDCT/405617006 C1320716
Synonyms	
Includes risk elements	Acute Myocardial infarction Ischemic heart disease Ischemic stroke
Type	biomedical
Modifiable	No
Observables	Myocardial infarction diagnosis Ischemic heart disease diagnosis Ischemic stroke diagnosis
Diagnosis condition	Acute Myocardial infarction diagnosis = yes OR Ischemic heart disease diagnosis = yes OR Ischemic stroke diagnosis = yes
Author	Stefanos
Reviewed	Dimitris

3.11. Cardiovascular events group 3

Risk Element	
Name	cardiovascular events group
Code	http://purl.bioontology.org/ontology/SNOMEDCT/405617006 C1320716
Synonyms	
Includes risk elements	Acute Myocardial infarction Ischemic stroke

Type	biomedical
Modifiable	No
Observables	Acute Myocardial infarction diagnosis Ischemic stroke diagnosis
Diagnosis condition	Acute Myocardial infarction diagnosis = yes OR Ischemic stroke diagnosis = yes
Author	Stefanos
Reviewed	Dimitris

3.12. Cardiovascular events group 4

Risk Element	
Name	cardiovascular events group
Code	http://purl.bioontology.org/ontology/SNOMEDCT/405617006 C1320716
Synonyms	
Includes risk elements	Ischemic heart disease Ischemic stroke
Type	biomedical
Modifiable	No
Observables	Ischemic heart disease diagnosis Ischemic stroke diagnosis
Diagnosis condition	Ischemic heart disease diagnosis = yes OR Ischemic stroke diagnosis = yes
Author	Stefanos
Reviewed	Dimitris

3.13. Cardiovascular events group 5

Risk Element	
Name	cardiovascular events group
Code	http://purl.bioontology.org/ontology/SNOMEDCT/405617006 C1320716
Synonyms	
Includes risk elements	Acute myocardial infarction Ischemic heart disease

	Heart failure Death due to cardiovascular event
Type	biomedical
Modifiable	No
Observables	Acute myocardial infarction diagnosis Ischemic heart disease diagnosis heart failure diagnosis Death diagnosis
Diagnosis condition	Acute myocardial infarction diagnosis = yes OR Ischemic heart disease diagnosis = yes OR Heart failure diagnosis = yes OR Death diagnosis = yes
Author	Stefanos
Reviewed	Dimitris

3.14. Central obesity

Risk Element	
Name	Central obesity
Code	http://purl.bioontology.org/ontology/SNOMEDCT/248311001 C0311277
Synonyms	
Type	Behavioural
Modifiable	Yes
Observables	Waist circumference (WC) Waist to hip ratio (WHR) Waist to height ratio (WtHR)
Diagnosis Condition	[Men: WC < 94 – normal 94 ≤ WC < 102 – decent WC ≥ 102 – too high Women: WC < 80 – normal 80 ≤ WC < 88 – decent WC ≥ 88 – too high] OR [Normal: male: WHR < 0.95

	female: WHR < 0.86 Abnormal: male: WHR ≥ 0.95 female: WHR ≥ 0.86] OR [Normal: 0.30 ≤ WtHR < 0.50 Abnormal: WtHR < 0.30 or WtHR ≥ 0.50]
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.15. Cholelithiasis

Risk Element	
Name	Cholelithiasis
Code	http://purl.bioontology.org/ontology/ICD9CM/574 C0008350
Synonyms	Biliary lithiasis, gallstones
Type	Biomedical
Modifiable	Yes
Observables	Cholelithiasis diagnosis
Diagnosis condition	Cholelithiasis diagnosis = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.16. Chronic kidney disease

Risk Element	
Name	Chronic kidney disease
Code	http://purl.bioontology.org/ontology/ICD9CM/585 C1561643
Synonyms	
Type	Biomedical
Modifiable	Yes
Observables	glomerular filtration rate (eGFR) OR Chronic kidney disease diagnosis
Diagnosis condition	[Chronic kidney disease = stage 1 OR eGFR ≥ 90]

	OR [Chronic kidney disease = stage 2 OR 60 ≤ eGFR ≤ 89] OR [Chronic kidney disease = stage 3A OR 45 ≤ eGFR ≤ 59] OR [Chronic kidney disease = stage 3B OR 30 ≤ eGFR ≤ 44] OR [Chronic kidney disease = stage 4 OR 15 ≤ eGFR ≤ 29] OR [Chronic kidney disease = stage 5 OR eGFR < 15]
Author	Stefanos
Reviewed	Kalliopi, Dimitris

3.17. Chronic kidney disease stage 5

Risk Element	
Name	Chronic kidney disease
Code	http://purl.bioontology.org/ontology/SNOMEDCT/433146000 C2316810
Synonyms	
Type	Biomedical
Modifiable	No
Observables	glomerular filtration rate (eGFR) OR Chronic kidney disease diagnosis
Diagnosis condition	Chronic kidney disease diagnosis = stage 5 OR eGFR < 15
Author	Stefanos
Reviewed	Kalliopi, Dimitris

3.18. Chronic obstructive pulmonary disease (COPD)

Risk Element	
Name	Chronic obstructive pulmonary disease (COPD)
Code	http://purl.bioontology.org/ontology/ICD10/J44 C0494659
Synonyms	Chronic obstructive lung disease
Type	Biomedical
Modifiable	No
Observables	Chronic obstructive pulmonary disease diagnosis
Diagnosis condition	Chronic obstructive pulmonary disease diagnosis = diagnosed
Author	Gintare
Reviewed	Dimitris, Kostas

3.19. Colorectal cancer

Risk Element	
Name	Colorectal cancer
Code	http://purl.bioontology.org/ontology/ICD9CM/153 C0007102
Synonyms	Malignant neoplasm of colon, colorectal carcinoma
Type	Biomedical, genetic, environmental
Modifiable	No
Observables	Colorectal cancer
Diagnosis condition	Colorectal cancer = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.20. Contrast agents

Risk Element	
Name	Contrast agents
Code	http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C390 C0009924
Synonyms	
Type	intervention
Modifiable	yes
Observables	contrast agents administration
Diagnosis condition	contrast agents administration = yes

Author	Dimitris
Reviewed	Kalliopi

3.21. Death

Risk Element	
Name	Death
Code	http://purl.bioontology.org/ontology/ICD10/R96 C0478196
Synonyms	Death
Type	Biomedical
Modifiable	No
Observables	Death diagnosis
Diagnosis condition	Death = diagnosed
Author	Gintare
Reviewed	Dimitris, Kostas

3.22. Death due to cardiovascular disease

Risk Element	
Name	Death: cardiovascular
Code	http://purl.bioontology.org/ontology/ICD10/I46 C0018790
Synonyms	Cardiac arrest
Type	Biomedical
Modifiable	No
Observables	Death: cardiovascular diagnosis
Diagnosis condition	Death: cardiovascular = diagnosed
Author	Gintare
Reviewed	Dimitris, Kostas

3.23. Depression

Risk Element	
Name	Depression
Code	http://purl.bioontology.org/ontology/ICD9CM/311 C0868892
Synonyms	
Type	Biomedical

Modifiable	Yes
Observables	Depression diagnosis
Diagnosis condition	Depression diagnosed
Author	Gintare
Reviewed	Stefanos

3.24. Diabetes

Risk Element	
Name	Diabetes
Code	http://purl.bioontology.org/ontology/ICD9CM/250 C0011849
Synonyms	
Type	biomedical
Modifiable	yes
Observables	Diabetes diagnosis Fasting plasma glucose levels HbA1c blood glucose at two hours after oral glucose tolerance test antidiabetic medication administration
Diagnosis condition	Fasting plasma glucose levels ≥ 126 mg/dL OR HbA1c ≥ 6.5% OR random plasma glucose levels ≥ 200 mg/dL OR glucose at two hours after oral glucose tolerance test ≥ 200 mg/dL OR antidiabetic medication administration = yes OR diabetes = diagnosed
Author	Zydrune, Gintare, Kalliopi
Reviewed	Dimitris, Stefanos

3.25. Diabetic nephropathy

Risk Element	
Name	Diabetic nephropathy
Code	http://purl.bioontology.org/ontology/SNOMEDCT/127013003 C0011882

Synonyms	Diabetic renal disease
Type	biomedical
Modifiable	no
Observables	Diabetic nephropathy diagnosis
Diagnosis condition	Diabetic nephropathy = diagnosed
Author	Zydrune, Kalliopi
Reviewed (2)	Stefanos

3.26. Diuretics

Risk Element	
Name	Drugs: diuretics
Code	http://purl.bioontology.org/ontology/LNC/LP18047-8 C0012798
Synonyms	
Type	intervention
Modifiable	yes
Observables	contrast agents administration
Diagnosis condition	contrast agents administration = yes
Author	Dimitris
Reviewed	Kalliopi

3.27. Dyslipidemia

Risk Element	
Name	Dyslipidemia
Code	http://purl.bioontology.org/ontology/ICD10/E78 C0494343
Synonyms	Hyperlipidemia, hypercholesterolemia, hyperlipoproteinemia, high serum cholesterol.
Type	Biomedical
Modifiable	Yes
Observables	Total cholesterol (TC) low-density lipoprotein cholesterol (LDL-C) high-density lipoprotein cholesterol (HDL-C) triglycerides (TG)
Diagnosis condition	dislipidemia diagnosis = yes
Author	Gintare
Reviewed	Dimitris, Kostas

3.28. Gastric cardia cancer

Risk Element	
Name	Gastric cardia cancer
Code	http://purl.bioontology.org/ontology/ICD9CM/151.0 C0024623
Synonyms	Malignant neoplasm of stomach, gastric carcinoma
Type	Biomedical, genetic, environmental
Modifiable	No
Observables	Gastric cardia cancer
Diagnosis condition	Gastric cardia cancer = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.29. Gastric non-cardia cancer

Risk Element	
Name	Gastric non-cardia cancer
Code	http://purl.bioontology.org/ontology/ICD9CM/151.0 C0024623
Synonyms	Malignant neoplasm of stomach, gastric carcinoma
Type	Biomedical, genetic, environmental
Modifiable	No
Observables	Gastric non-cardia cancer
Diagnosis condition	Gastric non-cardia cancer = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.30. Heart Failure

Risk Element	
Name	Heart failure
Code	http://purl.bioontology.org/ontology/ICD10/I50 C0018801
Synonyms	Congestive heart failure, cardiac insufficiency, chronic heart failure
Type	Biomedical
Modifiable	No
Observables	Heart failure diagnosis
Diagnosis condition	Heart failure = diagnosed

Author	Gintare, Zydrune
Reviewed	Kalliopi, Kostas

3.31. High density lipoprotein cholesterol serum concentration

Risk Element	
Name	High density lipoprotein cholesterol serum concentration
Code	http://purl.bioontology.org/ontology/SNOMEDCT/102737005 C0023822
Synonyms	
Type	Biomedical
Modifiable	Yes
Observables	High density lipoprotein cholesterol
Diagnosis condition	
Author	Kalliopi
Reviewed	Dimitris

3.32. Hospitalization

Risk Element	
Name	hospitalization
Code	http://purl.bioontology.org/ontology/SNOMEDCT/281685003 C0150124
Synonyms	
Type	clinical
Modifiable	yes
Observables	diagnosis
Diagnosis condition	hospitalization = yes
Author	Dimitris
Reviewed	Stefanos

3.33. Hyperkalemia

Risk Element	
Name	Hyperkalemia
Code	http://purl.bioontology.org/ontology/SNOMEDCT/14140009 C0020461

Synonyms	Hyperpotassaemia, K overload,
Type	biomedical
Modifiable	yes
Observables	Serum potassium
Diagnosis condition	Serum potassium > 5 mEq/l or mmol/L
Author	Neringa
Reviewed	Kalliopi, Dimitris

3.34. Hypertension

Risk Element	
Name	Hypertension
Code	http://purl.bioontology.org/ontology/ICD10/I10 C0085580
Synonyms	Essential hypertension, primary hypertension.
Type	Biomedical
Modifiable	Yes
Observables	Systolic blood pressure (SBP) Diastolic blood pressure (DBP)
Diagnosis condition	SBP ≥140 mmHg and/or DBP ≥ 90 mmHg OR [Grade 1 hypertension: 140–159 mmHg SBP and/or 90–99 mmHg DBP Grade 2 hypertension: 160–179 mmHg SBP and/or 100–109 mmHg DBP Grade 3 hypertension: ≥180 mmHg SBP and/or ≥110 mmHg DBP] OR antihypertensive medication administration = yes
Author	Neringa, Gintare, Zydrune
Reviewed	Kalliopi, Dimitris, Kostas
Reviewed (2)	

3.35. Hyperuricemia

Risk Element	
Name	Hyperuricemia
Code	http://purl.bioontology.org/ontology/SNOMEDCT/35885006 C0740394
Synonyms	
Type	biomedical
Modifiable	yes

Observables	Uric acid serum concentration
Diagnosis condition	Uric acid serum concentration >6.7 mg/dL or >0.4 mmol/L
Author	Laurynas
Reviewed	Kalliopi, Stefanos

3.36. Hypoglycaemia

Risk Element	
Name	Hypoglycaemia
Code	http://purl.bioontology.org/ontology/ICD9CM/251.2 C0020615
Synonyms	
Type	clinical
Modifiable	yes
Observables	Fasting Plasma Glucose
Diagnosis condition	Fasting Plasma Glucose < 50 mg%
Author	Stefanos
Reviewed	Kalliopi, Dimitris

3.37. Hypotension

Risk Element	
Name	Hypotension
Code	http://purl.bioontology.org/ontology/SNOMEDCT/67763001 C0520541
Synonyms	
Type	clinical
Modifiable	yes
Observables	blood pressure
Diagnosis condition	
Author	Dimitris
Reviewed	Kalliopi

3.38. Ischemic heart disease

Risk Element	
Name	Ischemic heart disease
Code	http://purl.bioontology.org/ontology/ICD9CM/410-414.99

	C0151744
Synonyms	Coronary artery disease, coronary heart disease
Type	Biomedical
Modifiable	No
Observables	Acute myocardial infarction Angina pectoris Old myocardial infarction
Diagnosis Condition	Acute myocardial infarction = diagnosed OR Angina pectoris = diagnosed OR Old myocardial infarction = diagnosed
Author	Kalliopi, Dimitris
Reviewed	Gintare, Kostas

3.39. Ischemic heart disease family history

Risk Element	
Name	Family history of ischemic heart disease
Code	http://purl.bioontology.org/ontology/ICD9CM/V17.3 C0260520
Synonyms	Family history of coronary artery disease, coronary heart disease
Type	Genetic
Modifiable	No
Observables	Family history of ischemic heart disease
Diagnosis condition	Family history of ischemic heart disease = yes
Author	Gintare
Reviewed	Kalliopi, Gintare, Kostas

3.40. Ischemic heart disease self history

Risk Element	
Name	Ischemic heart disease: self history
Code	http://purl.bioontology.org/ontology/ICD9CM/412 C0155668
Synonyms	Self history of coronary artery disease, coronary heart disease
Type	biomedical
Modifiable	no
Observables	Old myocardial infarction
Diagnosis Condition	Old myocardial infarction = diagnosed

Author	Kalliopi, Dimitris
Reviewed	Gintare, Kostas

3.41. Ischemic stroke

Risk Element	
Name	Ischemic stroke
Code	http://purl.bioontology.org/ontology/ICD9CM/434 C0028790
Synonyms	Occlusion of cerebral arteries
Type	Biomedical
Modifiable	No
Observables	Ischemic stroke diagnosis
Diagnosis condition	Ischemic stroke = yes
Author	Dimitris, Stefanos, Gintare
Reviewed	Kalliopi, Kostas

3.42. Left ventricular hypertrophy

Risk Element	
Name	Left ventricular hypertrophy
Code	http://purl.bioontology.org/ontology/SNOMEDCT/55827005 C0149721
Synonyms	LV hypertrophy
Type	Biomedical
Modifiable	No
Observables	Left ventricular hypertrophy
Diagnosis condition	Left ventricular hypertrophy = diagnosed
Author	Neringa
Reviewed	Kalliopi, Dimitris, Kostas

3.43. Obesity

Risk Element	
Name	Obesity
Code	http://purl.bioontology.org/ontology/ICD9CM/278.00 C0028754
Synonyms	

Type	Behavioral
Modifiable	Yes
Observables	BMI Body fat percentage (BFP)
Diagnosis Condition	BMI range – kg/m^2 — Category BMI < 15 — Very severely underweight 15 ≤ BMI < 16 — Severely underweight 16 ≤ BMI < 18.5 — Underweight 18.5 ≤ BMI < 25 — Normal (healthy weight) 25 ≤ BMI < 30 — Overweight 30 ≤ BMI < 35 — Obese Class I (Moderately obese) 35 ≤ BMI < 40 — Obese Class II (Severely obese) BMI ≥ 40 — Obese Class III (Very severely obese) OR Body fat percentage (BFP) Description — Women — Men Essential fat — 10 ≤ BFP ≤ 13 — 2 ≤ BFP ≤ 5 Athletes — 14 ≤ BFP ≤ 20 — 6 ≤ BFP ≤ 13 Fitness — 21 ≤ BFP ≤ 24 — 14 ≤ BFP ≤ 17 Average — 25 ≤ BFP ≤ 31 — 18 ≤ BFP ≤ 24 Obese — BFP ≥ 32 — BFP ≥ 25
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.44. Obstructive Sleep Apnoea

Risk Element	
Name	Obstructive sleep apnea (OSA)
Code	http://purl.bioontology.org/ontology/ICD10/G47.3 C0037315
Synonyms	Obstructive sleep apnea syndrome
Type	Biomedical
Modifiable	No
Observables	Apnoea–hypopnoea index (AHI)
Diagnosis condition	[5 ≤ AHI <15 OR OSA = mild]

	OR [15 ≤ AHI < 29.9 OR OSA = moderate] OR [AHI ≥ 30 OR OSA = severe]
Author	Gintare
Reviewed	Kalliopi, Dimitris, Kostas

3.45. Osteoarthritis

Risk Element	
Name	Osteoarthritis
Code	http://purl.bioontology.org/ontology/ICD9CM/715.0 C1384584
Synonyms	
Type	Biomedical
Modifiable	No
Observables	Osteoarthritis
Diagnosis condition	Osteoarthritis = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.46. Pancreatic cancer

Risk Element	
Name	Pancreatic cancer
Code	http://purl.bioontology.org/ontology/ICD9CM/157 C0346647
Synonyms	Malignant neoplasm of pancreas, pancreatic carcinoma
Type	Biomedical, genetic, environmental
Modifiable	No
Observables	Pancreatic cancer
Diagnosis condition	Pancreatic cancer = diagnosed
Author	Kalliopi
Reviewed	Dimitris, Gintare

3.47. Peripheral arterial disease

Risk Element	
Name	Peripheral arterial disease
Code	http://purl.bioontology.org/ontology/ICD10CM/I73.9 C0085096
Synonyms	Peripheral vascular disease
Type	Biomedical, behavioural
Modifiable	Yes
Observables	Ankle-branchial index (ABI)
Diagnosis condition	Peripheral vascular disease: ABI ≤ 0.9 - abnormal 0.91 ≤ ABI ≤ 0.99 – considered borderline abnormal Normal: 1.0 ≤ ABI ≤ 1.4
Author	Dimitris
Reviewed	Kalliopi

3.48. Peripheral vascular disease

Risk Element	
Name	Peripheral vascular disease
Code	http://purl.bioontology.org/ontology/ICD10CM/I73.9 C0085096
Synonyms	Peripheral artery disease
Type	Biomedical, behavioural
Modifiable	Yes
Observables	Ankle-branchial index (ABI)
Diagnosis condition	Peripheral vascular disease: ABI ≤ 0.9 - abnormal 0.91 ≤ ABI ≤ 0.99 – considered borderline abnormal Normal: 1.0 ≤ ABI ≤ 1.4
Author	Dimitris
Reviewed	Kalliopi

3.49. Physical activity

Risk Element	
Name	Physical activity

Code	http://purl.bioontology.org/ontology/SNOMEDCT/61686008 C0015259
Synonyms	
Type	behavioural, intervention
Modifiable	yes
Observables	physical activity
Diagnosis condition	[physical activity = moderate OR physical activity < 2.5 h per week of aerobic activity] OR [physical activity = high OR physical activity ≥ 2.5 h per week of aerobic activity]
Author	Stefanos
Reviewed	Kalliopi, Dimitris

3.50. Renin-angiotensin system dual blockade

Risk Element	
Name	Drugs: Renin-angiotensin system dual blockade (any)
Code	http://purl.bioontology.org/ontology/MEDDRA/10049415 C0877206
Synonyms	
Type	intervention
Modifiable	yes
Observables	Drugs: Renin-angiotensin system dual blockade (any) administration
Diagnosis condition	Drugs: Renin-angiotensin system dual blockade (any) administration = yes
Author	Dimitris
Reviewed	Kalliopi

3.51. Smoking

Risk Element	
Name	Smoking
Code	http://purl.bioontology.org/ontology/SNOMEDCT/365981007 C0453996
Synonyms	Tobacco smoking
Type	Behavioral
Modifiable	Yes
Observables	Smoking status, tobacco consumption, number of cigarettes smoked per day
Diagnosis condition	Smoking status = ex-smoker

	OR Smoking status = current OR Smoking status = never
Author	Dimitris
Reviewed	Kalliopi, Dimitris, Gintare

3.52. Statins

Risk Element	
Name	Drugs: Statins
Code	http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C1655 C0360714
Synonyms	
Type	intervention
Modifiable	yes
Observables	Drugs: Statins administration
Diagnosis condition	Drugs: Statins administration = yes
Author	Dimitris
Reviewed	Kalliopi

3.53. Triglycerides serum concentration

Risk Element	
Name	Triglycerides serum concentration
Code	http://purl.bioontology.org/ontology/SNOMEDCT/365796000 C1287372
Synonyms	
Type	Biomedical
Modifiable	Yes
Observables	Triglycerides
Diagnosis condition	
Author	Kalliopi
Reviewed	Dimitris

4. Observables

4.1. 2h glucose after oral glucose tolerance test

Observable	
Name	2h glucose after oral glucose tolerance test
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/Z01.3 C1313910
Synonyms	Post-Meal Blood Sugar or 2-hour postprandial blood sugar
Type	clinical
Data type	integer
Unit	mg/dl / mmol/L
Values/range	Normal: <140 mg/dl or 7.8 mmol/L Prediabetes: 140-199 mg/dl or 7.8-11.0 mmol/L Diabetes: ≥ 200 mg/dl or 11.1 mmol/L
Author	Stefanos
Reviewed 2	Dimitris

4.2. Acute kidney disease diagnosis

Observable	
Name	Acute kidney disease diagnosis
Code (UMLS, ICD, …)	
Synonyms	Acute kidney injury diagnosis
Type	clinical
Data type	
Unit	
Values/range	diagnosed mild moderate severe not diagnosed
Author	Kalliopi
Reviewed	Dimitris

4.3. Acute myocardial infarction diagnosis

Observable

Name	Acute myocardial infarction diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/410 C0155626
Synonyms	Cardiac infarction; infarction of heart, myocardium, ventricle
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Dimitris

4.4. Age

Observable	
Name	Age
Code (UMLS, ICD, …)	
Synonyms	
Type	personal
Data type	integer
Unit	years, months, days
Values/range	
Author	Kalliopi,
Reviewed	Gintare

4.5. Albuminuria

Observable	
Name	Aglbuminuria
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	integer
Unit	mass over time (mg/24h)
Values/range	
Author	Stefanos
Reviewed	Dimitris

4.6. Angina pectoris diagnosis

Observable	
Name	Angina pectoris diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/413 C0002962
Synonyms	
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi, Dimitris
Reviewed	Gintare

4.7. Ankle-branchial index

Observable	
Name	Ankle-branchial index (ABI)
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/446841001 C1328319
Synonyms	Ankle branchial pressure index
Type	clinical
Data type	real
Unit	-
Values/range	ABI ≤ 0.9 – abnormal 0.91 ≤ ABI ≤ 0.99 – considered borderline abnormal 1.0 ≤ ABI ≤ 1.4 – normal
Author	Dimitris, Gintare
Reviewed	Gintare

4.8. Apnoea– hypopnoea index

Observable	
Name	Apnoea– hypopnoea index
Code (UMLS, ICD, …)	
Synonyms	(AHI)
Type	clinical
Data type	integer

Unit	the number of apnoeas or hypopnoeas per hour of sleep
Values/range	Normal: < 5 per hour Mild OSA: AHI ≥ 5, but < 15 per hour Moderate OSA: AHI ≥ 15, but < 30 per hour Severe OSA: AHI ≥ 30 per hour
Author	
Reviewed	

4.9. Asthma diagnosis

Observable	
Name	Asthma diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/493 C0004096
Synonyms	Bronchial asthma
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.10. Atrial fibrillation diagnosis

Observable	
Name	Atrial fibrillation diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/I48 C0155709
Synonyms	Atrial fibrillation and flutter
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed
Author	
Reviewed	Kostas

4.11. Beta-blockers administration

Observable	
Name	β-blockers administration
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/LNC/LP18062-7 C0001645
Synonyms	β-blockers use
Type	clinical
Data type	text
Unit	-
Values/range	yes no
Author	Kalliopi
Reviewed	Gintare

4.12. Body Fat percentage

Observable			
Name	body fat percentage		
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/LNC/MTHU018853 C0518026		
Synonyms			
Type	personal and clinical		
Data type	real		
Unit	%		
Values/range	Description	Women	Men
	Essential fat	10–13%	2–5%
	Athletes	14–20%	6–13%
	Fitness	21–24%	14–17%
	Average	25–31%	18–24%
	Obese	32%+	25%+
Author	Kalliopi		
Reviewed	Gintare		

4.13. Body Mass Index

Observable	
Name	Body Mass Index

Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/V85 C2240399
Synonyms	BMI
Type	personal
Data type	real
Unit	kg/m^2
Values/range	BMI range – kg/m^2 : Category BMI < 15 : Very severely underweight 15 ≤ BMI < 16 : Severely underweight 16 ≤ BMI < 18.5 : Underweight 18.5 ≤ BMI < 25 : Normal (healthy weight) 25 ≤ BMI < 30 : Overweight 30 ≤ BMI < 35 : Obese Class I (Moderately obese) 35 ≤ BMI < 40 : Obese Class II (Severely obese) BMI ≥ 40 : Obese Class III (Very severely obese)
Author	Kalliopi
Reviewed	Gintare

4.14. Cholelithiasis diagnosis

Observable	
Name	Cholelithiasis diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/574 C0008350
Synonyms	Biliary lithiasis, gallstones
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.15. Chronic kidney disease diagnosis

Observable

Name	Chronic kidney disease diagnosed
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	text
Unit	
Values/range	diagnosed stage 1 stage 2 stage 3A stage 3B stage 4 stage 5 not diagnosed
Author	
Reviewed	

4.16. Chronic obstructive pulmonary disease diagnosis

Observable	
Name	Chronic obstructive pulmonary disease diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/J44 C0494659
Synonyms	Chronic obstructive lung disease diagnosis
Type	clinical
Data type	text
Unit	
Values/range	Stage I – Mild COPD – FEV1/FVC<0.70 – FEV_1≥ 80% normal Stage II – Moderate COPD – FEV1/FVC<0.70 – FEV_1 50-79% normal Stage III – Severe COPD – FEV1/FVC<0.70 – FEV_1 30-49% normal Stage IV – Very Severe COPD – FEV1/FVC<0.70 – FEV_1 <30% normal, or <50% normal with chronic respiratory failure present*
Author	Dimitris
Reviewed	Kostas

4.17. Colorectal cancer diagnosis

Observable	
Name	Colorectal cancer

Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/153 C0007102
Synonyms	Malignant neoplasm of colon, colorectal carcinoma
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.18. Contrast agents administration

Observable	
Name	Contrast agents: coronary angiography administration
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	text
Unit	
Values/range	yes no
Author	
Reviewed	

4.19. Death diagnosis

Observable	
Name	Death diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/R96 C0478196
Synonyms	
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed
Author	

Reviewed	Kostas

4.20. Depression diagnosis

Observable	
Name	Depression diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/428181000124104
Synonyms	Depression screening positive
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	
Reviewed 2	stefanos

4.21. Diabetes diagnosis

Observable	
Name	Diabetes diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/250 C0011849
Synonyms	Diabetes mellitus diagnosis
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.22. Diabetic nephropathy diagnosis

Observable	
Name	Diabetic nephropathy diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/127013003
Synonyms	Diabetic renal disease diagnosis
Type	clinical

Data type	text
Unit	
Values/range	diagnosed not diagnosed
Author	
Reviewed	stefanos

4.23. Diastolic blood pressure

Observable	
Name	Blood pressure (BP)
Code (UMLS, ICD, …)	
Synonyms	DBP
Type	clinical
Data type	real
Unit	mmHg
Values/range	Normal values: diastolic pressure ≤90 mmHg high normal BP: 85-89 mmHg. normal BP: 80-84 mmHg; Optimal: <80 mmHg; abnormal values: Grade 1 hypertension: 140–159 mmHg SBP and/or 90–99 mmHg DBP Grade 2 hypertension: 160–179 mmHg SBP and/or 100–109 mmHg DBP Grade 3 hypertension: ≥180 mmHg SBP and/or ≥110 mmHg DBP Isolated systolic hypertension ≥140 SBP mmHg and <90 mmHg DBP
Author	
Reviewed	

4.24. Diuretics administration

Observable	
Name	Diuretics administration
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	text
Unit	
Values/range	yes

	no
Author	
Reviewed	

4.25. Estimated glomerular filtration rate

Observable	
Name	Estimated glomerular filtration rate
Code (UMLS, ICD, …)	
Synonyms	eGFR
Type	clinical
Data type	real
Unit	ml/min/1.73 m^2
Values/range	Normal: >90 Stage 1: Mildly decreased: 60–89 Stage 2: Mildly to moderately decreased: 45–59 Stage 3: Moderately to severely decreased: 30–44 Stage 4:Severely decreased: 15–29 Stage 5: Kidney failure:<15
Author	
Reviewed	

4.26. Fasting plasma glucose

Observable	
Name	Plasma glucose
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/271062006
Synonyms	Fasting Blood Sugar; Fasting Blood Glucose; Fasting Plasma Glucose
Type	clinical
Data type	integer
Unit	mg/dl / mmol/L
Values/range	ormal: 3.9 to 5.5 mmol /l (70 to 100 mg/dl) Prediabetes or Impaired Glucose Tolerance: 5.6 to 7.0 mmol/l (101 to 126 mg/dl) Diagnosis of diabetes: more than 7.0 mmol/l (126 mg/dl)
Author	stefanos
Reviewed	Dimitris

4.27. Gastric cardia cancer diagnosis

Observable	
Name	Gastric cardia cancer
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/151.0 C0024623
Synonyms	Malignant neoplasm of stomach, gastric carcinoma
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.28. Gastric non-cardia cancer diagnosis

Observable	
Name	Gastric non-cardia cancer
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/151.0 C0024623
Synonyms	Malignant neoplasm of stomach, gastric carcinoma
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.29. Glycated haemoglobin (HbA1c)

Observable	
Name	glycated haemoglobin
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/33601001 C0019018
Synonyms	HbA1c
Type	Clinical
Data type	Real

Unit	%
Values/range	Normal: HbA1c < 5.7 Prediabetes: 5.7 ≤ HbA1c ≤ 6.4 Diabetes: HbA1c ≥ 6.5
Author	Kalliopi
Reviewed	Gintare

4.30. Haemoglobin (Hb)

Observable	
Name	Haemoglobin (Hb)
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/104720004
Synonyms	hemoglobin
Type	biomedical
Data type	integer
Unit	g/dL
Values/range	IF Sex = male, Normal: >13 IF Sex = female, Normal >12g/dL IF Sex = male, Abnormal <13 g/dL IF Sex = female, Abnormal <12g/dL
Author	
Reviewed 2	stefanos

4.31. Heart failure diagnosis

Observable	
Name	Heart failure diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/I50 C0018801
Synonyms	Cardiac failure, cardiac insufficiency, myocardial failure, weak heart.
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed
Author	Kostas
Reviewed	Dimitris

4.32. High-density lipoprotein cholesterol

Observable	
Name	(High-density lipoprotein cholesterol
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/102737005 C0023822
Synonyms	HDL-C
Type	Clinical
Data type	Number
Unit	mmol/L or mg/dL
Values/range	Normal: >1.0 mmol/L (>40 mg/dL) in men; >1.2 mmol/L (>45 mg/dL) in women Abnormal: <1.0 mmol/L (<40 mg/dL) in men; <1.2 mmol/L (<45 mg/dL) in women
Author	Kostas
Reviewed	

4.33. Hospitalization

Observable	
Name	hospitalization
Code (UMLS, ICD, …)	
Synonyms	
Type	Clinical, personal
Data type	Number
Unit	days
Values/range	
Author	Kostas
Reviewed	Dimitris

4.34. Hypertension Diagnosis

Observable	
Name	Hypertension diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/I10 C0085580
Synonyms	High blood pressure
Type	clinical
Data type	text

Unit	mmHg
Values/range	SBP ≥140 mmHg and/or DBP ≥ 90 mmHg OR [Grade 1 hypertension: 140mmHg<SBP<159mmHg and/or 90mmHg<DBP<99 mmHg Grade 2 hypertension: 160mmHg<SBP<179mmHg and/or 100mmHg<DBP<109 mmHg Grade 3 hypertension: ≥180 mmHg SBP and/or ≥110 mmHg DBP]
Author	
Reviewed	Kostas

4.35. Ischemic heart disease diagnosis

Observable	
Name	Ischemic heart disease diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD10/I20-I25.9 C0151744
Synonyms	Chronic ischemic heart disease
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed
Author	
Reviewed	Kostas

4.36. Ischemic heart disease family history

Observable	
Name	Ischemic heart disease diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/410-414.99 C0151744
Synonyms	Coronary artery disease, coronary heart disease diagnosis
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi

Reviewed	Gintare

4.37. Ischemic heart disease self history

Observable	
Name	Ischemic heart disease self history
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	text
Unit	
Values/range	yes no
Author	Kalliopi
Reviewed	Gintare

4.38. Ischemic stroke diagnosis

Observable	
Name	Ischemic stroke diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/434 C0028790
Synonyms	
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Dimitris, Stefanos, Gintare
Reviewed	Gintare

4.39. Left ventricular hypertrophy diagnosis

Observable	
Name	Left ventricular hypertrophy diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/55827005 C0149721
Synonyms	LV hypertrophy

Type	Clinical
Data type	text
Unit	
Values/range	Mild Moderate Severe
Author	Kostas
Reviewed	Dimitris

4.40. Low-density lipoprotein cholesterol

Observable	
Name	LDL-C (Low-density lipoprotein cholesterol)
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/102739008 C0023824
Synonyms	LDL cholesterol
Type	Clinical
Data type	Number
Unit	mmol/L or mg/dL
Values/range	Normal <3.36 mmol/L (≤130 mg/dL) for subjects at low risk <2.6 mmol/L (≤100 mg/dL) for subjects at moderate risk; <1.8 mmol/L (≤70 mg/dL) for subjects at high risk
Author	Kostas
Reviewed	Dimitris

4.41. Acute myocardial infarction self history

Observable	
Name	Old myocardial infarction diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/412 C0155668
Synonyms	
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi, Dimitris

Reviewed	Gintare

4.42. Non-High density lipoprotein cholesterol

Observable	
Name	Non-HDL-C cholesterol serum concentration
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/312260007 C0729627
Synonyms	Non high density lipoprotein cholesterol
Type	Clinical
Data type	Real
Unit	mmol/L or mg/dL
Values/range	Abnormal Border line high : 130<Non HDL-C<159mg/dL High : 160<Non HDL-C<189mg/dL Very high : >190 mg/dL
Author	Kostas
Reviewed	Dimitris

4.43. Obstructive sleep apnea diagnosis

Observable	
Name	Obstructive sleep apnea diagnosis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/78275009 C0520679
Synonyms	Obstructive sleep apnea syndrome
Type	clinical
Data type	text
Unit	
Values/range	diagnosed mild moderate severe not diagnosed
Author	
Reviewed	Kostas

4.44. Osteoarthritis diagnosis

Observable	
Name	Osteoarthritis
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/715.0 C1384584
Synonyms	
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.45. Pancreatic cancer diagnosis

Observable	
Name	Pancreatic cancer
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/ICD9CM/157 C0346647
Synonyms	Malignant neoplasm of pancreas, pancreatic carcinoma
Type	clinical
Data type	text
Unit	-
Values/range	diagnosed not diagnosed
Author	Kalliopi
Reviewed	Gintare

4.46. Peripheral arterial disease diagnosis

Observable	
Name	Peripheral arterial disease diagnosis
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	text
Unit	-

Values/range	diagnosed not diagnosed
Author	Stefanos
Reviewed	Dimitris

4.47. Physical activity

Observable	
Name	physical exercise
Code (UMLS, ICD, …)	
Synonyms	
Type	personal
Data type	text
Unit	
Values/range	no low moderate high
Author	Kostas
Reviewed	Dimitris

4.48. Renin-angiotensin system dual blockade (any) administration

Observable	
Name	Renin-angiotensin system dual blockade administration
Code (UMLS, ICD, …)	-
Synonyms	-
Type	clinical
Data type	text
Unit	
Values/range	yes no
Author	Stefanos
Reviewed	Dimitris

4.49. Serum creatinine

Observable

Name	serum creatinine level
Code (UMLS, ICD, …)	
Synonyms	
Type	biomedical
Data type	integer
Unit	µmol per liter or mg per deciliter
Values/range	Normal men = 0,7 – 1,4 mg/dL (71 – 115 µmol/L) women = 0,6 – 1,1 mg/dL (53 – 97 µmol/L) Abnormal 200 µmol per liter [2.26 mg per deciliter], Doubling value= nephropathy
Author	Stefanos
Reviewed	Dimitris

4.50. Serum potassium

Observable	
Name	Serum potassium
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/88480006
Synonyms	K- potassium
Type	clinical
Data type	real
Unit	mEq/L or mmol/L
Values/range	Normal: 3.6-5.2 mEq/L or mmol/L Increasedserum potassium vaue-moderate hyperkalemia 5.0 < Serum Potassium < 6.0 mEq/liter or mmol/L) High serum potassium value- life threatening hyperkalemia > 6.0 mEq/liter or mmol/L).
Author	Stefanos
Reviewed 2	Dimitris

4.51. Sex

Observable	
Name	Sex
Code (UMLS, ICD, …)	
Synonyms	
Type	personal

Data type	text
Unit	
Values/range	female male
Author	Stefanos
Reviewed	Dimitris

4.52. Smoking status

Risk Element	
Name	Smoking status
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/LNC/LP114183-9 C1519386
Synonyms	
Type	personal
Data type	text
Units	-
Diagnosis condition	Smoking status = ex-smoker OR Smoking status = current OR Smoking status = never
Author	Dimitris
Reviewed	Gintare

4.53. Statin administration

Observable	
Name	Statin administration
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	text
Unit	
Values/range	yes Atorvastatin Simvastatin Rosuvastatin Pravastatin

	Lovastatin no
Author	Dimitris
Reviewed	Stefanos

4.54. Systolic blood pressure

Observable	
Name	Systolic blood pressure (BP)
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical
Data type	real
Unit	mmHg
Values/range	Normal values: systolic pressure ≤140 mmHg high normal BP: 130-139 mmHg normal BP: 120-129 mmHg Optimal: <120 mmHg; abnormal values: Grade 1 hypertension: 140–159 mmHg SBP and/or 90–99 mmHg DBP Grade 2 hypertension: 160–179 mmHg SBP and/or 100–109 mmHg DBP Grade 3 hypertension: ≥180 mmHg SBP and/or ≥110 mmHg DBP Isolated systolic hypertension ≥140 SBP mmHg and <90 mmHg DBP
Author	Kalliopi
Reviewed	Gintare

4.55. Time after myocardial infarction event

Observable	
Name	Time after acute myocardial infarction event
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/416524004 C1563038
Synonyms	Time of illness onset
Type	clinical
Data type	integer
Unit	days
Values/range	diagnosed not diagnosed

Author	Kostas
Reviewed	Dimitris

4.56. Tobacco consumption

Risk Element	
Name	Tobacco consumption
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/MESH/D064424 C0543414
Synonyms	Smoking intensity
Type	Personal
Data type	Integer
Units	-
Diagnosis condition	1 ≤ tobacco consumption (g/day) ≤ 14 15 ≤ tobacco consumption (g/day) ≤ 24 Tobacco consumption (g/day) > 24
Author	Dimitris
Reviewed	Gintare

4.57. Total cholesterol

Observable	
Name	Total cholesterol (TC)
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/390956002 C1272107
Synonyms	Plasma total cholesterol level
Type	Clinically measured
Data type	Real
Unit	mmol/L or mg/dL
Values/range	Normal: <5 mmol/L (l<190 mg/dL) Abnronal: >5 mmol/L (>190 mg/dL)
Author	Kostas
Reviewed	Dimitris

4.58. Triglycerides (TG)

Observable	
Name	Triglycerides serum concentration (TG)

Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/271245006 C0542495
Synonyms	Serum triglyceride levels
Type	Clinically measured
Data type	Number
Unit	mmol/L or mg/dL
Values/range	Ideal:<1.1 mmol/L (<100 mg/dL) Normal: <1.7 mmol/L (<150 mg/dL) Abnormal: >1.7 mmol/L (>150 mg/dL)
Author	Kostas
Reviewed	Dimitris

4.59. Uric acid serum concentration

Observable	
Name	Uric acid serum concentration
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/1710001
Synonyms	
Type	clinical
Data type	real
Unit	mg/dL or mmol/L
Values/range	Normal: < 6.7 mg% mg/dL or <0.4 mmol/L Abnormal: >6.7 mg/dL or >0.4 mmol/L
Author	stefanos
Reviewed 2	Dimitris

4.60. Urine output

Observable	
Name	Urine output
Code (UMLS, ICD, …)	
Synonyms	
Type	clinical, personal
Data type	real
Unit	ml/kg/h
Values/range	
Author	stefanos
Reviewed 2	Dimitris

4.61. Waist circumference

Observable	
Name	waist circumference
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/276361009 C0455829
Synonyms	
Type	personal
Data type	integer
Unit	cm
Values/range	Men: WC < 94 – normal 94 ≤ WC < 102 – decent WC ≥ 102 – too high Women: WC < 80 – normal 80 ≤ WC < 88 – decent WC ≥ 88 – too high
Author	Kalliopi
Reviewed	Gintare

4.62. Waist to height ratio

Observable	
Name	Waist to height ratio (WtHR)
Code (UMLS, ICD, …)	http://purl.obolibrary.org/obo/CMO_0000020
Synonyms	
Type	personal
Data type	real
Unit	-
Values/range	Normal: 0.30 ≤ WtHR < 0.50 Abnormal: WtHR < 0.30 or WtHR ≥ 0.50
Author	Kalliopi
Reviewed	Gintare

4.63. Waist to hip ratio

Observable	
Name	waist to hip ratio (WHR)
Code (UMLS, ICD, …)	http://purl.bioontology.org/ontology/SNOMEDCT/248367009

	C0205682
Synonyms	
Type	personal
Data type	Real
Unit	
Values/range	Normal: male: WHR < 0.95 female: WHR < 0.86 Abnormal: male: WHR ≥ 0.95 female: WHR ≥ 0.86
Author	Kalliopi
Reviewed	Gintare

5. Evidence Sources

5.1. PMID = 01866765

Evidence source	01866765
Evidence source PMID	Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study, Stroke. 1991 Aug;22(8):983-8.
Evidence source type	observational
OCEBM Level	1

5.2. PMID = 02496858

Evidence source	02496858
Evidence source PMID	Shinton R, Beevers G. Meta-analysis of relation between cigarette smoking and stroke. BMJ. 1989 Mar 25;298(6676):789-94.
Evidence source type	meta-analysis
OCEBM Level	1

5.3. PMID = 08025994

Evidence source	08025994
Evidence source PMID	Post WS, Larson MG, Levy D. Impact of left ventricular structure on the incidence of hypertension. The Framingham Heart Study. Circulation. 1994 Jul;90(1):179-85. doi: 10.1161/01.CIR.90.1.179
Evidence source type	observational
OCEBM Level	1

5.4. PMID = 09552903

Evidence source PMID	09552903
Evidence source	Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ. 1998;316(7137):1043-7.
Evidence source type	Longitudinal population study
OCEBM Level	2

5.5. PMID = 10069784

Evidence source PMID	10069784
Evidence source	Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, age, cardiovascular risk factors, and coronary heart disease: a prospective follow-up study of 14 786 middle-aged men and women in Finland. Circulation. 1999 Mar 9;99(9):1165-72.
Evidence source type	Cohort study
OCEBM Level	3

5.6. PMID = 10770144

Evidence source PMID	10770144
Evidence source	Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AB, Lebowitz MD; Pickering TG; for the Sleep Heart Health Study. Association of Sleep-Disordered Breathing, Sleep Apnea, and Hypertension in a Large Community-Based Study. *JAMA.* 2000;283(14):1829-1836. doi:10.1001/jama.283.14.1829
Evidence source type	Cross-sectional analyses of a community-based multicenter study
OCEBM Level	3

5.7. PMID = 10972692

Evidence source PMID	10972692
Evidence source	Halimi JM, Giraudeau B, Vol S, Cacès E, Nivet H, Lebranchu Y, Tichet J. Effects of current smoking and smoking discontinuation on renal function and proteinuria in the general population. Kidney Int. 2000 Sep;58(3):1285-92.
Evidence source type	observational
OCEBM Level	2

5.8. PMID = 11282794

Evidence source PMID	11282794
Evidence source	Hooi JD, Kester AD, Stoffers HE, Overdijk MM, van Ree JW, Knottnerus JA., Incidence of and risk factors for asymptomatic peripheral arterial occlusive disease: a longitudinal study. Am J Epidemiol. 2001 Apr 1;153(7):666-72.
Evidence source type	longitudinal population study
OCEBM Level	2

5.9. PMID = 11352882

Evidence source PMID	11352882

Evidence source	Sundström J, Lind L, Arnlöv J, Zethelius B, Andrén B, Lithell HO. Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men. Circulation. 2001 May 15;103(19):2346-51.
Evidence source type	Comparative Study
OCEBM Level	3

5.10. PMID = 11390335

Evidence source PMID	11390335
Evidence source	Iribarren C, Karter AJ, Go AS, Ferrara A, Liu JY, Sidney S, Selby JV. Glycemic control and heart failure among adult patients with diabetes. Circulation. 2001 Jun 5;103(22):2668-73.
Evidence source type	cohort
OCEBM Level	3

5.11. PMID = 11468199

Evidence source PMID	11468199
Evidence source:	Sesso HD, Lee IM, Gaziano JM, Rexrode KM, Glynn RJ, Buring JE. Maternal and Paternal History of Myocardial Infarction and Risk of Cardiovascular Disease in Men and Women. Circulation. 2001;104:393-398
Evidence source type:	Population study
OCEBM Level	2

5.12. PMID = 12151467

Evidence source PMID	12151467
Evidence source:	Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, Kannel WB, Vasan RS. Obesity and the risk of heart failure. N Engl J Med. 2002 Aug 1;347(5):305-13.
Evidence source type:	observational
OCEBM Level	2

5.13. PMID = 12695299

Evidence source PMID	12695299
Evidence source:	Albert CM, Chae CU, Grodstein F, Rose LM, Rexrode KM, Ruskin JN, Stampfer MJ, Manson JE. Prospective Study of Sudden Cardiac Death Among Women in the United States. Circulation. 2003;107:2096-2101
Evidence source type:	Prospective cohort study

OCEBM Level	3

5.14. PMID = 12843775

Evidence source PMID	12843775
Evidence source:	Stengel B, Tarver–Carr ME, Powe NR, Eberhardt MS, Brancati FL, Lifestyle Factors, Obesity and the Risk of Chronic Kidney Disease; Epidemiology 14 2003.
Evidence source type:	Cohort study
OCEBM Level	3

5.15. PMID = 14732743

Evidence source PMID	14732743
Evidence source:	O'Hare AM, Glidden DV, Fox CS, Hsu CY, High prevalence of peripheral arterial disease in persons with renal insufficiency: results from the National Health and Nutrition Examination Survey 1999-2000.. Circulation. 2004 Jan 27;109(3):320-3. Epub 2004 Jan 19.
Evidence source type:	Cross-sectional national study
OCEBM Level	

5.16. PMID = 15385656

Evidence source PMID	15385656
Evidence source	Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004 Sep 23;351(13):1296-305.
Evidence source type	Longitudinal, retrospective epidemiologic study
OCEBM Level	

5.17. PMID = 15562125

Evidence source PMID	15562125
Evidence source	Wang TJ, Parise H, Levy D, D'Agostino RB Sr, Wolf PA, Vasan RS, Benjamin EJ. Obesity and the risk of new-onset atrial fibrillation. JAMA. 2004 Nov 24;292(20):2471-7.
Evidence source type	observational
OCEBM Level	2

5.18. PMID = 15562129

Evidence source PMID	15562129
Evidence source	Fox CS, Coady S, Sorlie PD, Levy D, Meigs JB, D'Agostino RB Sr, Wilson PW, Savage PJ. Trends in cardiovascular complications of diabetes. JAMA. 2004 Nov 24;292(20):2495-9.
Evidence source type	observational
OCEBM Level	2

5.19. PMID = 16039877

Evidence source PMID	16039877
Evidence source	Curkendall SM, DeLuise C, Jones JK, Lanes S, Stang MR, Goehring E Jr, She D. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada cardiovascular disease in COPD patients. Ann Epidemiol. 2006 Jan;16(1):63-70.
Evidence source type	cohort
OCEBM Level	3

5.20. PMID = 16157837

Evidence source PMID	16157837
Evidence source:	Selvin E, Coresh J, Golden SH, Brancati FL, Folsom AR, Steffes MW. Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in communities study. Arch Intern Med. 2005 Sep 12;165(16):1910-6.
Evidence source type:	cohort
OCEBM Level	3

5.21. PMID = 16310551

Evidence source PMID	16310551
Evidence source	Drury PL, Ting R, Zannino D, Ehnholm C, Flack J, Whiting M, Fassett R, Ansquer JC, Dixon P, Davis TM, Pardy C, Colman P, Keech A. Estimated glomerular filtration rate and albuminuria are independent predictors of cardiovascular events and death in type 2 diabetes mellitus: the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study. Diabetologia. 2011 Jan;54(1):32-43. doi: 10.1007/s00125-010-1854-1. Epub 2010 Jul 30.
Evidence source type	Multinational, randomized, double-blind placebo-controlled trial
OCEBM Level	1

5.22. PMID = 16697315

Evidence source PMID	16697315
Evidence source:	Smith GL, Lichtman JH, Bracken MB, Shlipak MG, Phillips CO, DiCapua P, Krumholz HM. Renal impairment and outcomes in heart failure: systematic review and meta-analysis. J Am Coll Cardiol. 2006 May 16;47(10):1987-96.
Evidence source type:	systematic review and meta-analysis
OCEBM Level	1

5.23. PMID = 17082208

Evidence source PMID	17082208
Evidence source:	Nicholson A, Kuper H, Hemingway H. Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies.
Evidence source type:	Meta-analysis
OCEBM Level	1

5.24. PMID = 17327354

Evidence source PMID	17327354
Evidence source	Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. Diabetes Care. 2007;30(3):744-52.
Evidence source type	systematic review
OCEBM Level	1

5.25. PMID = 17541263

Evidence source PMID	17541263
Evidence source:	Jones-Burton C, Seliger SL, Scherer RW, Mishra SI, Vessal G, Brown J, Weir MR, Fink JC. Cigarette smoking and incident chronic kidney disease: a systematic review. Am J Nephrol. 2007;27(4):342-51
Evidence source type:	Systematic review
OCEBM Level	1

5.26. PMID = 18261929

Evidence source PMID	18261929
Evidence source:	Gu Q, Burt VL, Paulose-Ram R, Yoon S, Gillum RF. High blood pressure and cardiovascular disease mortality risk among U.S. adults: the third National Health

	and Nutrition Examination Survey mortality follow-up study. Ann Epidemiol. 2008 Apr;18(4):302-9.
Evidence source type:	follow-up
OCEBM Level	3

5.27. PMID = 18490538

Evidence source PMID	18490538
Evidence source	Messerli FH, Bangalore S, Julius S. Risk/benefit assessment of beta-blockers and diuretics precludes their use for first-line therapy in hypertension. Circulation. 2008 May 20;117(20):2706-15;
Evidence source type	
OCEBM Level	

5.28. PMID = 18755344

Evidence source PMID	18755344
Evidence source	Groenveld HF, Januzzi JL, Damman K, van Wijngaarden J, Hillege HL, van Veldhuisen DJ, van der Meer P. Anemia and mortality in heart failure patients a systematic review and meta-analysis. J Am Coll Cardiol. 2008 Sep 2;52(10):818-27. doi: 10.1016/j.jacc.2008.04.061.
Evidence source type	systematic review and meta-analysis
OCEBM Level	1

5.29. PMID = 19046219

Evidence source PMID	19046219
Evidence source	Elley CR, Kenealy T, Robinson E, Drury PL. Glycated haemoglobin and cardiovascular outcomes in people with Type 2 diabetes: a large prospective cohort study. Diabet Med. 2008 Nov;25(11):1295-301.
Evidence source type	cohort
OCEBM Level	3

5.30. PMID = 19320986

Evidence source PMID	19320986
Evidence source	Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health. 2009 Mar 25;9:88. doi: 10.1186/1471-2458-9-88.
Evidence source type	Systematic review and meta-analysis

OCEBM Level	1

5.31. PMID = 19368979

Evidence source PMID	19368979
Evidence source:	Nishiyama K, Morimoto T, Furukawa Y, Nakagawa Y, Ehara N, Taniguchi R, Ozasa N, Saito N, Hoshino K, Touma M, Tamura T, Haruna Y, Shizuta S, Doi T, Fukushima M, Kita T, Kimura T. Chronic obstructive pulmonary disease—An independent risk factor for long-term cardiac and cardiovascular mortality in patients with ischemic heart disease. International Journal of Cardiology 2010;143:178–183
Evidence source type:	Cohort study
OCEBM Level	3

5.32. PMID = 19705980

Evidence source PMID	19705980
Evidence source	Cameron AJ, Dunstan DW, Owen N, Zimmet PZ, Barr EL, Tonkin AM, Magliano DJ, Murray SG, Welborn TA, Shaw JE. Health and mortality consequences of abdominal obesity: evidence from the AusDiab study. Med J Aust. 2009 Aug 17;191(4):202-8
Evidence source type	prospective, national, population based study
OCEBM Level	3

5.33. PMID = 19903920

Evidence source PMID	19903920
Evidence source	Emerging Risk Factors Collaboration, Di Angelantonio E, Sarwar N, Perry P, Kaptoge S, Ray KK, Thompson A, Wood AM, Lewington S, Sattar N, Packard CJ, Collins R, Thompson SG, Danesh J. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009 Nov 11;302(18):1993-2000.
Evidence source type	meta-analysis
OCEBM Level	1

5.34. PMID = 19933936

Evidence source PMID	19933936
Evidence source	Velagaleti RS, Massaro J, Vasan RS, Robins SJ, Kannel WB, Levy D. Relations of Lipid Concentrations to Heart Failure Incidence The Framingham Heart Study. Circulation. 2009;120:2345-2351. doi: 10.1161/CIRCULATIONAHA.109.830984
Evidence source type	Cohort study
OCEBM Level	3

5.35. PMID = 20167359

Evidence source PMID	20167359
Evidence source	Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, Seshasai SR, McMurray JJ, Freeman DJ, Jukema JW, Macfarlane PW, Packard CJ, Stott DJ,Westendorp RG, Shepherd J, Davis BR, Pressel SL, Marchioli R, Marfisi RM, Maggioni AP, Tavazzi L, Tognoni G, Kjekshus J, Pedersen TR, Cook TJ, Gotto AM,Clearfield MB, Downs JR, Nakamura H, Ohashi Y, Mizuno K, Ray KK, Ford I. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. Lancet. 2010 Feb 27;375(9716):735-42.
Evidence source type	meta-analysis
OCEBM Level	1

5.36. PMID = 20191515

Evidence source PMID	20191515
Evidence source	Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2010 Feb;62(2):170-80
Evidence source type	systematic review and meta-analysis
OCEBM Level	1

5.37. PMID = 20299666

Evidence source PMID	20299666
Evidence source:	Strazzullo P, D'Elia L, Cairella G, Garbagnati F, Cappuccio FP, Scalfi L. Excess body weight and incidence of stroke: meta-analysis of prospective studies with 2 million participants. Stroke. 2010 May;41(5):e418-26.
Evidence source type:	Systematic review and meta-analysis
OCEBM Level	1

5.38. PMID = 20668832

Evidence source PMID	20668832
Evidence source:	Drury PL, Ting R, Zannino D, Ehnholm C, Flack J, Whiting M, Fassett R, Ansquer JC, Dixon P, Davis TM, Pardy C, Colman P, Keech A. Estimated glomerular filtration rate and albuminuria are independent predictors of cardiovascular events and death in type 2 diabetes mellitus: the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study. Diabetologia. 2011 Jan;54(1):32-43. doi: 10.1007/s00125-010-1854-1.
Evidence source type:	randomized trial
OCEBM Level	2

5.39. PMID = 20824805

Evidence source PMID	20824805
Evidence source:	Grayson PC, Kim SY, LaValley M, Choi HK. Hyperuricemia and incident hypertension: a systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2011 Jan;63(1):102-10.
Evidence source type:	systematic review and meta-analysis
OCEBM Level	1

5.40. PMID = 21852664

Evidence source PMID	21852664
Evidence source:	Thomas G, Sehgal AR, Kashyap SR, Srinivas TR, Kirwan JP, Navaneethan SD. Metabolic syndrome and kidney disease: a systematic review and meta-analysis. Clin J Am Soc Nephrol. 2011 Oct;6(10):2364-73.
Evidence source type:	systematic review and meta-analysis
OCEBM Level	1

5.41. PMID = 22020036

Evidence source PMID	22020036
Evidence source:	Dong JY, Zhang YH, Tong J, Qin LQ. Depression and Risk of Stroke A Meta-Analysis of Prospective Studies. Stroke. 2012;43:32-37
Evidence source type:	A meta-analysis of prospective studies
OCEBM Level	1

5.42. PMID = 22113526

Evidence source PMID	22113526
Evidence source	Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. Kidney Int. 2012 Mar;81(5):442-8.
Evidence source type	Systematic review and meta-analysis
OCEBM Level	1

5.43. PMID = 22139711

Evidence source PMID	22139711
Evidence source	Chintan S Desai, Hongyan Ning and Donald M Lloyd-Jones. Competing cardiovascular outcomes associated with electrocardiographic leftventricular hypertrophy: the AtherosclerosisRisk in Communities Study. Heart 2012 98: 330-334.doi: 10.1136/heartjnl-2011-300819

Evidence source type	multicenter cohort follow up study
OCEBM Level	3

5.44. PMID = 22342847

Evidence source PMID	22342847
Evidence source	Jain N, Kotla S, Little BB, Weideman RA, Brilakis ES, Reilly RF, Banerjee S. Predictors of hyperkalemia and death in patients with cardiac and renal disease.Am J Cardiol. 2012 May 15;109(10):1510-3. doi: 10.1016/j.amjcard.2012.01.367. Epub 2012 Feb 18
Evidence source type	Comparative Study
OCEBM Level	

5.45. PMID = 22470299

Evidence source PMID	22470299
Evidence source	Li J, Siegrist J. Physical activity and risk of cardiovascular disease--a meta-analysis of prospective cohort studies., Int. J. Environ. Res. Public Health 2012, 9, 391-407
Evidence source type	meta-analysis
OCEBM Level	1

5.46. PMID = 22508734

Evidence source	22508734
Evidence source PMID	Fink HA, Ishani A, Taylor BC, Greer NL, MacDonald R, Rossini D, Sadiq S, Lankireddy S, Kane RL, Wilt TJ. Screening for, monitoring, and treatment of chronic kidney disease stages 1 to 3: a systematic review for the U.S. Preventive Services Task Force and for an American College of Physicians Clinical Practice Guideline. Ann Intern Med. 2012 Apr 17;156(8):570-81. doi: 10.7326/0003-4819-156-8-201204170-00004
Evidence source type	systematic review and meta-analysis
OCEBM Level	1

5.47. PMID = 22828826

Evidence source PMID	22828826
Evidence source:	Loke YK, Brown JW, Kwok CS, Niruban A, Myint PK. Association of obstructive sleep apnea with risk of serious cardiovascular events: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):720-8. doi: 10.1161/CIRCOUTCOMES.111.964783
Evidence source type:	systematic review and meta-analysis

OCEBM Level	1

5.48. PMID = 22988888

Evidence source PMID	22988888
Evidence source:	Wang X, Bi Y, Zhang Q, Pan F. Obstructive sleep apnoea and the risk of type 2 diabetes: A meta-analysis of prospective cohort studies. Respirology 2013 Jan;18:140–146. doi: 10.1111/j.1440-843.2012.02267.x
Evidence source type:	Meta-analysis
OCEBM Level	1

5.49. PMID = 23144362

Evidence source PMID	23144362
Evidence source	Kodama S, Horikawa C, Fujihara K, Heianza Y, Hirasawa R, Yachi Y, Sugawara A, Tanaka S, Shimano H, Iida KT, Saito K, Sone H. Comparisons of the strength of associations with future type 2 diabetes risk among anthropometric obesity indicators, including waist-to-height ratio: a meta-analysis. Am J Epidemiol. 2012 Dec 1;176(11):959-69. doi: 10.1093/aje/kws172. Epub 2012 Nov 9.
Evidence source type	meta-analysis
OCEBM Level	1

5.50. PMID = 23271790

Evidence source PMID	23271790
Evidence source:	Ho JE, Lyass A, Lee DS, Vasan RS, Kannel WB, Larson MG, Levy D. Predictors of New-Onset Heart Failure Differences in Preserved Versus Reduced Ejection Fraction. Circ Heart Fail 2013;6:279-286. doi: 10.1161/CIRCHEARTFAILURE.112.972828
Evidence source type:	Cohort study
OCEBM Level	3

5.51. PMID = 23322741

Evidence source PMID	23322741
Evidence source:	James MT, Samuel SM, Manning MA, Tonelli M, Ghali WA, Faris P, Knudtson ML, Pannu N, Hemmelgarn BR. Contrast-induced acute kidney injury and risk of adverse clinical outcomes after coronary angiography: a systematic review and meta-analysis. Circ Cardiovasc Interv. 2013 Feb;6(1):37-43
Evidence source type:	systematic review and meta-analysis
OCEBM Level	1

5.52. PMID = 23349764

Evidence source PMID	23349764
Evidence source:	Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS One. 2013;8(1):e53916.
Evidence source type:	Systematic review of prospective studies
OCEBM Level	2

5.53. PMID = 23351816

Evidence source PMID	23351816
Evidence source:	Lawler PR, Filion KB, Dourian T, Atallah R, Garfinkle M, Eisenberg MJ. Anemia and mortality in acute coronary syndromes: a systematic review and meta-analysis. Am Heart J. 2013 Feb;165(2):143-53.e5. doi: 10.1016/j.ahj.2012.10.024. Epub 2012 Dec 4.
Evidence source type:	systematic review and meta-analysis
OCEBM Level	1

5.54. PMID = 23358488

Evidence source PMID	23358488
Evidence source	Makani H, Bangalore S, Desouza KA, Shah A, Messerli FH. Efficacy and safety of dual blockade of the renin-angiotensin system: meta-analysis of randomised trials. BMJ. 2013 Jan 28;346:f360.
Evidence source type	Meta-analysis of randomised trials
OCEBM Level	1

5.55. PMID = 23697611

Evidence source PMID	23697611
Evidence source:	Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, Gong G, Li G. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Observables Prev. 2013 Aug;22(8):1395-408.
Evidence source type:	Meta-analysis
OCEBM Level	1

5.56. PMID = 23915883

Evidence source PMID	23915883

Evidence source:	Fowkes FGR, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, Norman PE, Sampson UKA, Williams LJ, Mensah GA, Criqui MH. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet 2013; 382: 1329–40. doi:10.1016/S0140-6736(13)61249-0
Evidence source type:	systematic review and analysis
OCEBM Level	1

5.57. PMID = 23922053

Evidence source PMID	23922053
Evidence source	Lu L, Mackay DF, Pell JP. Meta-analysis of the association between cigarette smoking and peripheral arterial disease, Heart. 2014;100(5):414-23
Evidence source type	Meta-analysis
OCEBM Level	1

5.58. PMID = 23933579

Evidence source PMID	23933579
Evidence source	Huang H, Huang B, Li Y, Huang Y, Li J, Yao H, Jing X, Chen J, Wang J. Uric acid and risk of heart failure: a systematic review and meta-analysis. Eur J Heart Fail. 2014 Jan;16(1):15-24.
Evidence source type	systematic review and meta-analysis
OCEBM Level	1

5.59. PMID = 24468137

Evidence source PMID	24468137
Evidence source	Li M, Hou W, Zhang X, Tang Z. Hyperuricemia and risk of stroke: a systematic review and meta-analysis of prospective studies. Atherosclerosis. 2014 Feb;232(2):265-70.
Evidence source type	Systematic review and meta-analysis
OCEBM Level	1

5.60. PMID = 24859435

Evidence source PMID	24886432
Evidence source:	Peters SA, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014 May 25.

Evidence source type:	systematic review and meta-analysis
OCEBM Level	1