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D.2.2. Functional Requirements & CARRE Information Model

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Table of Contents

List of Figures

List of Tables

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.

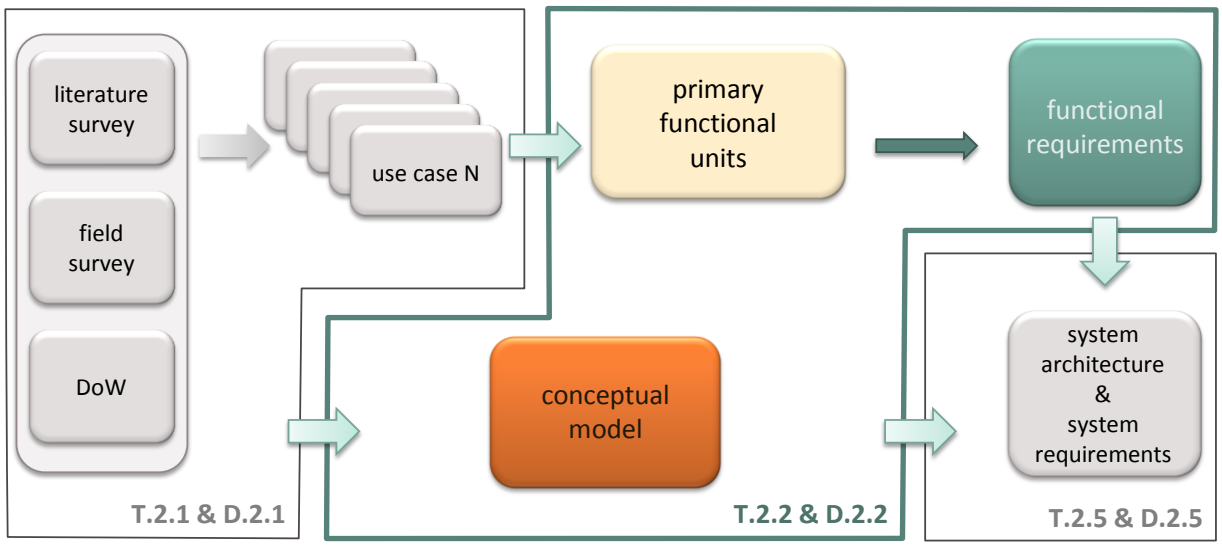

Figure 1. Process for deriving CARRE functional requirements and conceptual model.

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.

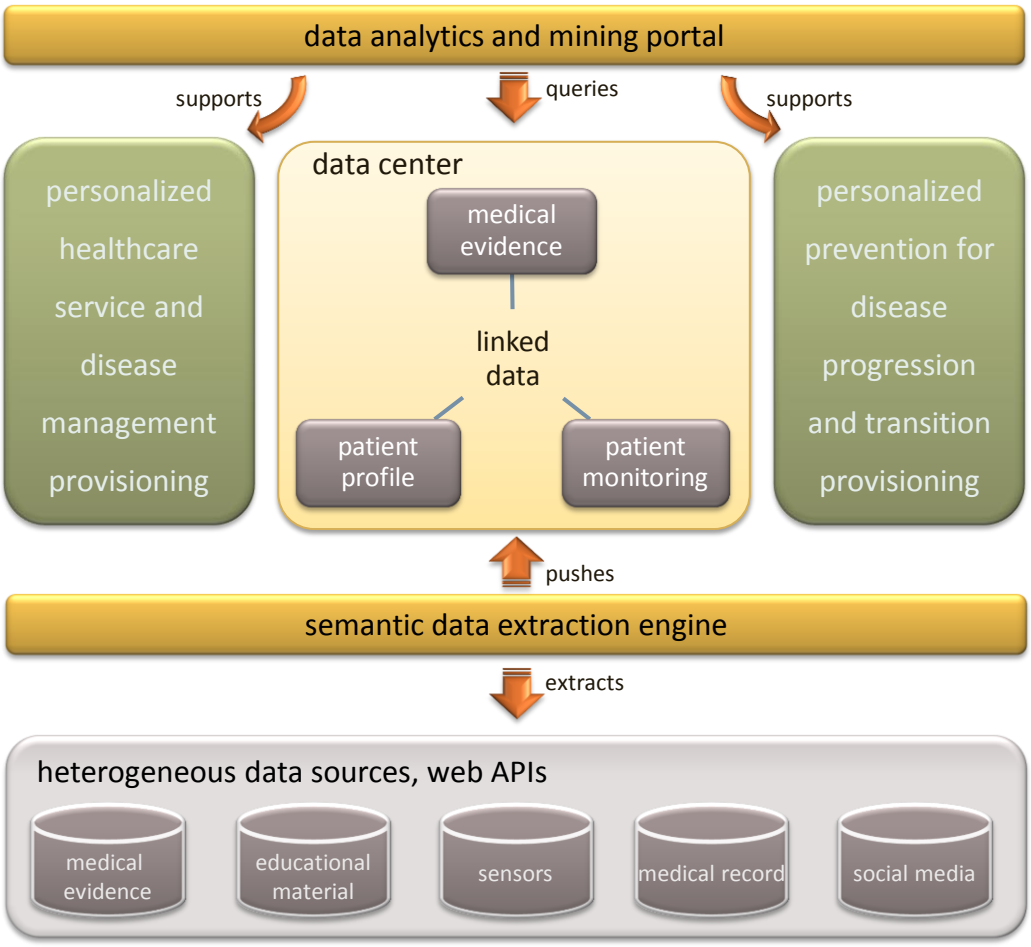

Figure 2. Overview of CARRE service environment as described in the DoW.

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):

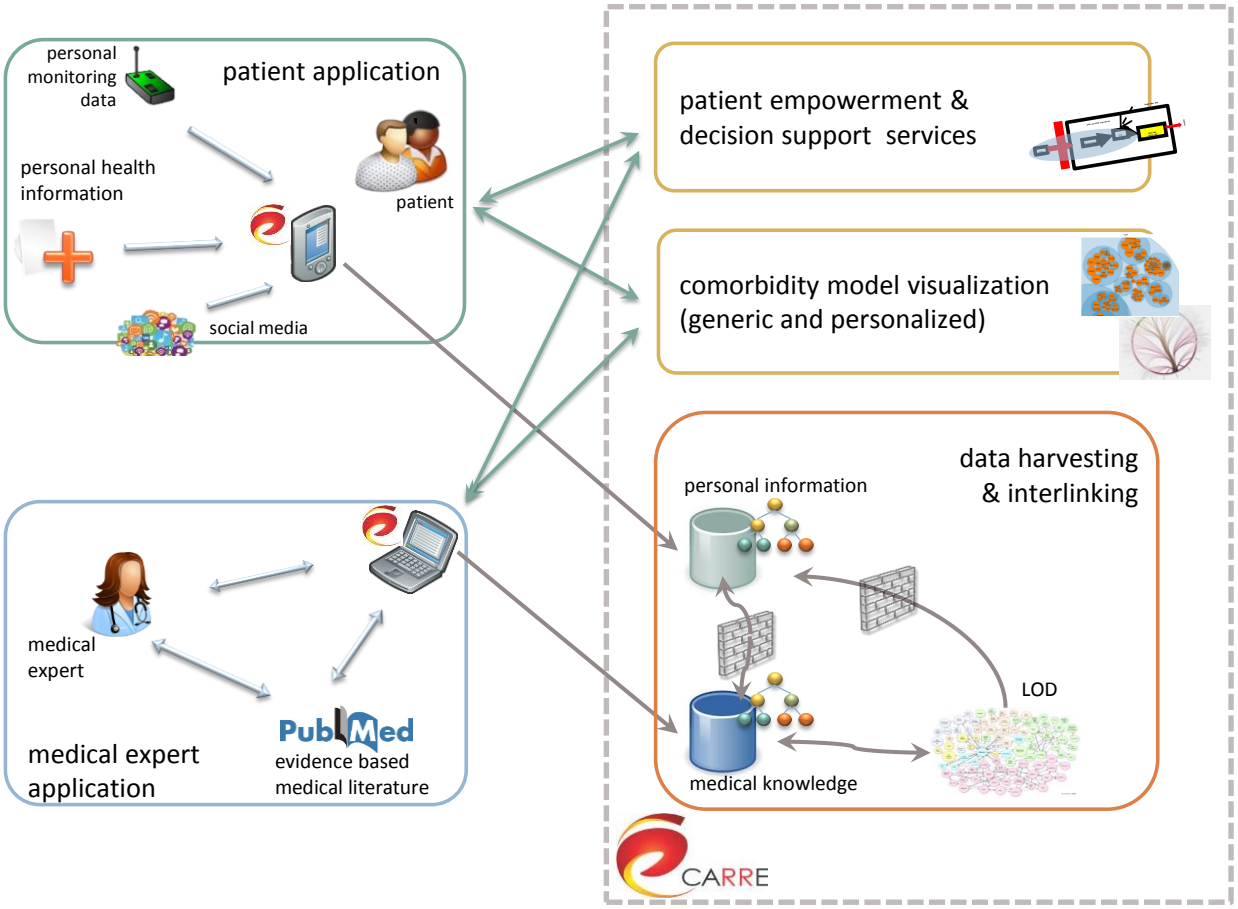

Figure 3. CARRE primary functional units.

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.

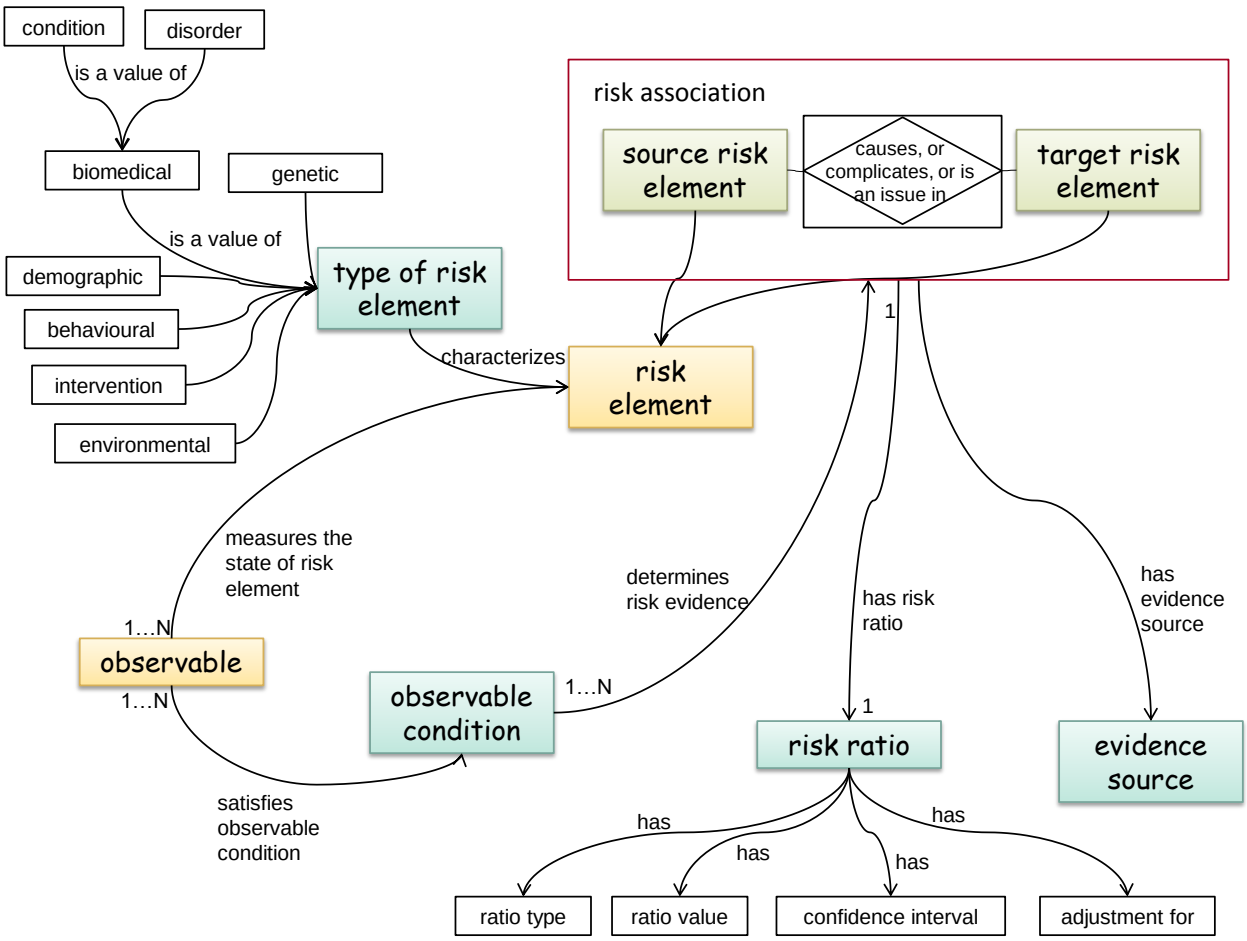

Figure 4. CARRE basic concepts and their relationships.

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.

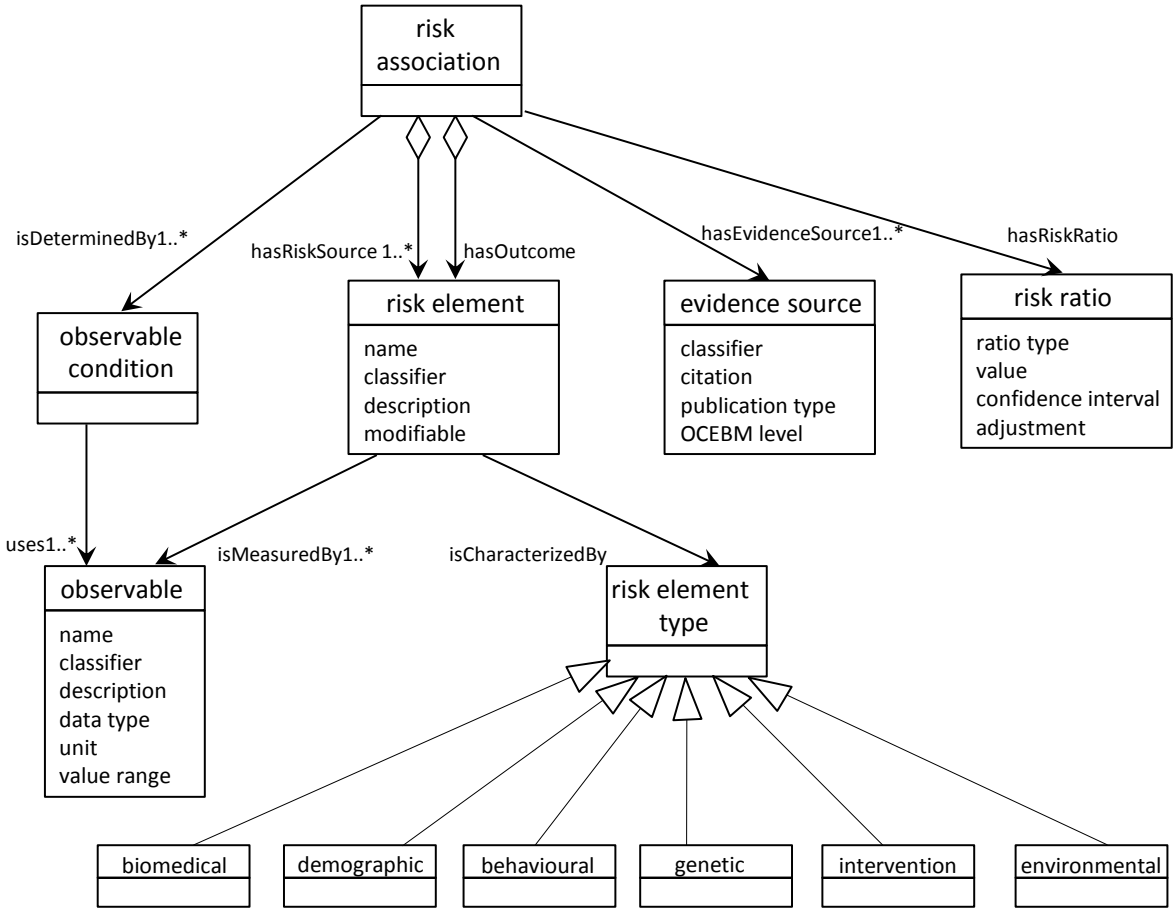

Figure 5. Risk factor class diagram.

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. The Drupal content management system[5] has been customised to reflect the structure of the model presented here, so that observables, evidence sources, risk elements and associations can be entered via web forms, and automatically translated to RDF. The system maintains referential integrity, so that if "diabetes" is entered as a risk element entity, then a risk association representing an observed link between diabetes and hypertension will refer to the existing diabetes risk element entity. Users are supported in the reuse of data already entered into the system by the user interface, which allows existing relevant entities to be selected via drop-down lists wherever possible.

In order to add evidence sources from the clinical literature, the system provides a search interface to PubMed[6], enabling publications to be located and their unique PubMed identifiers to be inserted into the system easily and conveniently.

The system is available at http://carre.kmi.open.ac.uk.

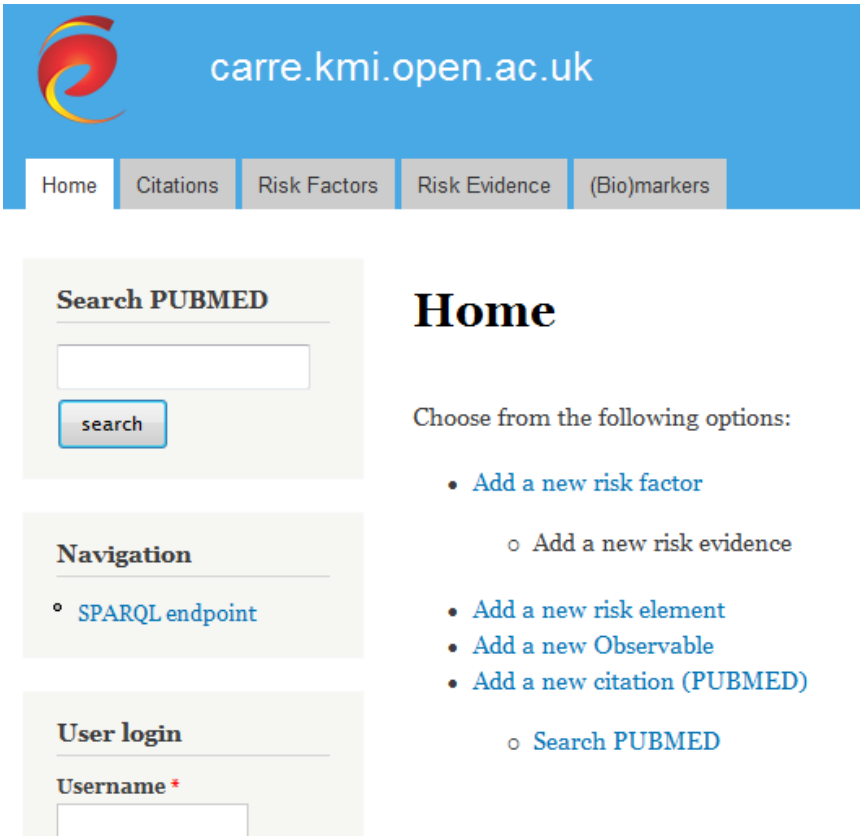

Figure 6. Home page of Drupal-based semantic data entry system.

[3] http://www.w3.org/DesignIssues/LinkedData.html
[4] http://www.w3.org/RDF/
[5] https://www.drupal.org/
[6] http://www.ncbi.nlm.nih.gov/pubmed

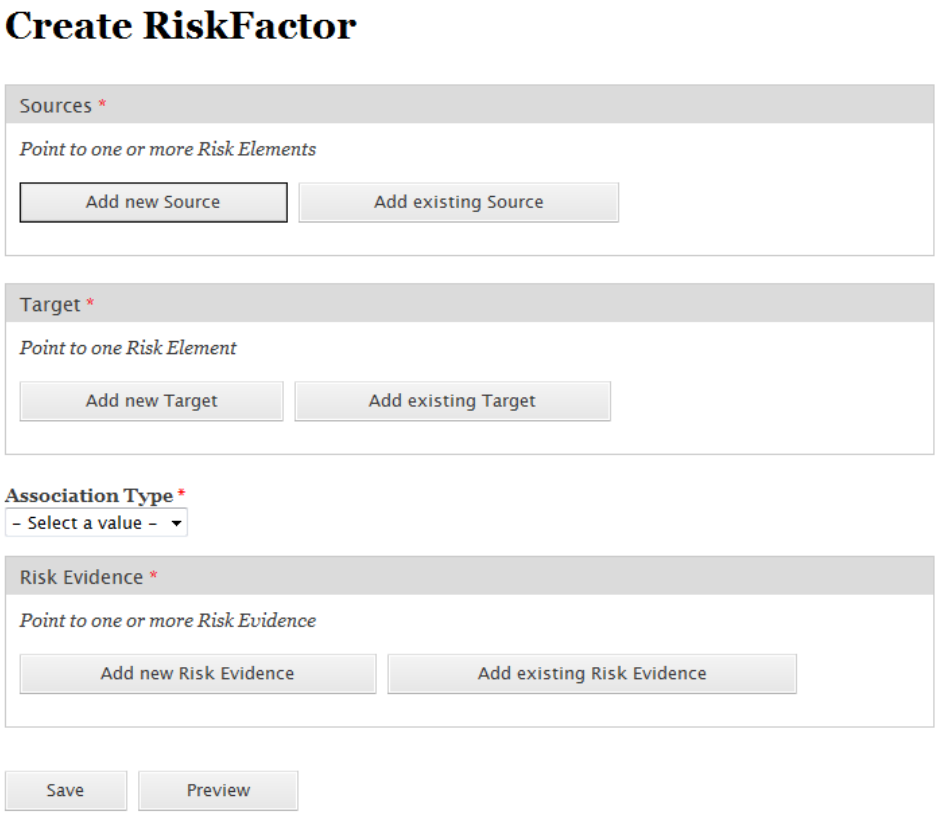

Figure 7. Create a new Risk Association

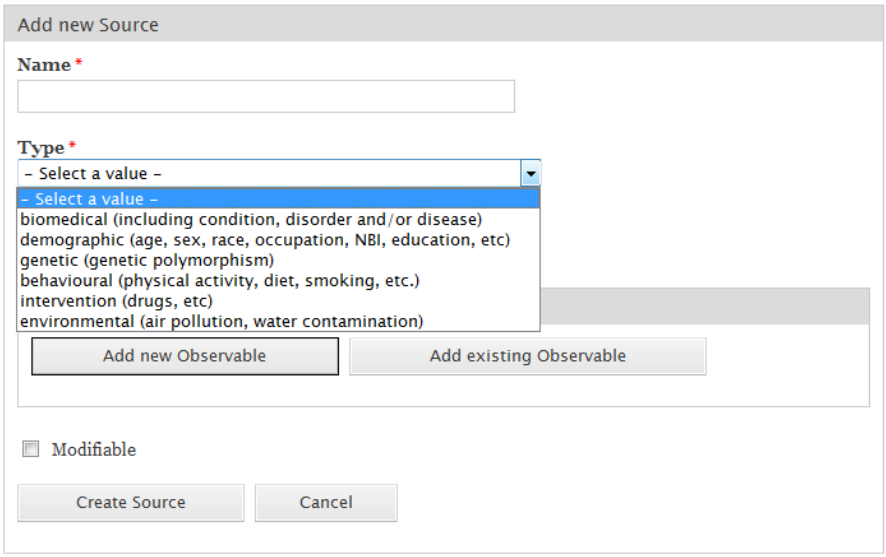

Figure 8. Create a new source Risk Element

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, 2014.

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 different risk factors with their respective risk associations (total of 268). The involved risk elements (total of 45) attributes tables are presented in Section 3. Respective observables (total of 47) are given in Section 4. Finally, Section 5 presents the attributes tables for the sources of evidence mentioned in risk association descriptions (total of 62).

2. Risk Associations

2.1. Acute kidney injury → Chronic kidney disease

Risk Association	
Risk Source:	Acute kidney injury (AKI)
Risk Target:	Chronic kidney disease
Association Type:	Is an issue in
RiskID:	REID1 – REID4
Author	Laurynas
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = diagnosed
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, Ploumis
Reviewed	Stefanos, Ploumis

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, Ploumis
Reviewed	Stefanos, Ploumis

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, Ploumis
Reviewed	Stefanos, Ploumis

2.2. Acute kidney injury → Death

Risk Association	
Risk Source:	Acute kidney injury
Risk Target:	Death
Association Type:	Causes
RiskID:	REID1
Author	Laurynas
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Acute kidney disease diagnosis
Observable Condition:	Acute kidney disease diagnosis = diagnosed
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
RiskID:	REID1 – REID4
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:	5.18
Confidence Interval:	4.20 – 6.39
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis

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

Ratio Type:	Risk ratio
Ratio Value:	9.08
Confidence Interval:	7.16 – 11.53
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis

Risk Evidence ID3	
RiskID:	3
Observables:	Age AND sex
Observable Condition:	54 ≤ age ≤ 59 AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	9.01
Confidence Interval:	5.62 – 14.44
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis

Risk Evidence ID4	
RiskID:	4
Observables:	Age AND Sex
Observable Condition:	60 ≤ age ≤ 64 AND sex = female
Ratio Type:	Risk ratio
Ratio Value:	24.12
Confidence Interval:	15.24 – 38.87
Adjusted for:	Smoking, HDL cholesterol ratio, systolic blood pressure, BMI, diabetes
Evidence source PMID	10069784
Author	Kalliopi
Reviewed	Stefanos, Ploumis

2.4. Age → Peripheral arterial disease

Risk Association	
Risk Source:	Age
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi, Dimitris
Reviewed	Kalliopi, 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, Dimitris
Reviewed	Kalliopi, Dimitris

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, Dimitris
Reviewed	Kalliopi, Dimitris

2.5. Atrial fibrillation → Ischemic stroke

Risk Association	
Risk Source:	Atrial fibrillation

Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi
Reviewed by	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	Atrial fibrillation diagnosis = diagnosed 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

Risk Evidence ID2	
RiskID:	2
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	Atrial fibrillation diagnosis = diagnosed 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

Risk Evidence ID3	
RiskID:	3
Observables:	Atrial fibrillation diagnosis

	AND Age
Observable Condition:	Atrial fibrillation diagnosis = diagnosed 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

Risk Evidence ID4	
RiskID:	4
Observables:	Atrial fibrillation diagnosis AND Age
Observable Condition:	Atrial fibrillation diagnosis = diagnosed AND 50 ≤ age ≤ 59
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

2.6. Anemia AND Acute myocardial infarction → Death

Risk Association	
Risk Source:	Anemia AND Acute myocardial infarction
Risk Target:	Death
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare
Reviewed	Stefanos, Ploumis

Risk Evidence ID1

RiskID:	1
Observable:	Hemoglobin (Hb) level AND Acute myocardial infarction AND Time after Acute myocardial infarction event
Observable Condition:	Hb <12.5 g/dL AND Acute myocardial infarction diagnosis = diagnosed AND Time after Acute myocardial infarction event = 30 days
Ratio Type:	Hazard ratio
Ratio Value:	1.75
Confidence Interval:	1.02 – 3.01
Adjusted for:	Age, sex, history of type 2 diabetes mellitus, congestive heartfailure, 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:	Hemoglobin (Hb) level AND Acute myocardial infarction diagnosis AND Time after Acute myocardial infarction event
Observable Condition:	Hb < 12.5 g/dL AND Acute myocardial infarction diagnosis = diagnosed AND Time after Acute myocardial infarction event = 365 days
Ratio Type:	Hazard ratio
Ratio Value:	1.63
Confidence Interval:	1.10 – 2.40
Adjusted for:	Age, sex, history of type 2 diabetes mellitus, congestive heartfailure, revascularization, treatment with thrombolysis, Killip class on presentation, and renal function
Evidence source PMID	23351816
Author	Gintare
Reviewed	Stefanos, Ploumis

2.7. Anemia AND Heart Failure → Death

Risk Association	
Risk Source:	Anemia AND Heart Failure
Risk Target:	Death
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	

Risk Evidence ID1	
RiskID:	1
Observable:	Hemoglobin (Hb) level AND Heart Failure diagnosis
Observable Condition:	Hb <12.5 g/dL AND Heart failure diagnosis = diagnosed
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	Dimitris

2.8. Atrial fibrillation → Heart failure

Risk Association	
Risk Source:	Atrial fibrillation
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1

Observables:	Atrial fibrillation diagnosis
Observable Condition:	Atrial fibrillation diagnosis = diagnosed
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	Dimitris

2.9. Chronic kidney disease → Death

Risk Association	
Risk Source:	Chronic kidney disease
Risk Target:	Death
Association Type:	causes
RiskID:	REID1 – REID4
Author:	Stefanos
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	Chronic kidney disease diagnosis = stage 3A OR $45 \leq eGFR \leq 59$
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:	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	Chronic kidney disease diagnosis = stage 3**B** OR 30 ≤ eGFR ≤ 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:	Stefanos, Ploumis

Risk Evidence ID3	
RiskID:	3
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	Chronic kidney disease diagnosis = stage 4 OR 15 ≤ eGFR ≤ 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:	Stefanos, Ploumis

Risk Evidence ID4	
RiskID:	4

Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	Chronic kidney disease diagnosis = stage 5 OR eGFR < 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:	Stefanos, Ploumis

2.10. Chronic kidney disease → Hospitalization

Risk Association	
Risk Source:	Chronic Kidney Disease (CKD)
Risk Target:	Hospitalization
Association Type:	causes
RiskID:	REID1 – REID4
Author:	Stefanos
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	45 ≤ eGFR ≤ 59 OR Chronic kidney disease diagnosis = stage 3A
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:	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	30 ≤ eGFR ≤ 44 OR Chronic kidney disease diagnosis = stage 3**B**
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:	Stefanos, Ploumis

Risk Evidence ID3	
RiskID:	3
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	15≤eGFR≤29 OR Chronic kidney disease diagnosis = stage 4
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:	Stefanos, Ploumis

Risk Evidence ID4	
RiskID:	4
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	eGFR < 15 OR Chronic kidney disease diagnosis = stage 5
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:	Stefanos, Ploumis

2.11. Chronic kidney disease → 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
RiskID:	REID1 – REID4
Author:	Stefanos
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	45 ≤ eGFR ≤ 59 OR

	Chronic kidney disease diagnosis = stage 3A
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, and prior hospitalizations.
Evidence source PMID	15385656
Author:	Stefanos
Reviewed:	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	30 ≤ eGFR ≤ 44 OR Chronic kidney disease diagnosis = stage 3B
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:	Stefanos, Ploumis

Risk Evidence ID3	
RiskID:	3
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	15 ≤ eGFR ≤ 29 OR Chronic kidney disease diagnosis = stage 4
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:	Stefanos, Ploumis

Risk Evidence ID4	
RiskID:	4
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	eGFR < 15 OR Chronic kidney disease diagnosis = stage 5
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:	Stefanos, Ploumis

2.12. Chronic Kidney Disease → Peripheral arterial disease

Risk Association	
Risk Source:	Chronic kidney disease
Risk Target:	Peripheral Arterial Disease
Association Type:	causes
RiskID:	REID1
Author:	Stefanos
Reviewed	Dimitris, Kalliopi

Risk Evidence ID1

RiskID:	1
Observable:	Chronic kidney disease diagnosis OR eGFR
Observable Condition:	eGFR < 60 ml/min OR [Chronic kidney disease diagnosis = stage 3 OR Chronic kidney disease diagnosis = stage 4 OR Chronic kidney disease diagnosis = stage 5]
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

2.13. Chronic kidney disease AND Heart failure → Death

Risk Association	
Risk Source:	Chronic kidney disease AND Heart Failure
Risk Target:	Death
Association Type:	Issue in
RiskID:	REID1
Author	Dimitris
Reviewed	

Risk Evidence ID1	
RiskID:	1
Observable:	[Chronic kidney disease diagnosis OR eGFR] AND Heart failure diagnosis
Observable Condition:	[eGFR < 90 ml/min/1.73m^2 OR Chronic kidney disease diagnosis = stage 2 OR Chronic kidney disease diagnosis = stage 3 OR Chronic kidney disease diagnosis = stage 4

	OR Chronic kidney disease diagnosis = stage 5] AND Heart failure diagnosis = diagnosed
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	

2.14. Chronic kidney disease AND (Hypertension OR Heart failure) → Hyperkalemia

Risk Association	
Risk Source:	Chronic kidney disease AND (Hypertension OR Heart failure)
Risk Target:	Hyperkalemia
Association Type:	Issue in
RiskID:	REID1
Author	Neringa
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	(Chronic kidney disease diagnosis OR eGFR) AND (hypertension OR heart failure)
Observable Condition:	(eGFR < 60 ml/min/1.73m^2 OR Chronic kidney disease diagnosis = stage 3 OR Chronic kidney disease diagnosis = stage 4 OR Chronic kidney disease diagnosis = stage 5) AND (Hypertension diagnosis = diagnosed OR Heart failure diagnosis = diagnosed)
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

2.15. 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
RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Chronic obstructive pulmonary disease diagnosis
Observable Condition:	Chronic obstructive pulmonary disease diagnosis = diagnosed
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, and triple vessel disease
Evidence source PMID	19368979
Author	Gintare
Reviewed	Gintare, Kalliopi, Dimitris

2.16. Depression → Ischemic stroke

Risk Association	
Risk Source:	Depression
Risk Target:	Ischemic stroke
Association Type:	is an issue in

RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Depression diagnosis
Observable Condition:	Depression diagnosis = diagnosed
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, and history of cardiac disease
Evidence source PMID	22020036
Author	Gintare
Reviewed	Gintare, Kalliopi, Dimitris

2.17. Depression → Ischemic heart disease

Risk Association	
Risk Source:	Depression
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk evidence ID1	
RiskID:	1
Observable	Depression diagnosis
Observable Condition:	Depression diagnosis = diagnosed
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 (LV) function
Evidence source PMID	17082208

Author	Gintare
Reviewed	Gintare, Kalliopi, Dimitris

2.18. Diabetes → Death: due to cardiovascular disease

Risk Association	
Risk Source:	Diabetes
Risk Target:	Death: due to cardiovascular disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes diagnosis AND Sex
Observable Condition:	Diabetes diagnosis = diagnosed 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, and prior report of Ischemic heart disease. Hypertension, smoking, hypercholesterolemia, parental history of myocardial infarction, BMI
Evidence source PMID	12695299
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.19. Diabetes → Heart failure

Risk Association	
Risk Source:	Diabetes
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	Diabetes diagnosis
Observable Condition:	Diabetes diagnosis = diagnosed
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	Dimitris

2.20. Diabetes → Ischemic heart disease

Risk Association	
Risk Source:	Diabetes
Risk Target:	Ischemic heart disease
Association Type:	causes
RiskID:	REID1, REID2
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID1:	1
Observables:	Diabetes diagnosis AND Sex
Observable Condition:	Diabetes diagnosis = diagnosed AND Sex = female
Ratio Type:	RR
Ratio Value:	2.82
Confidence Interval:	2.35 – 3.38
Adjusted for:	
Evidence source PMID	24859435
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	Diabetes diagnosis AND Sex
Observable Condition:	Diabetes diagnosis = diagnosed AND Sex = male
Ratio Type:	RR
Ratio Value:	2.16
Confidence Interval:	1.82 – 2.56
Adjusted for:	
Evidence source PMID	24859435
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

2.21. Diabetes → Ischemic heart disease OR Ischemic stroke

Risk Association	
Risk Source:	Diabetes
Risk Target:	Ischemic heart disease OR Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable	Diabetes diagnosis
Observable Condition:	Diabetes diagnosis = diagnosed
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 and body mass index
Evidence source PMID	15562129
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

2.22. Diabetes → Peripheral vascular disease

Risk Association	
Risk Source:	Diabetes
Risk Target:	Peripheral vascular disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes diagnosis
Observable Condition:	Diabetes diagnosis = diagnosed
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

2.23. Diabetes: disease control → Heart failure

Risk Association	
Risk Source:	Diabetes: disease control
Risk Target:	Heart failure
Association Type:	issue in
RiskID:	REID1 – REID4
Author	Zydrune
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 7.0 ≤ HbA1c < 8.0

Ratio Type:	Hazard ratio
Ratio Value:	1.15
Confidence Interval:	0.93–1.43
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 ID2	
RiskID:	2
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 8.0% ≤ HbA1c < 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 ID3	
RiskID:	3
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 9.0% ≤ HbA1c < 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 ID4

RiskID:	4
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis= diagnosed AND HbA1c ≥ 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

2.24. Diabetes: disease control → Ischemic heart disease

Risk Association	
Risk Source:	Diabetes: disease control
Risk Target:	Ischemic Heart Disease
Association Type:	issue in
RiskID:	REID1 – REID5
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND HbA1c < 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, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 5.2% ≤ HbA1c < 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, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 5.7% ≤ HbA1c < 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, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis =diagnosed AND 6.5% ≤ HbA1c < 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, Dimitris

Risk Evidence ID5	
RiskID:	5
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND HbA1c ≥ 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, Dimitris

2.25. Diabetes: disease control → Ischemic heart disease OR Ischemic stroke

Risk Association	
Risk Source:	Diabetes: disease control
Risk Target:	Ischemic heart disease OR Ischemic stroke
Association Type:	issue in
RiskID:	REID1 – REID6
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes diagnosis = diagnosed AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND HbA1c < 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 and urine albumin : creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 6.0% ≤ HbA1c < 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 and urine albumin : creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 7.0% ≤ HbA1c < 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 and urine albumin : creatinine ratio
Evidence source PMID	19046219

Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 8.0% ≤ HbA1c < 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 and urine albumin : creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observable:	Diabetes diagnosis AND HbA1c
Observable Condition:	Diabetes diagnosis = diagnosed AND 9.0% ≤ HbA1c < 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 and urine albumin : creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observable:	Diabetes diagnosis AND HbA1c

Observable Condition:	Diabetes diagnosis = diagnosed AND HbA1c ≥ 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 and urine albumin : creatinine ratio
Evidence source PMID	19046219
Author	Dimitris
Reviewed	Kalliopi, Dimitris

2.26. Diabetic nephropathy → Acute myocardial infarction OR Ischemic stroke

Risk Association	
Risk Source:	Diabetic nephropathy
Risk Target:	Acute myocardial infarction OR Ischemic stroke
Association Type:	issue in
RiskID:	REID1 – REID18
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	eGFR AND Diabetes diagnosis
Observable Condition:	60 ≤ eGFR ≤89 AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.14
Confidence Interval:	1.01–1.29
Adjusted for:	age, sex, duration of diabetes, smoking status, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, diabetic retinopathy, treatment with ACE inhibitors or angiotensin-receptor blockers, treatment group and log of the UACR (as a continuous covariate)
Evidence source PMID	20668832
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	eGFR AND Diabetes diagnosis
Observable Condition:	30≤ eGFR ≤69 AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.59
Confidence Interval:	1.28–1.98
Adjusted for:	age, sex, duration of diabetes, smoking status, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, diabetic retinopathy, treatment with ACE inhibitors or angiotensin-receptor blockers, treatment group and log of the UACR (as a continuous covariate)
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	60 ≤ eGFR ≤ 89 AND Uric acid serum concentration < 2.5 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.11
Confidence Interval:	0.95–1.29
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	60 ≤ eGFR ≤ 89 AND Uric acid serum concentration < 3.5 mg/mmol AND Sex = female AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.11
Confidence Interval:	0.95–1.29
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	30 ≤ eGFR ≤ 59 AND Uric acid serum concentration < 2.5 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.63
Confidence Interval:	1.20–2.20
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group

Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes
Observable Condition:	30 ≤ eGFR ≤ 59 AND Uric acid serum concentration < 3.5 mg/mmol AND Sex = female AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.63
Confidence Interval:	1.20–2.20
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID7	
RiskID:	7
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	eGFR > 90 AND Uric acid serum concentration > 2.5 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.25

Confidence Interval:	1.01–1.54
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID8	
RiskID:	8
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	eGFR > 90 AND Uric acid serum concentration > 3.5 mg/mmol AND Sex = female AND Diabetes = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.25
Confidence Interval:	1.01–1.54
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID9	
RiskID:	9
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	60 ≤ eGFR ≤ 89 AND Uric acid serum concentration > 2.5 mg/mmol AND Sex = male

	AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.43
Confidence Interval:	1.18–1.72
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID10	
RiskID:	10
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes
Observable Condition:	60 ≤ eGFR ≤ 89 AND Uric acid serum concentration > 3.5 mg/mmol AND Sex = female AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.43
Confidence Interval:	1.18–1.72
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID11	
RiskID:	11
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes
Observable Condition:	30 ≤ eGFR ≤ 59

	AND Uric acid serum concentration > 2.5 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.94
Confidence Interval:	1.37–2.73
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID12	
RiskID:	12
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes
Observable Condition:	30 ≤ eGFR ≤ 59 AND Uric acid serum concentration > 3.5 mg/mmol AND Sex = female AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.94
Confidence Interval:	1.37–2.73
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID13	
RiskID:	13
Observable:	eGFR

	AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	eGFR > 90 AND Uric acid serum concentration > 25 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.19
Confidence Interval:	0.76–1.85
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID14	
RiskID:	14
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	eGFR > 90 AND Uric acid serum concentration > 35 mg/mmol AND Sex = female AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.19
Confidence Interval:	0.76–1.85
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID15	
RiskID:	15
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	60 ≤ eGFR ≤ 89 AND Uric acid serum concentration > 25 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.77
Confidence Interval:	1.33–2.36
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID16	
RiskID:	16
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	60 ≤ eGFR ≤ 89 AND Uric acid serum concentration > 35 mg/mmol AND Sex = female AND Diabetes diagnosed = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	1.77
Confidence Interval:	1.33–2.36
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551

Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID17	
RiskID:	17
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes diagnosis
Observable Condition:	30 ≤ eGFR ≤ 59 AND Uric acid serum concentration >25 mg/mmol AND Sex = male AND Diabetes diagnosis = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	2.30
Confidence Interval:	1.48–3.55
Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

Risk Evidence ID18	
RiskID:	18
Observable:	eGFR AND Uric acid serum concentration AND Sex AND Diabetes
Observable Condition:	30 ≤ eGFR ≤ 59 AND Uric acid serum concentration > 35 mg/mmol AND Sex = female AND Diabetes = diagnosed
Ratio Type:	Hazard ratio
Ratio Value:	2.30
Confidence Interval:	1.48–3.55

Adjusted for:	age, sex, duration of diabetes, smoking, BMI, systolic BP, HbA1c, HDL-cholesterol, LDL-cholesterol, triacylglycerol, retinopathy, renin–angiotensin–aldosterone inhibition and treatment group
Evidence source PMID	16310551
Author	Zydrune
Reviewed	Kalliopi, Dimitris

2.27. Drugs: β-blockers → Diabetes

Risk Association	
Risk Source:	Drugs: β-blockers
Risk Target:	Diabetes
Association Type:	issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	β-blockers administration
Observable Condition:	β-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, Dimitris

2.28. Drugs: contrast agents: coronary angiography → Acute kidney injury

Risk Association	
Risk Source:	Contrast agents: coronary angiography
Risk Target:	Acute kidney injury
Association Type:	causes
RiskID:	REID1
Author:	Dimitris
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	coronary angiography contrast agents administration
Observable Condition:	coronary angiography 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

2.29. Drugs: diuretics → Diabetes

Risk Association	
Risk Source:	Drugs: diuretics
Risk Target:	Diabetes
Association Type:	issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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, Dimitris

2.30. Drugs: renin-angiotensin system dual blockade (any) → Hyperkalemia

Risk Association	
Risk Source:	Dual blockade of the renin-angiotensin system (any)
Risk Target:	Hyperkalemia
Association Type:	Causes
RiskID:	REID1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	Drug therapy
Observable Condition:	[Use of ACEI AND use of ATII inhibitors] OR [Use of ACE AND use of Renin inhibitors] OR [Use of ATII inhibitors AND use of Renin inhibitors]
Ratio Type:	RR
Ratio Value:	1.55
Confidence Interval:	1.32-1.82
Adjusted for:	-
Evidence source PMID	23358488
Author	Laurynas
Reviewed	Dimitris

2.31. Drugs: renin-angiotensin system dual blockade (any) → Hypotension

Risk Association	
Risk Source:	Dual blockade of the renin-angiotensin system (any)
Risk Target:	Hypotension
Association Type:	Causes
RiskID:	REID1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Renin-angiotensin system dual blockade administration
Observable Condition:	[Use of ACEI AND use of ATII inhibitors] OR [Use of ACE AND use of Renin inhibitors] OR

	[Use of ATII inhibitors AND use of Renin inhibitors]
Ratio Type:	RR
Ratio Value:	1.66
Confidence Interval:	1.38 - 1.98
Adjusted for:	-
Evidence source PMID	23358488
Author	Laurynas
Reviewed	Dimitris

2.32. Drugs: renin-angiotensin system dual blockade (any) AND Heart failure → Acute kidney injury

Risk Association	
Risk Source:	Dual blockade of the renin-angiotensin system (any) AND Heart failure
Risk Target:	Acute kidney injury
Association Type:	Causes
RiskID:	REID1
Author	Laurynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Heart failure AND Renin-angiotensin system dual blockade administration
Observable Condition:	Heart failure AND {[Use of ACEI AND use of ATII inhibitors] OR [Use of ACE AND use of Renin inhibitors] OR [Use of ATII inhibitors AND use of Renin inhibitors] }
Ratio Type:	RR
Ratio Value:	2.19
Confidence Interval:	1.82 - 2.65
Adjusted for:	-
Evidence source PMID	23358488
Author	Laurynas
Reviewed	Dimitris

2.33. Drugs: statins → Diabetes

Risk Association	
Risk Source:	Drug therapy: statins
Risk Target:	Diabetes
Association Type:	issue in
RiskID:	REID1 – REID5
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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, Dimitris

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, Dimitris

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, Dimitris

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, Dimitris

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, Dimitris

2.34. Drugs: statins AND Chronic kidney disease stage = 1 to 3 → Chronic kidney disease = stage 5

Risk Association	
Risk Source:	Drugs: Statins AND Chronic kidney disease diagnosis = stage 1 to 3

Risk Target:	Chronic kidney disease = stage 5
Association Type:	Is an issue in
RiskID:	REID1
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 = stage 1 OR Chronic kidney disease diagnosis = stage 2 OR Chronic kidney disease diagnosis = stage 3 OR $90 \leq eGFR \leq 30$)
Ratio Type:	RR
Ratio Value:	0.98
Confidence Interval:	0.62-1.56
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos
Reviewed	Dimitris

2.35. Drugs: statins AND Chronic kidney disease stage = 1 to 3→ Death

Risk Association	
Risk Source:	Use of statins in Chronic kidney disease stage 1-3
Risk Target:	Death
Association Type:	Is an issue in
RiskID:	REID1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1

Observable:	Statin administration AND Chronic kidney disease diagnosis
Observable Condition:	(Chronic kidney disease diagnosis = stage 1 OR Chronic kidney disease diagnosis = stage 2 OR Chronic kidney disease diagnosis = stage 3 OR 90 ≤ eGFR ≤ 30) 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

2.36. Drugs: statins AND Chronic kidney disease → Ischemic stroke

Risk Association	
Risk Source:	Use of statins in CKD 1-3
Risk Target:	Ischemic stroke
Association Type:	Is an issue in
RiskID:	REID1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Statin administration AND Chronic kidney disease diagnosis
Observable Condition:	(Chronic kidney disease diagnosis = stage 1 OR Chronic kidney disease diagnosis = stage 2 OR Chronic kidney disease diagnosis = stage 3 OR

	90 ≤ eGFR ≤ 30) 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

2.37. Drugs: Statins AND Chronic kidney disease stage 1 to 3 → Myocardial Infraction

Risk Association	
Risk Source:	Use of statins in Chronic kidney disease stage 1-3
Risk Target:	Myocardial infarction
Association Type:	Is an issue in
RiskID:	REID1
Author	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Statin administration AND Chronic kidney disease diagnosis
Observable Condition:	(Chronic kidney disease diagnosis = stage 1 OR Chronic kidney disease diagnosis = stage 2 OR Chronic kidney disease diagnosis = stage 3 OR 90 ≤ eGFR ≤ 30) 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

2.38. Dyslipidemia → Heart Failure

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Gintare
Reviewed	Stefanos, Ploumis

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

Risk Evidence ID2	
RiskID:	2
Observable:	High-density lipoprotein cholesterol (HDL-C) AND Sex
Observable Condition:	50 ≤ HDL-C ≤ 64mg/dL AND Sex = female
Ratio Type:	Hazard ratio
Ratio Value:	0.77

Confidence Interval:	0.65 – 0.91
Adjusted for:	Age, sex, 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 (HDL-C) AND Sex
Observable Condition:	HDL-C ≥ 55 mg/dL AND Sex = male
Ratio Type:	Hazard ratio
Ratio Value:	0.60
Confidence Interval:	0.48 – 0.74
Adjusted for:	Age, sex, 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 (HDL-C) AND Sex
Observable Condition:	HDL-C ≥ 65 mg/dL AND Sex = female
Ratio Type:	Hazard ratio
Ratio Value:	0.60
Confidence Interval:	0.48 – 0.74
Adjusted for:	Age, sex, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, and smoking
Evidence source PMID	19933936
Author	Gintare
Reviewed	Stefanos, Ploumis

2.39. Dyslipidemia → Ischemic heart disease

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
RiskID:	REID1 – REID3
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Non-HDL cholesterol serum concentration
Observable Condition:	Non-HDL ≥ 169 mg%
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, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	HDL cholesterol serum concentration
Observable Condition:	HDL ≤ 50 mg%
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, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Tryglicerides serum concentration
Observable Condition:	Tryglicerides ≥ 150mg%

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, Dimitris

2.40. Dyslipidemia → Ischemic stroke

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1 – REID3
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Non-HDL cholesterol serum concentration
Observable Condition:	Non-HDL cholesterol ≥ 169 mg%
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, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	HDL cholesterol serum concentration
Observable Condition:	HDL cholesterol ≤ 50 mg%
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, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Tryglicerides serum concentration
Observable Condition:	Tryglicerides ≥ 150mg%
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, Dimitris

2.41. Dyslipidemia → Peripheral arterial disease

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Total cholesterol (TC) serum concentration
Observable Condition:	Total cholesterol > 200 mg/dL
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:	LDL-C
Observable Condition:	LDL-C > 130 mg/dL
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:	HDL-C
Observable Condition:	HDL-C < 40 mg/dL
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 (TG) serum concentration
Observable Condition:	Triglycerides >150 mg/dL
Ratio Type:	Odds ratio
Ratio Value:	1.22
Confidence Interval:	1.10–1.35
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

2.42. Heart failure → Ischemic stroke

Risk Association	
Risk Source:	Heart failure
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi
Reviewed by	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Heart failure diagnosis AND Age
Observable Condition:	Heart failure diagnosis = diagnosed 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	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	Heart failure diagnosis AND Age
Observable Condition:	Heart failure diagnosis= diagnosed 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	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Heart failure diagnosis AND Age
Observable Condition:	Heart failure diagnosis= diagnosed 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	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	Heart failure diagnosis AND Age
Observable Condition:	Heart failure diagnosis = diagnosed 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	Kalliopi, Dimitris

2.43. Hyperkalemia AND Chronic kidney disease → Death

Risk Association	
Risk Source:	Hyperkalemia AND Chronic kidney disease
Risk Target:	death
Association Type:	cause
RiskID:	REID1
Author	Neringa

Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	serum potassium AND (Chronic kidney disease diagnosis OR eGFR)
Observable Condition:	Serum potassium > 5.0 mEq/L AND (Chronic kidney disease diagnosis = stage 3 OR Chronic kidney disease diagnosis = stage 4 OR Chronic kidney disease diagnosis = stage 5 OR eGFR ≤ 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

2.44. Hypertension → Chronic kidney disease

Risk Association	
Risk Source:	Hypertension
Risk Target:	Chronic kidney disease (CKD)
Association Type:	Causes
RiskID:	REID1
Author	Laurynas
Reviewed	Dimitiris

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

	systolic blood pressure ≥ 140 mmHg AND/OR diastolic blood pressure ≥ 90 mmHg
Ratio Type:	Odds ratio
Ratio Value:	2.0
Confidence Interval:	1.8 - 2.2
Adjusted for:	age, sex, smoking status and GFR
Evidence source PMID	21852664
Author	Dimitris
Reviewed	kalliopi, Dimitris

2.45. Hypertension → Death: cardiovascular

Risk Association	
Risk Source:	Hypertension
Risk Target:	Death: due to cardiovascular disease
Association Type:	Is an issue
RiskID:	REID1, REID 2
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure
Observable Condition:	120mmHg ≤ Systolic blood pressure ≤ 139mmHg, AND/OR 80mmHg ≤ Diastolic blood pressure ≤ 89mmHg
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, Dimitris

Risk Evidence ID2	
RiskID:	2

Observable:	Blood pressure
Observable Condition:	Systolic blood pressure ≥ 140mmHg, AND/OR Diastolic blood pressure ≥ 90mmHg
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, Dimitris

2.46. Hypertension → Heart Failure

Risk Association	
Risk Source:	Hypertension
Risk Target:	Heart failure
Association Type:	Causes
RiskID:	REID1
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure OR Hypertension diagnosis
Observable Condition:	Hypertension diagnosis = diagnosed OR systolic blood pressure ≥ 140 mmHg AND/OR diastolic blood pressure ≥ 90 mmHg AND/OR antihypertensive drug administration = yes
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

2.47. Hypertension → Ischemic stroke

Risk Association	
Risk Source:	Hypertension
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi, Dimitris
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observables:	Hypertension diagnosis AND Age
Observable Condition:	Hypertension diagnosis = diagnosed 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, Dimitris
Reviewed	Stefanos, Ploumis

Risk Evidence ID2	
RiskID:	2
Observables:	Hypertension diagnosis AND Age
Observable Condition:	Hypertension diagnosis = diagnosed 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, Dimitris
Reviewed	Stefanos, Ploumis

Risk Evidence ID3	
RiskID:	3
Observables:	Hypertension diagnosis AND Age
Observable Condition:	Hypertension diagnosis = diagnosed 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, Dimitris
Reviewed	Stefanos, Ploumis

Risk Evidence ID4	
RiskID:	4
Observables:	Hypertension diagnosis AND Age
Observable Condition:	Hypertension diagnosis = diagnosed 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, Dimitris
Reviewed	Stefanos, Ploumis

2.48. Hypertension → Peripheral arterial disease

Risk Association	
Risk Source:	Hypertension
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in

RiskID:	REID1
Author	Gintare
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure OR Hypertension diagnosis
Observable Condition:	Hypertension diagnosis = diagnosed OR systolic blood pressure ≥ 140 mmHg AND/OR diastolic blood pressure ≥ 90 mmHg
Ratio Type:	Odds ratio
Ratio Value:	1.47
Confidence Interval:	1.37–1.57
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare
Reviewed	Dimitris

2.49. Hyperuricemia →Heart failure

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration
Observable Condition:	Uric acid serum concentration > 6.8 mg%
Ratio Type:	Hazard ratio
Ratio Value:	1.65
Confidence Interval:	1.41 – 1.94

Adjusted for:	-
Evidence source PMID	23933579
Author	Dimitris
Reviewed	Dimitris

2.50. Hyperuricemia → Hypertension

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Hypertension
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration
Observable Condition:	Uric acid serum concentration > 6.8 mg%
Ratio Type:	RR
Ratio Value:	1.41
Confidence Interval:	1.23 – 1.58
Adjusted for:	Multivariable adjusted
Evidence source PMID	20824805
Author	Dimitris
Reviewed	Dimitris

2.51. Hyperuricemia → Ischemic heart disease

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris, Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration
Observable Condition:	Uric acid serum concentration > 6.8 mg%
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	Dimitris, Kalliopi

2.52. Hyperuricemia → Ischemic stroke

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Larynas
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration AND Sex
Observable Condition:	Uric acid serum concentration > 6.8 mg% 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

Risk Evidence ID2

RiskID:	2
Observables:	Uric acid serum concentration AND Sex
Observable Condition:	Uric acid serum concentration > 6.8 mg% 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

2.53. 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
RiskID:	REID1 – REID4
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 = diagnosed 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

Risk EvidenceID2	
RiskID:	2
Observables:	Ischemic heart disease diagnosis AND age AND sex
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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

Risk Evidence ID3	
RiskID:	3
Observables:	Ischemic heart disease diagnosis AND age AND sex
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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

Risk Evidence ID4

RiskID:	4
Observables:	Ischemic heart disease diagnosis AND age AND sex
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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

2.54. Ischemic heart disease → Ischemic stroke

Risk Association	
Risk Source:	Ischemic heart disease
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi, Dimitris
Reviewed by	

Risk Evidence ID1	
RiskID:	1
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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, Dimitris
Reviewed by	

Risk Evidence ID2	
RiskID:	2
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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, Dimitris
Reviewed by	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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, Dimitris
Reviewed by	

Risk Evidence ID4	
RiskID:	4
Observables:	Ischemic heart disease diagnosis AND Age
Observable Condition:	Ischemic heart disease diagnosis = diagnosed 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, Dimitris
Reviewed by	

2.55. Ischemic heart disease AND Chronic kidney disease → Death

Risk Association	
Risk Source:	Ischemic heart disease AND Chronic kidney disease
Risk Target:	Death
Association Type:	cause
RiskID:	REID1
Author	Neringa
Reviewed	Stefanos, Ploumis

Risk Evidence ID1	
RiskID:	1
Observable:	Ischemic heart disease diagnosis AND (Chronic kidney disease diagnosis OR eGFR)
Observable Condition:	Ischemic heart disease diagnosis = diagnosed AND (Chronic kidney disease diagnosis = stage 3 OR Chronic kidney disease diagnosis = stage 4 OR Chronic kidney disease diagnosis = stage 5 OR eGFR ≤ 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

2.56. 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
RiskID:	REID1
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 = diagnosed OR Ischemic stroke diagnosis = diagnosed
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

2.57. 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
RiskID:	REID1 – REID6
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1

RiskID:	1
Observable:	Ischemic heart disease family history AND Sex
Observable Condition:	Ischemic heart disease 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 & maternal 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 & maternal 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

2.58. 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
RiskID:	REID1 – REID6
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 & 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 & 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

2.59. 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
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris

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	Dimitris

2.60. Left ventricular hypertrophy → 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
RiskID:	REID1, REID2
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk EvidenceID1	
RiskID:	1
Observables:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	Left ventricular hypertrophy diagnosis = diagnosed 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 = diagnosed 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

2.61. Left ventricular hypertrophy → Death: cardiovascular

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Death: cardiovascular
Association Type:	issue in
RiskID:	REID1
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	Left ventricular hypertrophy diagnosis = diagnosed 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

2.62. Left ventricular hypertrophy → Heart failure

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Heart failure

Association Type:	Issue in
RiskID:	REID1, REID2
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	Left ventricular hypertrophy diagnosis = diagnosed AND Sex = male
Ratio Type:	relative 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 = diagnosed AND Sex = female
Ratio Type:	relative Hazard ratio
Ratio Value:	2.75
Confidence Interval:	1.94-3.91
Adjusted for:	-
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

2.63. Left ventricular hypertrophy → Hypertension

Risk Association	
Risk Source:	Left ventricular hypertrophy

Risk Target:	Hypertension
Association Type:	Issue in
RiskID:	REID1
Author	Neringa
Reviewed	Dimitris, Kalliopi

Risk Evidence ID1	
RiskID:	REID1
Observable:	Left ventricular hypertrophy diagnosis
Observable Condition:	Left ventricular hypertrophy diagnosis = diagnosed
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

2.64. Left ventricular hypertrophy → Ischemic stroke

Risk Assocation	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Ischemic stroke
Association Type:	Issue in
RiskID:	REID1, REID2
Author	Neringa
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	REID1
Observable:	Left ventricular hypertrophy diagnosis AND Sex
Observable Condition:	Left ventricular hypertrophy diagnosis = diagnosed AND Sex = male
Ratio Type:	relative 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 = diagnosed AND Sex = female
Ratio Type:	relative Hazard ratio
Ratio Value:	2.77
Confidence Interval:	1.70 – 4.52
Adjusted for:	-
Evidence source PMID	22139711
Author	Neringa
Reviewed	Kalliopi, Dimitris

2.65. Obesity → Asthma

Risk Association	
Risk Source:	Obesity
Risk Target:	asthma
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi
Reviewed	Dimitris

Risk EvidenceID1	
RiskID1:	1
Observables:	BMI AND Sex
Observable Condition:	$25 \leq BMI \leq 30$ AND Sex = male
Ratio Type:	Relative Risk

Ratio Value:	1.20
Confidence Interval:	1.08 – 1.33
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID2:	2
Observables:	BMI AND sex
Observable Condition:	BMI > 30 AND Sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.43
Confidence Interval:	1.14 – 1.79
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID3	
RiskID3:	3
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 30 AND Sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.25
Confidence Interval:	1.05 – 1.49
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID4	
RiskID4:	4

Observables:	BMI AND Sex
Observable Condition:	BMI > 30 AND Sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.78
Confidence Interval:	1.36 – 2.32
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

2.66. Obesity → Atrial fibrillation

Risk Association	
Risk Source:	Obesity
Risk Target:	Atrial fibrillation
Association Type:	Is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 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 murmur, interim media thickness
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID2:	2
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 30 AND Sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.13
Confidence Interval:	0.84 – 1.52
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	BMI AND Sex
Observable Condition:	BMI >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 murmur, interim media thickness
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	BMI AND Sex
Observable Condition:	BMI >30 AND Sex = female
Ratio Type:	Hazard ratio

Ratio Value:	1.46
Confidence Interval:	1.03 – 2.07
Evidence source PMID	15562125
Author	Kalliopi
Reviewed	Dimitris

2.67. Obesity → Cancer: colorectal cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: colorectal cancer
Association Type:	is an issue in
RiskID:	REID1
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	BMI > 30
Ratio Type:	Relative Risk
Ratio Value:	1.33
Confidence Interval:	1.25 – 1.42
Adjusted for:	-
Evidence source PMID	23349764
Author	Kalliopi
Reviewed	Dimitris

2.68. Obesity → Cancer: gastric cardiac cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: gastric cardiac cancer
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID3:	1
Observables:	BMI
Observable Condition:	25 ≤ BMI ≤ 30
Ratio Type:	Relative Risk
Ratio Value:	1.21
Confidence Interval:	
Adjusted for:	-
Evidence source PMID	23697611
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI > 30
Ratio Type:	Relative Risk
Ratio Value:	1.82
Confidence Interval:	
Adjusted for:	-
Evidence source PMID	23697611
Author	Kalliopi
Reviewed	Dimitris

2.69. Obesity → Cancer: pancreatic cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: pancreatic cancer
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI

Observable Condition:	25 ≤ BMI ≤ 30
Ratio Type:	Relative Risk
Ratio Value:	1.28
Confidence Interval:	0.94 – 1.75
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris

Risk EvidenceID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI > 30
Ratio Type:	Relative Risk
Ratio Value:	2.29
Confidence Interval:	1.65 – 3.19
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi
Reviewed	Dimitris

2.70. Obesity → Death: cardiovascular

Risk Association	
Risk Source:	Obesity
Risk Target:	Sudden cardiac death
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 29.9 AND Sex = female

Ratio Type:	Relative Risk
Ratio Value:	1.06
Confidence Interval:	0.72-1.56
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

Risk Evidence ID2	
RiskID:	2
Observable:	BMI
Observable Condition:	BMI ≥ 30
Ratio Type:	Relative Risk
Ratio Value:	1.63
Confidence Interval:	1.10-2.43
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

2.71. Obesity → Diabetes

Risk Association	
Risk Source:	Obesity
Risk Target:	Diabetes
Association Type:	causes
RiskID:	REID1 – REID4
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:	1.61
Confidence Interval:	1.41 – 1.84
Adjusted for:	
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	23 ≤ BMI ≤ 34
Ratio Type:	RR
Ratio Value:	1.61
Confidence Interval:	1.40 – 1.84
Adjusted for:	
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	Waist circumference
Observable Condition:	79.3 < WC < 107.5
Ratio Type:	RR
Ratio Value:	1.65
Confidence Interval:	1.42 – 1.91
Adjusted for:	
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris

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:	1.61
Confidence Interval:	1.35 – 1.93

Adjusted for:	
Evidence source PMID	23144362
Author	Kalliopi
Reviewed	Dimitris

2.72. Obesity → Cholelithiasis

Risk Association	
Risk Source:	Obesity
Risk Target:	Cholelithiasis
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 30 AND Sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.09
Confidence Interval:	0.87 – 1.37
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	BMI > 30 AND Sex = male
Ratio Type:	Relative Risk
Ratio Value:	1.43

Confidence Interval:	1.04 – 1.96
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 30 AND Sex = female
Ratio Type:	Relative Risk
Ratio Value:	1.44
Confidence Interval:	1.05 – 1.98)
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	BMI AND sex
Observable Condition:	BMI >30 AND Sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.32
Confidence Interval:	1.17 – 4.57
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

2.73. Obesity → Heart Failure

Risk Association	
Risk Source:	Obesity
Risk Target:	Heart failure
Association Type:	Is an issue in
RiskID:	REID1 – REID7
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 30 AND Sex = female
Ratio Type:	Hazard ratio
Ratio Value:	1.5
Confidence Interval:	
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, and presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, and myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	30 ≤ BMI ≤ 35 AND Sex = female
Ratio Type:	hazard ratio
Ratio Value:	1.6
Confidence Interval:	
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, and presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, and myocardial

	infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris

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

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

Risk Evidence ID5	
RiskID5:	5
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 30 AND Sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.2
Confidence Interval:	95%
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, and presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, and myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID6	
RiskID:	6
Observables:	BMI AND Sex
Observable Condition:	30 ≤ BMI ≤ 35 AND Sex = male
Ratio Type:	Hazard ratio
Ratio Value:	1.8
Confidence Interval:	
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, and presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, and myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID7	
RiskID:	7
Observables:	BMI AND Sex
Observable Condition:	35 ≤ BMI ≤ 40

	AND Sex = male
Ratio Type:	Hazard ratio
Ratio Value:	2.8
Confidence Interval:	
Adjusted for:	age, total serum cholesterol level, cigarette smoking, alcohol consumption, and presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, and myocardial infarction at base line
Evidence source PMID	12151467
Author	Kalliopi
Reviewed	Dimitris

2.74. Obesity → Ischemic heart disease

Risk Association	
Risk Source:	Obesity
Risk Target:	Ischemic heart disease
Association Type:	Is an issue in
RiskID:	REID1 – REID8
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI AND Sex
Observable Condition:	25 ≤ BMI ≤ 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

Risk Evidence ID2

RiskID:	2
Observables:	BMI AND Sex
Observable Condition:	BMI >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

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	94 ≤ WC ≤ 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

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC >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

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 ≤ WC ≤ 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

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 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

Risk Evidence ID7	
RiskID:	7
Observables:	BMI

	AND Sex
Observable Condition:	25 ≤ BMI ≤ 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

Risk Evidence ID8	
RiskID8:	8
Observables:	BMI AND Sex
Observable Condition:	BMI >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

2.75. Obesity → Ischemic stroke

Risk Association	
Risk Source:	Obesity
Risk Target:	Ischemic stroke
Association Type:	Is an issue in
RiskID:	REID1, REID2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1

RiskID:	1
Observables:	BMI
Observable Condition:	25 ≤ BMI ≤ 30
Ratio Type:	Risk ratio
Ratio Value:	1.22
Confidence Interval:	1.05 – 1.41
Adjusted for:	-
Evidence source PMID	20299666
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI >30
Ratio Type:	Risk ratio
Ratio Value:	1.64
Confidence Interval:	1.36 – 1.99
Adjusted for:	-
Evidence source PMID	20299666
Author	Kalliopi
Reviewed	Dimitris

2.76. Obesity → Osteoarthritis

Risk Association	
Risk Source:	Obesity
Risk Target:	Osteoarthritis
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	25 ≤ BMI ≤ 30

Ratio Type:	Relative Risk
Ratio Value:	1.80
Confidence Interval:	1.75 – 1.85
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI > 30
Ratio Type:	Relative Risk
Ratio Value:	1.96
Confidence Interval:	1.88 – 2.04
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi
Reviewed	Dimitris

2.77. Obesity: central → Acute myocardial infarction OR Old myocardial infarction

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Acute myocardial infarction OR Old myocardial infarction
Association Type:	is an issue in
RiskID:	REID – REID 4
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND sex
Observable Condition:	94 ≤ WC ≤102 AND sex = male
Ratio Type:	Odds ratio

Ratio Value:	1
Confidence Interval:	0.5 – 4.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC >102 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	2.75
Confidence Interval:	1.08- 7.03
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80 ≤ WC ≤88 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	1.5
Confidence Interval:	0.1- 7.5
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4

Observables:	Waist circumference (WC) AND sex
Observable Condition:	WC > 88 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	1.43
Confidence Interval	0.37- 5.50
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

2.78. Obesity: central → Diabetes

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Diabetes
Association Type:	Causes
RiskID:	REID1 – REID8
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	88.2 ≤ WC ≤ 94.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	3.9
Confidence Interval:	1.0 – 8.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2

RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	94.3 ≤ WC ≤ 99.3 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	3.9
Confidence Interval:	1.0 – 8.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	99.4 ≤ WC ≤ 106.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	7.8
Confidence Interval:	2.0 -14.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 106.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	8
Confidence Interval:	4.0 – 18.0

Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	73.7 ≤ WC ≤ 80.3 AND sex = female
Ratio Type:	Odds ratio
Ratio Value:	2
Confidence Interval:	0,5 -4.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80.4 ≤ WC ≤ 87.0 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	1
Confidence Interval:	0.3 - 2.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID7	
RiskID:	7
Observables:	Waist circumference (WC) AND Sex

Observable Condition:	87.1 ≤ WC ≤ 96.2 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	4
Confidence Interval:	2.0 – 8.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID8	
RiskID:	8
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 96.2 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	6
Confidence Interval:	4.0 – 10.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

2.79. Obesity: central → Dyslipidemia: HDL cholesterol serum concentration

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Dyslipidemia: HDL cholesterol serum concentration
Association Type:	Is an issue in
RiskID:	REID1 – REID8
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC)

	AND Sex
Observable Condition:	88.2 ≤ WC ≤ 94.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	2
Confidence Interval:	1.5 -4.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND sex
Observable Condition:	94.3 ≤ WC ≤ 99.3 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	1.7 – 4.2
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	99.4 ≤ WC ≤ 106.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	4
Confidence Interval:	2.0 – 8.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980

Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 106.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	1.7- 4.2
Adjusted for:	age and smoking status
Evidence source PMID	1970598
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	73.7 ≤ WC ≤ 80.2 AND Sex = female
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	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80.4 ≤ WC ≤ 87 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	Kalliopi, Dimitris

Risk Evidence ID7	
RiskID:	7
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	87.1 ≤ WC ≤ 96.2 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	3.9
Confidence Interval:	2.5 - 6.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID8	
RiskID:	8
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 96.2 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	3.5
Confidence Interval:	1.5- 4.3
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

2.80. Obesity: central → Dyslipidemia: Triclycerides serum concentration

Risk Association	
Risk Source:	Obesity: central
Risk Target:	Dyslipidemia: Triclycerides serum concentratiion
Association Type:	Is an issue in
RiskID:	REID1 – REID8
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	88.2 ≤ WC ≤94.2 AND Sex = male
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	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	94.3 ≤ WC ≤ 99.3 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	3.5
Confidence Interval:	2.0 - 4.2
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	99.4 ≤ WC ≤ 106.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	1.6- 3.9
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 106.2 AND Sex = male
Ratio Type:	Odds ratio
Ratio Value:	2.5
Confidence Interval:	1.3-3.8
Confidence Interval:	95%
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	73.7 ≤ WC ≤ 80.3 AND Sex = female
Ratio Type:	Odds ratio

Ratio Value:	3
Confidence Interval:	1.2- 4.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80.4 ≤ WC ≤ 87 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	5
Confidence Interval:	3.9- 8.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID7	
RiskID:	7
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	87.1 ≤ WC ≤ 96.2 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	7
Confidence Interval:	5.0 – 12.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

Risk Evidence ID8	
RiskID:	8

Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 96.2 AND Sex = female
Ratio Type:	Odds ratio
Ratio Value:	8
Confidence Interval:	7.0 – 14.0
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

2.81. Obesity: central → Hypertension

Risk Association	
Risk Source:	Central obesity
Risk Target:	Hypertension
Association Type:	causes
RiskID:	REID1 – REID8

Risk Evidence ID1	
RiskID:	1
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	88.2 ≤ WC ≤ 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	Kalliopi, Dimitris

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

	AND Sex
Observable Condition:	94.3 ≤ WC ≤ 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	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	99.4 ≤ WC ≤ 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	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 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	Kalliopi, Dimitris

Risk Evidence ID5	
RiskID:	5
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	73.7 ≤ WC ≤ 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	Kalliopi, Dimitris

Risk Evidence ID6	
RiskID:	6
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	80.4 ≤ WC ≤ 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	Kalliopi, Dimitris

Risk Evidence ID7	
RiskID:	7
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	87.1 ≤ WC ≤ 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	Kalliopi, Dimitris

Risk Evidence ID8	
RiskID:	8
Observables:	Waist circumference (WC) AND Sex
Observable Condition:	WC > 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	Kalliopi, Dimitris

2.82. Obstructive sleep apnoea → Death: cardiovascular

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Death due to Cardiovascular disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare
Reviewed	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	AHI
Observable Condition:	AHI > 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	Gintare

2.83. Obstructive sleep apnoea → Diabetes

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Diabetes
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	AHI OR Obstructive sleep apnea diagnosis
Observable Condition:	5 ≤ AHI <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

Risk Evidence ID2	
RiskID:	2
Observable:	AHI

	OR Obstructive sleep apnea diagnosis
Observable Condition:	AHI ≥ 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

2.84. Obstructive sleep apnoea → Heart failure

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	

Risk Evidence ID1	
RiskID:	1
Observable:	Obstructive sleep apnea diagnosis
Observable Condition:	Obstructive sleep apnea diagnosis = diagnosed
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	Dimitris

2.85. Obstructive sleep apnoea → Hypertension

Risk Association

Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Hypertension
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	AHI
Observable Condition:	1.5 ≤ AHI < 4.9
Ratio Type:	Odds ratio
Ratio Value:	1.07
Confidence Interval:	0.91-1.26
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	AHI OR \ Obstructive sleep apnea diagnosis
Observable Condition:	5 ≤ AHI < 14.9 OR Obstructive sleep apnea diagnosis = mild
Ratio Type:	Odds ratio
Ratio Value:	1.20
Confidence Interval:	1.01-1.42
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID3	
RiskID:	3
Observable:	AHI OR Obstructive sleep apnea diagnosis

Observable Condition:	15 ≤ AHI < 29.9 OR Obstructive sleep apnea diagnosis = moderate
Ratio Type:	Odds ratio
Ratio Value:	1.25
Confidence Interval:	1.00-1.56
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID4	
RiskID:	4
Observable:	AHI OR Obstructive sleep apnea diagnosis
Observable Condition:	AHI ≥ 30 OR Obstructive sleep apnea diagnosis = severe
Ratio Type:	Odds ratio
Ratio Value:	1.37
Confidence Interval:	1.03-1.83
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare
Reviewed	Kalliopi, Dimitris

2.86. 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
RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1

Observable:	Obstructive sleep apnea diagnosis
Observable Condition:	Obstructive sleep apnea diagnosis = diagnosed
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

2.87. Obstructive sleep apnoea → Ischemic stroke

Risk Association	
Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare
Reviewed	Kalliopi, Dimitris

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

2.88. Physical Activity→ Diabetes

Risk Association	
Risk Source:	Physical activity
Risk Target:	Diabetes type 2
Association Type:	is an issue in
RiskID:	1
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Physical activity
Observable Condition:	Physical activity = moderate
Ratio Type:	RR
Ratio Value:	0.83
Confidence Interval:	0.75–0.91
Adjusted for:	BMI
Evidence source PMID	17327354
Author	Dimitris
Reviewed	Kalliopi, Dimitris

2.89. Physical Activity → Ischemic heart disease

Risk Association	
Risk Source:	Physical activity
Risk Target:	Ischemic heart disease
Association Type:	Is an issue in
RiskID:	REID1 – REID4
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris
Reviewed	Kalliopi, Dimitris

2.90. Physical activity → Ischemic stroke

Risk Association	
Risk Source:	Physical activity
Risk Target:	Ischemic stroke
Association Type:	Is an issue in
RiskID:	REID1 – REID4
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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, Dimitris

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, Dimitris

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, Dimitris

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, Dimitris

2.91. Physical activity AND Chronic kidney disease → Death

Risk Association	
Risk Source:	Physical activity AND Chronic kidney disease
Risk Target:	Death
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Laurynas
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Physical activity AND Chronic kidney disease diagnosis
Observable Condition:	Physical activity = moderate AND Chronic kidney disease diagnosis = stage 5
Ratio Type:	Relative risk
Ratio Value:	1.2
Confidence Interval:	0.7–1.8
Adjusted for:	age, sex, race, body-mass index
Evidence source PMID	12843775
Author	Laurynas
Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Physical activity AND Chronic kidney disease diagnosis
Observable Condition:	Physical activity = high AND Chronic kidney disease diagnosis = stage 5
Ratio Type:	Relative risk

Ratio Value:	2.2
Confidence Interval:	1.3–3.8
Adjusted for:	age, sex, race, body-mass index
Evidence source PMID	12843775
Author	Laurynas
Reviewed	Kalliopi, Dimitris

2.92. Smoking → Death: cardiovascular

Risk Factor	
Risk Source:	Smoking status
Risk Target:	Death: cardiovascular
Association Type:	is an issue in
RiskID:	REID1 – REID4
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 smoking intensity AND sex
Observable Condition:	status = Current AND 1 ≤smoking intensity ≤ 14 cigarettes/day

	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 Smoking intensity AND Sex
Observable Condition:	Smoking status = Current AND 15 ≤ Smoking intensity ≤ 24 cigarettes/day 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 Smoking intensity AND Sex
Observable Condition:	Smoking status = Current AND Smoking intensity ≥ 25 cigarettes/day 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

2.93. Smoking → Albuminuria

Risk Association	
Risk Source:	Smoking
Risk Target:	Albuminuria
Association Type:	Causes
RiskID:	REID1, REID2
Author:	Stefanos
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	Smoking status = Current Smoker
Ratio Type:	Relative Risk
Ratio Value:	3.26
Confidence Interval:	1.66 - 6.80
Adjusted for:	
Evidence source PMID	10972692
Author:	Stefanos
Reviewed:	Dimitris

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:	
Evidence source PMID	10972692

Author:	Stefanos
Reviewed:	Dimitris

2.94. Smoking → Chronic Kidney Disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Chronic kidney disease
Association Type:	Is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Dimitris

Risk Evidence ID1	
RiskID:	1
Observables:	Smoking status AND Sex
Observables Condition:	Smoking status = current 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	Dimitris

2.95. Smoking → Heart failure

Risk Association	
Risk Source:	Smoking
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris
Reviewed	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	Smoking status = Current
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	Dimitris

2.96. Smoking → Ischemic heart disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Ischemic heart disease
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status AND Sex
Observable Condition:	Smoking status = Current AND Sex = male
Ratio Type:	Relative risk
Ratio Value:	1.43
Confidence Interval:	1.26-1.62
Adjusted for:	arterial blood pressure, total and high density lipoprotein cholesterol concentrations, triglyceride concentrations, diabetes, body mass index, height, alcohol intake, physical activity, and level of education
Evidence source PMID	09552903
Author	Dimitris

Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status AND Sex
Observable Condition:	Smoking status = Current AND Sex = female
Ratio Type:	Relative risk
Ratio Value:	2.24
Confidence Interval:	1.85-2.71
Adjusted for:	arterial blood pressure, total and high density lipoprotein cholesterol concentrations, triglyceride concentrations, diabetes, body mass index, height, alcohol intake, physical activity, and level of education
Evidence source PMID	09552903
Author	Dimitris
Reviewed	Kalliopi, Dimitris

2.97. Smoking → Ischemic stroke

Risk Association	
Risk Source:	Smoking
Risk Target:	Ischemic stroke
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Dimitris
Reviewed	Kalliopi, Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	Smoking status = Current
Ratio Type:	Relative risk
Ratio Value:	1.5
Confidence Interval:	1.4 – 1.6
Adjusted for:	-
Evidence source PMID	2496858
Author	Dimitris

Reviewed	Kalliopi, Dimitris

Risk Evidence ID2	
RiskID:	2
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:	-
Evidence source PMID	2496858
Author	Dimitris
Reviewed	Kalliopi, Dimitris

2.98. Smoking → Peripheral Arterial Disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Peripheral arterial disease
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Dimitris
Reviewed	Kalliopi, Dimitris

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

Risk Evidence ID2

RiskID:	2
Observable:	Smoking status
Observable Condition:	Smoking status = Ex-smoker
Ratio Type:	Relative risk
Ratio Value:	1.67
Confidence Interval:	1.54 - 1.81
Adjusted for:	-
Evidence source PMID	23922053
Author	Dimitris
Reviewed	Kalliopi, Dimitris

3. Risk Elements

3.1. Acute kidney injury

Risk Element	
Name	Acute Kidney Injury http://purl.bioontology.org/ontology/ICD9CM/584 C0022660
Type	biomedical
Modifiable	yes
Observables	serum creatinine urine output diagnosis
Diagnosis Condition	[(serum creatine +0.3 of baseline OR serum creatine +150-200% of baseline) 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	Stefanos, Ploumis, Kalliopi

3.2. Acute myocardial infarction

Risk Element	
Name	Acute myocardial infarction http://purl.bioontology.org/ontology/ICD9CM/410 C0155626
Type	Biomedical
Modifiable	No
Observables	Acute myocardial infarction
Diagnosis Condition	Acute myocardial infarction = diagnosed
Author	Kalliopi, Dimitris
Reviewed	Kalliopi, Dimitris

3.3. Age

Risk Element	
Name	Age http://purl.bioontology.org/ontology/SNOMEDCT/71395006 C0001783
Type	demographic
Modifiable	no
Observables	age
Diagnosis condition	N/A
Author	Kalliopi
Reviewed	Kalliopi

3.4. Albuminuria

Risk Element	
Name	Albuminuria

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

3.5. Anemia

Risk Element	
Name	Anemia http://purl.bioontology.org/ontology/SNOMEDCT/271737000 C0002871 C1510654
Type	Biomedical
Modifiable	Yes
Observables	Hemoglobin level
Diagnosis condition	Hb ≤ 12.5 g/dL
Author	Gintare
Reviewed	Kalliopi, Dimitris

3.6. Asthma

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

3.7. Atrial fibrillation

Risk Element	
Name	Atrial fibrillation http://purl.bioontology.org/ontology/ICD9CM/427.31 C0004238
Type	biomedical
Modifiable	yes
Observables	Atrial fibrillation
Diagnosis condition	Atrial fibrillation = diagnosed
Author	Neringa
Reviewed	Kalliopi, Dimitris

3.8. Cholelithiasis

Risk Element	
Name	Cholelithiasis http://purl.bioontology.org/ontology/ICD9CM/574 C0008350
Type	Biomedical
Modifiable	yes
Observables	Cholelithiasis
Diagnosis condition	Cholelithiasis = diagnosed
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

3.9. Chronic kidney disease

Risk Element	
Name	Chronic kidney disease http://purl.bioontology.org/ontology/ICD9CM/585 C1561643
Type	Biomedical
Modifiable	Yes
Observables	glomerular filtration rate (eGFR)
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

3.10. Chronic obstructive pulmonary disease (COPD)

Risk Element	
Name	Chronic obstructive pulmonary disease (COPD) http://purl.bioontology.org/ontology/ICD9CM/490-496.99 C0178278
Type	Biomedical
Modifiable	Yes
Observables	Chronic obstructive pulmonary disease diagnosis
Diagnosis condition	Chronic obstructive pulmonary disease diagnosis = diagnosed
Author	Gintare
Reviewed	Kalliopi, Dimitris

3.11. Cancer: Colorectal

Risk Element	
Name	Colorectal Cancer http://purl.bioontology.org/ontology/ICD9CM/153 C0007102
Type	Biomedical, genetic, environmental
Modifiable	no

Observables	Colorectal Cancer
Diagnosis condition	Colorectal Cancer = diagnosed
Author	Kalliopi
Reviewed	kalliopi, Dimitris

3.12. Cancer: Gastric cardiac cancer

Risk Element	
Name	Gastric cardiac Cancer http://purl.bioontology.org/ontology/ICD9CM/151.0 C0153417
Type	Biomedical, genetic, environmental
Modifiable	no
Observables	Colorectal Cancer
Diagnosis condition	Colorectal Cancer = diagnosed
Author	Kalliopi
Reviewed	kalliopi, Dimitris

3.13. Cancer: Pancreatic

Risk Element	
Name	Pancreatic Cancer http://purl.bioontology.org/ontology/ICD9CM/157 C0346647
Type	Biomedical, genetic, environmental
Modifiable	no
Observables	Colorectal Cancer
Diagnosis condition	Colorectal Cancer = diagnosed
Author	Kalliopi
Reviewed	kalliopi, Dimitris

3.14. Death

Risk Element	
Name	Death http://purl.bioontology.org/ontology/ICD9CM/798 C0520806
Type	biomedical
Modifiable	no

Observables	Death
Diagnosis condition	Death = diagnosed
Author	Gintare
Reviewed	Kalliopi, Dimitris

3.15. Death: due to cardiovascular disease

Risk Element	
Name	Death: cardiovascular http://purl.bioontology.org/ontology/SNOMEDCT/95281009 C0085298
Type	biomedical
Modifiable	no
Observables	Death: cardiovascular
Diagnosis condition	Death: cardiovascular = diagnosed
Author	Gintare
Reviewed	Kalliopi, Dimitris

3.16. Depression

Risk Element	
Name	Depression http://purl.bioontology.org/ontology/ICD9CM/311 C0868892
Type	Biomedical
Modifiable	Yes
Observables	Depression Antidepressant medication
	Depression = diagnosed OR Antidepressant medication administration = yes
Author	Gintare
Reviewed	Gintare

3.17. Diabetes

Risk Element	
Name	Diabetes

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

3.18. Diabetes: disease control

Risk Element	
Name	see 2.28—2.30
Type	clinical
Modifiable	yes
Observables	Diabetes AND HbA1c
Diagnosis condition	Diabetes = diagnosed AND HbA1c > 5.7
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

3.19. Diabetic nephropathy

Risk Element	
Name	Diabetic nephropathy http://purl.bioontology.org/ontology/ICD9CM/250.4 C0011881
Type	biomedical
Modifiable	no
Observables	Diabetic nephropathy
Diagnosis condition	Diabetic nephropathy = diagnosed
Author	Zydrune
Reviewed	Kalliopi, Dimitris

3.20. Drugs: β-blockers

Risk Element	
Name	Drugs: β-blockers
Type	Intervention
Modifiable	yes
Observables	drug administration
Diagnosis condition	drug administration = yes
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

3.21. Drugs: Contrast agents

Risk Element	
Name	Contrast agents
Type	intervention
Modifiable	yes
Observables	contrast agents administration
Diagnosis condition	contrast agents administration = yes
Author	Dimitris
Reviewed	Kalliopi, Dimitris

3.22. Drugs: Diuretics

Risk Element

Name	Drugs: diuretics
Type	intervention
Modifiable	yes
Observables	contrast agents administration
Diagnosis condition	contrast agents administration = yes
Author	Dimitris
Reviewed	Kalliopi, Dimitris

3.23. Drugs: Renin-angiotensin system dual blockade (any)

Risk Element	
Name	Drugs: Renin-angiotensin system dual blockade (any)
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, Dimitris

3.24. Drugs: Statins

Risk Element	
Name	Drugs: Statins
Type	intervention
Modifiable	yes
Observables	Drugs: Statins administration
Diagnosis condition	Drugs: Statins administration = yes
Author	Dimitris
Reviewed	Kalliopi, Dimitris

3.25. Dyslipidemia

Risk Element	
Name	Dyslipidemia http://purl.bioontology.org/ontology/ICD9CM/272 C0154251
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 = diagnosed
Author	Gintare
Reviewed	Kalliopi, Dimitris

3.26. Heart Failure

Risk Element	
Name	Heart failure http://purl.bioontology.org/ontology/ICD9CM/428 C0018801
Type	Biomedical
Modifiable	yes
Observables	Heart failure
Diagnosis condition	Heart failure = diagnosed
Author	Gintare, Zydrune
Reviewed	Kalliopi, Dimitris

3.27. Hospitalization

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

3.28. Hyperkalemia

Risk Element	
Name	Hyperkalemia http://purl.bioontology.org/ontology/ICD9CM/276.7 C0020461

Type	biomedical
Modifiable	yes
Observables	Serum potassium
Diagnosis condition	Serum potassium > 5 mEq/l
Author	Neringa
Reviewed	Kalliopi, Dimitris

3.29. Hypertension

Risk Element	
Name	Hypertension http://purl.bioontology.org/ontology/ICD9CM/401-405.99 C0020538
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	Neringa, Kalliopi, Dimitris

3.30. Hyperuricemia

Risk Element	
Name	Hyperuricemia http://purl.bioontology.org/ontology/SNOMEDCT/35885006 C0740394
Type	biomedical
Modifiable	yes
Observables	Uric acid serum concentration
Diagnosis condition	Uric acid serum concentration > 7 mg%
Author	Laurynas
Reviewed	Kalliopi, Dimitris

3.31. Hypoglycaemia

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

3.32. Hypotension

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

3.33. Ischemic heart disease

Risk Element	
Name	Ischemic heart disease http://purl.bioontology.org/ontology/ICD9CM/410-414.99 C0151744
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	Kalliopi, Dimitris

3.34. Ischemic heart disease: Family history of

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

3.35. Ischemic heart disease: Self history

Risk Element	
Name	Ischemic heart disease: self history http://purl.bioontology.org/ontology/ICD9CM/412 C0155668
Type	Biomedical
Modifiable	No
Observables	Old myocardial infarction
Diagnosis Condition	Old myocardial infarction = diagnosed
Author	Kalliopi, Dimitris
Reviewed	Kalliopi, Dimitris

3.36. Ischemic stroke

Risk Element	
Name	Ischemic stroke http://purl.bioontology.org/ontology/ICD9CM/434

	C0028790
Type	biomedical
Modifiable	no
Observables	Ischemic stroke
Diagnosis condition	Ischemic stroke = diagnosed
Author	Dimitris, Stefanos, Gintare
Reviewed	Kalliopi, Dimitris

3.37. Left ventricular hypertrophy

Risk Element	
Name	Left ventricular hypertrophy http://purl.bioontology.org/ontology/SNOMEDCT/55827005 C0149721
Type	biomedical
Modifiable	yes
Observables	Left ventricular hypertrophy
Diagnosis condition	Left ventricular hypertrophy = diagnosed
Author	Neringa
Reviewed	Kalliopi, Dimitris

3.38. Obesity

Risk Element		
Name	Obesity http://purl.bioontology.org/ontology/ICD9CM/278.00 C0028754	
Type	behavioral	
Modifiable	yes	
Observables	BMI, body fat percentage	
Diagnosis Condition	BMI range – kg/m^2	Category
	less than 15	Very severely underweight
	from 15.0 to 16.0	Severely underweight
	from 16.0 to 18.5	Underweight
	from 18.5 to 25	Normal (healthy weight)
	from 25 to 30	Overweight
	from 30 to 35	Obese Class I (Moderately obese)

	from 35 to 40 Obese Class II (Severely obese) over 40 Obese Class III (Very severely obese) OR 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	Kalliopi, Dimitris

3.39. Obesity: Central

Risk Element	
Name	Central obesity http://purl.bioontology.org/ontology/SNOMEDCT/248311001 C0311277
Type	behavioural
Modifiable	yes
Observables	waist circumference waist to hip ratio waist to height ratio
	[Men Normal: < 94 in men decent: 80 to 88 too high: >88 women normal: <80 decent: 94 to 102 too high: >102] OR [Normal: 0.30- 0.49 Abnormal: <0.30 or >0.50] OR [Normal: male: <0.95 female: <0.8

	Abnormal: male: >0.96 female: >0.81]
Author	Kalliopi
Reviewed	Kalliopi, Dimitris

3.40. Obstructive Sleep Apnoea

Risk Element	
Name	Obstructive sleep apnea (OSA) http://purl.bioontology.org/ontology/ICD9CM/327.23 C0520679
Type	Biomedical
Modifiable	Yes
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

3.41. Osteoarthritis

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

3.42. Peripheral arterial disease

Risk Element	
Name	Peripheral arterial disease http://purl.bioontology.org/ontology/ICD9CM/440.2 C3495604
Type	Biomedical, behavioural
Modifiable	yes
Observables	ankle-branchial index
Author	Dimitris, Kalliopi
Reviewed	Dimitris, Kalliopi

3.43. Peripheral vascular disease

Risk Element	
Name	Peripheral vascular disease http://purl.bioontology.org/ontology/ICD10CM/I73.9 C0085096
Type	Biomedical, behavioural
Modifiable	yes
Observables	
Author	Dimitris, Kalliopi
Reviewed	Dimitris, Kalliopi

3.44. Physical activity

Risk Element	
Name	Physical activity http://purl.bioontology.org/ontology/SNOMEDCT/61686008 C0015259
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, Dimitris
Reviewed	Kalliopi, Dimitris

3.45. Smoking

Risk Element	
Name	Smoking http://purl.bioontology.org/ontology/SNOMEDCT/365981007 C0453996
Type	behavioral
Modifiable	yes
Observables	smoking status
Diagnosis condition	smoking status = ex-smoker OR smoking status = current OR smoking status = never
Author	Dimitris
Reviewed	Kalliopi, Dimitris

4. Observables

4.1. Acute kidney disease diagnosis

Observable	
Name	Acute kidney disease diagnosis
Type	personal
Data type	text
Unit	
Values/range	diagnosed mild moderate severe not diagnosed

4.2. Acute myocardial infarction diagnosis

Observable	
Name	Acute myocardial infarction diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.3. Age

Observable	
Name	Age
Type	personal
Data type	integer
Unit	years, months, days
Values/range	

4.4. AHI (Apnoea– hypopnoea index)

Observable	
Name	Apnoea– hypopnoea index (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

4.5. Atrial fibrillation diagnosis

Observable	
Name	Atrial fibrillation diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed

	not diagnosed

4.6. β-blockers administration

Observable	
Name	β-blockers administration
Type	clinical
Data type	text
Unit	
Values/range	yes no

4.7. Blood Glucose: 2h glucose after oral glucose tolerance test

Observable	
Name	2h glucose after oral glucose tolerance test
Type	clinical
Data type	integer
Unit	mg/dl
Values/range	Normal: <140 Prediabetes: 140-199 Diabetes: ≥ 200

4.8. Blood Glucose: fasting

Observable	
Name	Plasma glucose
Type	clinical
Data type	integer
Unit	mmol/l
Values/range	Normal: Fasting plasma glucose 3.3 – 6.1 mmol/l Abnormal: Fasting plasma glucose ≥7.0mmol/l

4.9. Blood pressure

Observable	
Name	Blood pressure (BP)
Type	clinical

Data type	real
Unit	mmHg
Values/range	Normal values: systolic pressure ≤140 mmHg and/or diastolic pressure ≤90 mmHg high normal BP: SBP 130-139 mmHg and/or DBP 85-89 mmHg. normal BP: SBP 120-129 mmHg and/or DBP 80-84 mmHg; Optimal: SBP<120 mmHg and DBP<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

4.10. BMI (Body Mass Index)

Observable		
Name	BMI	
Type	personal	
Data type	integer	
Unit	kg/m^2	
Values/range	BMI range – kg/m^2	Category
	less than 15	Very severely underweight
	from 15.0 to 16.0	Severely underweight
	from 16.0 to 18.5	Underweight
	from 18.5 to 25	Normal (healthy weight)
	from 25 to 30	Overweight
	from 30 to 35	Obese Class I (Moderately obese)
	from 35 to 40	Obese Class II (Severely obese)
	over 40	Obese Class III (Very severely obese)

4.11. Body Fat percentage

Observable	
Name	body fat percentage
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%+

4.12. Chronic kidney disease diagnosis

Observable	
Name	Chronic kidney disease diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed stage 1 stage 2 stage 3A stage 3B stage 4 stage 5 not diagnosed

4.13. Chronic obstructive pulmonary disease diagnosis

Observable	
Name	Chronic obstructive pulmonary disease diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.14. Contrast agents: coronary angiography administration

Observable	
Name	Contrast agents: coronary angiography administration

Type	clinical
Data type	text
Unit	
Values/range	yes no

4.15. Depression diagnosis

Observable	
Name	Depression diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.16. Diabetes diagnosis

Observable	
Name	Diabetes diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.17. Diuretics administration

Observable	
Name	Diuretics administration
Type	clinical
Data type	text
Unit	
Values/range	yes no

4.18. eGFR

Observable	
Name	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

4.19. Fasting Plasma Glucose Levels

Observable	
Name	Fasting Plasma Glucose levels
Type	clinical, personal
Data type	integer
Unit	mg/dl
Values/range	Normal: <100 Prediabetes: 100 to 126 Diabetes: ≥ 126
Author	Kalliopi
Reviewed	

4.20. HbA1c

Observable	
Name	HbA1c
Type	clinical
Data type	real
Unit	%
Values/range	Normal: <5.7 Prediabetes: 5.7 to 6.4 Diabetes: ≥6.5

4.21. Haemoglobin (Hb)

Observable	
Name	Haemoglobin (Hb)
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

4.22. HDL-C (High-density lipoprotein cholesterol)

Observable	
Name	HDL-C (High-density lipoprotein cholesterol)
Type	Clinical
Data type	Real
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

4.23. Heart failure diagnosis

Observable	
Name	Heart failure diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.24. Hypertension Diagnosis

Observable	
Name	Hypertension diagnosis

Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.25. Ischemic heart disease diagnosis

Observable	
Name	Ischemic heart disease diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.26. Ischemic heart disease family history

Observable	
Name	Ischemic heart disease family history
Type	clinical
Data type	text
Unit	
Values/range	yes maternal paternal maternal & paternal no

4.27. Ischemic heart disease self history

Observable	
Name	Ischemic heart disease self history
Type	clinical
Data type	text
Unit	
Values/range	yes no

4.28. Ischemic stroke diagnosis

Observable	
Name	Stroke diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.29. LDL-C (Low-density lipoprotein cholesterol)

Observable	
Name	LDL-C (Low-density lipoprotein cholesterol)
Type	Clinical
Data type	Real
Unit	mmol/L or mg/dL
Values/range	Normal <3 mmol/L (less than ~115 mg/dL) for subjects at low or moderate risk; <2.5 mmol/L (less than ~100 mg/dL) for subjects at high risk Abnormal >3 mmol/L (more than ~115 mg/dL) for subjects at low or moderate risk ; >2.5 mmol/L (more than ~100 mg/dL) for subjects at high risk

4.30. Left ventricular hypertrophy diagnosis

Observable	
Name	Left ventricular hypertrophy diagnosis
Type	Clinical
Data type	text
Unit	
Values/range	diagnosed not diagnosed

4.31. Non-HDL-C

Observable	
Name	Non-HDL-C cholesterol serum concentration
Type	Clinical

Data type	Real
Unit	mmol/L or mg/dL
Values/range	

4.32. Obstructive sleep apnea diagnosis

Observable	
Name	Obstructive sleep apnea diagnosis
Type	clinical
Data type	text
Unit	
Values/range	diagnosed mild moderate severe not diagnosed

4.33. Physical activity

Observable	
Name	physical exercise
Type	personal
Data type	text
Unit	
Values/range	no moderate high

4.34. Renin-angiotensin system dual blockade administration

Observable	
Name	Renin-angiotensin system dual blockade administration
Type	clinical
Data type	text
Unit	
Values/range	yes no

4.35. Serum creatinine level

Observable	
Name	serum creatinine level
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

4.36. Serum potassium

Observable	
Name	Serum potassium
Type	clinical
Data type	real
Unit	mEq/L
Values/range	Normal: 3.5-5.3 mEq/L Moderate 5.0 < Serum Potassium < 6.0 mEq/liter (5.0-6.0 mmol/L) High: serum potassium value > 6.0 mEq/liter (>6.0 mmol/L).

4.37. Sex

Observable	
Name	Sex
Type	personal
Data type	text
Unit	
Values/range	female male

4.38. Smoking intensity

Risk Element	
Name	Smoking intensity

Type	Personal
Data type	text
Unit	
Values/range	heavy: Cigarettes per day > 20 moderate: 1 < cigarettes per day < 20 occasional: cigarettes per day < 1]

4.39. Smoking status

Risk Element	
Name	Smoking status
Type	personal
Data type	text
Units	
Diagnosis condition	ex-smoker current never

4.40. Statin administration

Observable	
Name	Statin administration
Type	clinical
Data type	text
Unit	
Values/range	yes Atorvastatin Simvastatin Rosuvastatin Pravastatin Lovastatin no

4.41. Time after myocardial infarction event

Observable	
Name	Time after acute myocardial infarction event
Type	clinical
Data type	integer

Unit	days
Values/range	diagnosed not diagnosed

4.42. Total cholesterol

Observable	
Name	Total cholesterol (TC)
Type	Clinically measured
Data type	Real
Unit	mmol/L or mg/dL
Values/range	Normal: <5 mmol/L (less than ~190 mg/dL) Abnronal: >5 mmol/L (more than ~190 mg/dL)

4.43. Triglycerides (TG)

Observable	
Name	Triglycerides serum concentration (TG)
Type	Clinically measured
Data type	Real
Unit	mmol/L or mg/dL
Values/range	Normal: <1.8 mmol/L (less than~70 mg/dL) Abnormal: >1.8 mmol/L (more than~70 mg/dL)

4.44. Uric acid serum concentration

Observable	
Name	Uric acid serum concentration
Type	clinical
Data type	real
Unit	mg%
Values/range	Normal: 2.5 – 6.8 mg% Abnormal: >6.8mg%

4.45. Waist circumference

Observable	
Name	waist circumference

Type	personal
Data type	integer
Unit	cm
Values/range	Men Normal: < 94 in men decent: 80 to 88 too high: >88 women normal: <80 decent: 94 to 102 too high: >102

4.46. Waist to height ratio

Observable	
Name	waist to height ratio
Type	personal
Data type	real
Unit	
Values/range	Normal: 0.30- 0.49 Abnormal: <0.30 or >0.50

4.47. Waist to hip ratio

Observable	
Name	waist to hip ratio
Type	personal
Data type	real
Unit	
Values/range	Normal: male: <0.95 female: <0.8 Abnormal: male: >0.96 female: >0.81

5. Evidence Sources

5.1. 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

5.2. 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	1-2

5.3. 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

5.4. 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	

5.5. 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	1-2

5.6. 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	
OCEBM Level	

5.7. 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

5.8. 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

5.9. 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	

5.10. 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	1-2

5.11. 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

5.12. 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

5.13. 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	

5.14. 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	

5.15. 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	1-2

5.16. 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

5.17. 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

5.18. 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

5.19. 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

5.20. PMID = 16738019

Evidence source PMID	16738019
Evidence source:	Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, McAlister F, Garg AX. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol. 2006 Jul;17(7):2034-47.
Evidence source type:	systematic review
OCEBM Level	1

5.21. 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	1-2

5.22. 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

5.23. 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

5.24. 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

5.25. 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	

5.26. PMID = 1866765

Evidence source PMID	1866765
Evidence source	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	longitudinal study
OCEBM Level	1-2

5.27. 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

5.28. 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

5.29. 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

5.30. 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

5.31. 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

5.32. 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

5.33. 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

5.34. 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

5.35. 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

5.36. 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

5.37. 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

5.38. 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

5.39. 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	2-3

5.40. 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	1-2

5.41. 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

5.42. 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

5.43. 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	

5.44. 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

5.45. 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

5.46. 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

5.47. 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

5.48. 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

5.49. 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

5.50. 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

5.51. 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	1

5.52. 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;6(1):37-43.
Evidence source type:	systematic review and meta-analysis
OCEBM Level	1

5.53. 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

5.54. 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

5.55. 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

5.56. 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

5.57. 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

5.58. PMID = 24360912

Evidence source PMID	24360912
Evidence source	Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014 Apr;14(2):122-30.
Evidence source type	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

5.61. PMID = 24913219

Evidence source PMID	24913219
Evidence source	Heiwe S, Jacobson SH. Exercise Training in Adults With CKD:A Systematic Review and Meta-analysis. Am J Kidney Dis. 2014Jun6.pii:S0272-6386(14)00735-5.doi: 10.1053/j.ajkd.2014.03.020
Evidence source type	Systematic Review and Meta-analysis
OCEBM Level	1

5.62. PMID = 2496858

Evidence source PMID	2496858
Evidence source	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