FP7-ICT-611140 CARRE

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

D.2.2. Functional Requirements & CARRE Information Model

DUTH, VULSK, OU

June 2014

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Disclaimer

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

Document Control Page

Project

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

Deliverable

Deliverable No.:	D.2.2
Deliverable Title:	Functional Requirements & CARRE information model
Responsible Partner:	DUTH – Eleni Kaldoudi
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Input from:	All partners
Peer Reviewers:	E. Liu (BED), D. Stundys (VULSK), J. Piwinski (PIAP), A. Third (OU)
Task:	T.2.2. Functional Requirements & CARRE information model
Task duration:	5 months: 1 Feb 2014 to 30 Jun 2014
Work Package:	WP2: Domain analysis, requirements and design
Work Package Leader:	DUTH – Eleni Kaldoudi
Due Date:	30 June 2014
Actual Delivery Date:	9 July 2014
Dissemination Level:	PU
Nature:	R & Web Demonstrator
Files and format:	Deliverable report: 1 pdf file Software: CARRE Risk Model Semantic Data Entry System http://carre.kmi.open.ac.uk
Version:	03
Status:	☐ Draft ☒ Consortium reviewed ☒ WP leader accepted ☒ Coordinator accepted ☐ EC accepted

Document Revision History

Version	Date	Modifications	Contributors
v01.1	07 May 2014	new content – outline	Eleni Semertzidou Eleni Kaldoudi
v01.2	10 June	Introduction Functional units Comorbidities conceptual model	Eleni Kaldoudi Eleni Semertzidou input from Technical meeting in London 6-7 May 2014
v02	24 June	editing, figures Appendices	Eleni Kaldoudi Koula Zigeridou all authors
v03	09 July	revised version based on reviews	Eleni Kaldoudi

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Executive Summary

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

About CARRE

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

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

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

Terms and Definitions

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

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

1. Introduction

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

1.1. Functional Requirements and Conceptual Modelling

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

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

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

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

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

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

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

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

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

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

1.2. Methodology

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

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

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

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

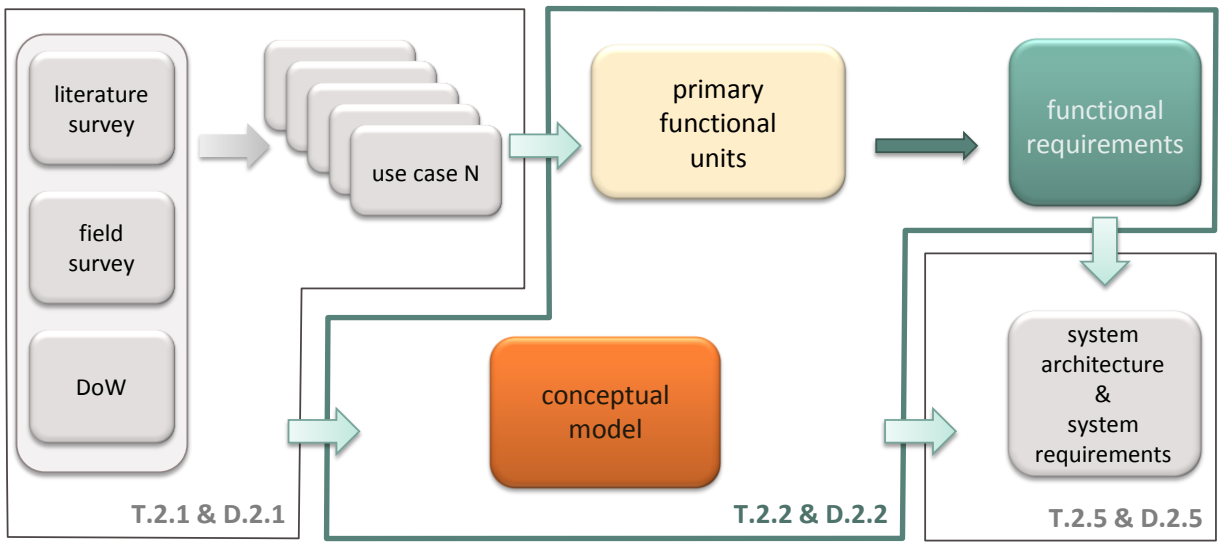

Figure 1. Process for deriving CARRE functional requirements and conceptual model.

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

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

2. Prerequisites

2.1. CARRE Concept

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

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

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

CARRE research aims to create technology in order to:

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

– calculate informed estimations for disease progression and transition,

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

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

2.2. CARRE Objectives

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

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

The project **objectives** include:

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

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

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

Major **expected technological breakthroughs** include:

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

2.3. CARRE Predefined Framework

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

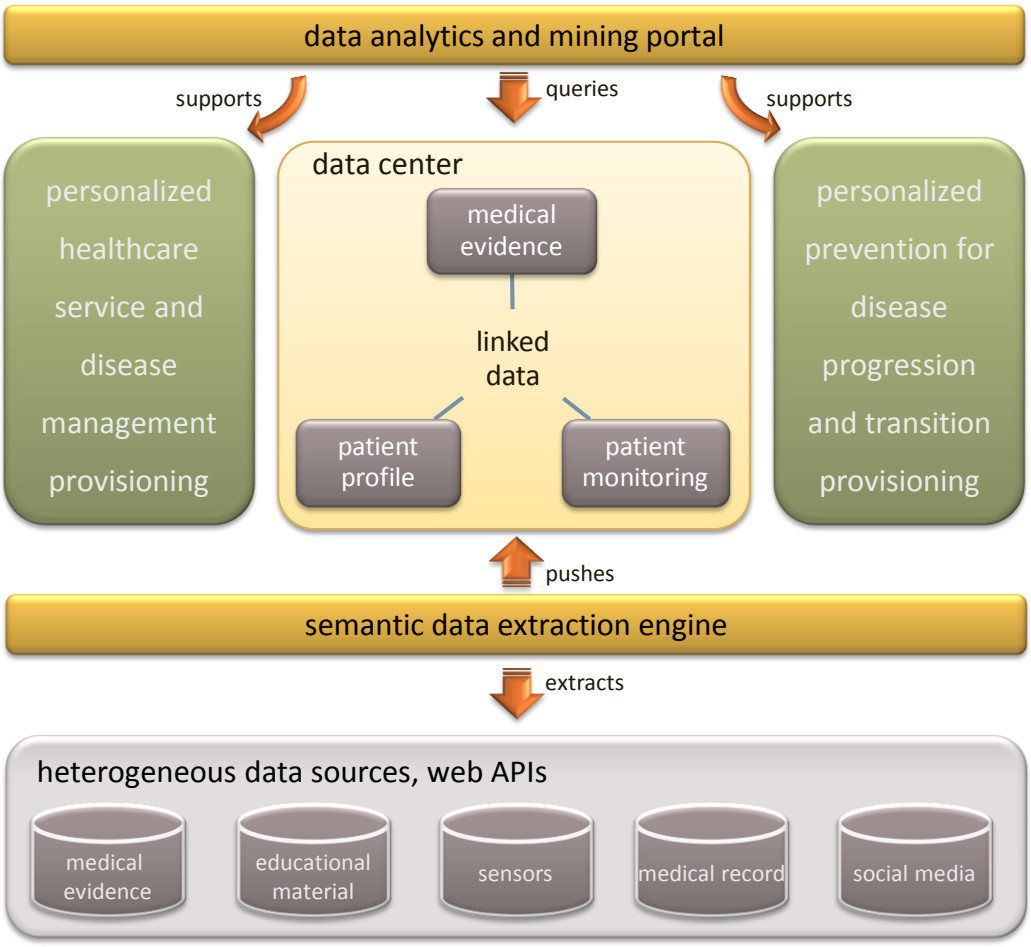

Figure 2. Overview of CARRE service environment as described in the DoW.

The overall environment includes six major components:

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

3. Primary Functional Units

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

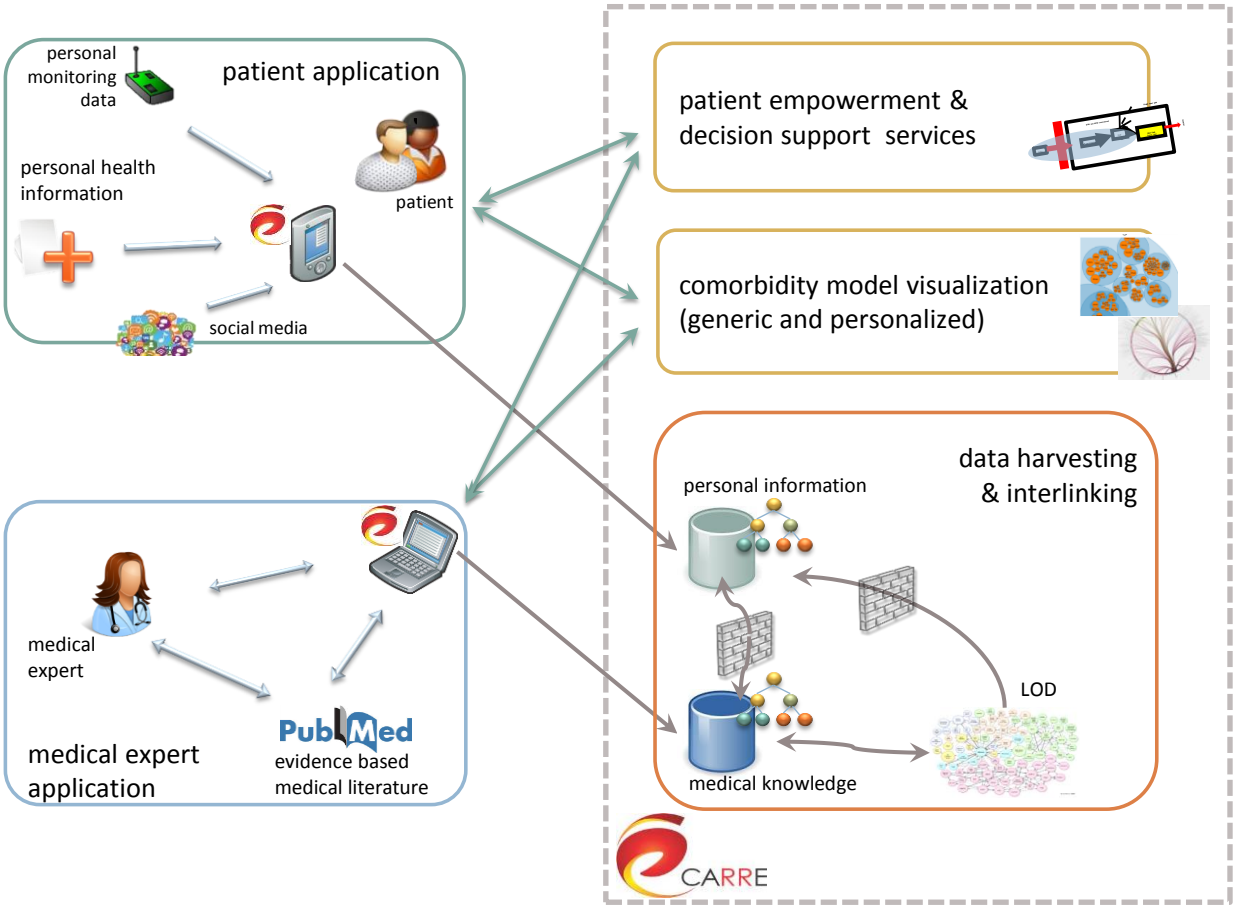

Figure 3. CARRE primary functional units.

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

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

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

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

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

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

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

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

4. Conceptual Model of Comorbidities

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

4.1. Core Concepts and Concepts Relationships

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

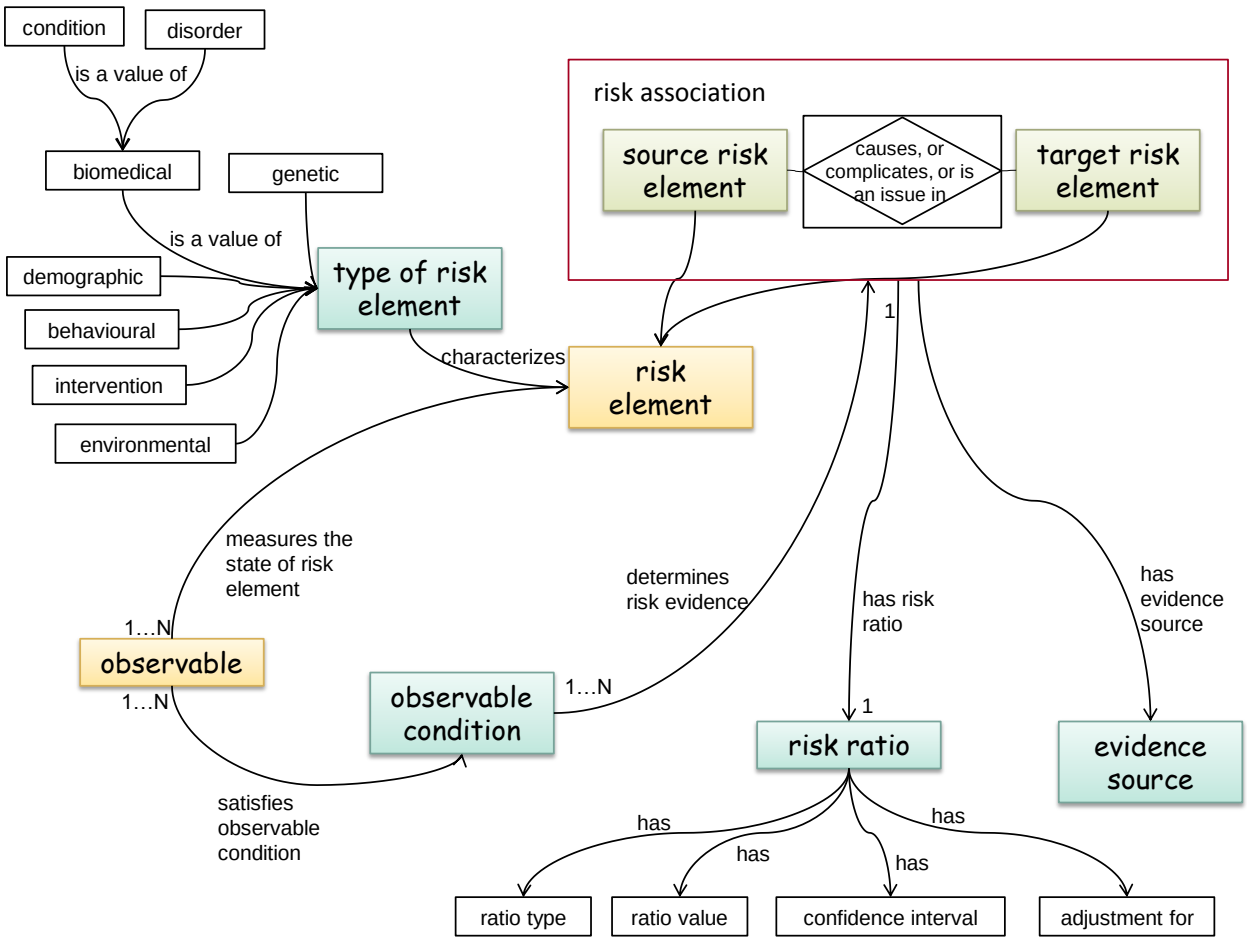

Figure 4. CARRE basic concepts and their relationships.

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

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

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

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

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

4.2. Concept Attributes Tables

The basic concepts in modelling comorbidity are:

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

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

Table 1. Risk Association (RA) Attributes

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

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

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

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

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

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

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

4.3. Class Diagram

An overview of a class diagram is given in

Figure 5.

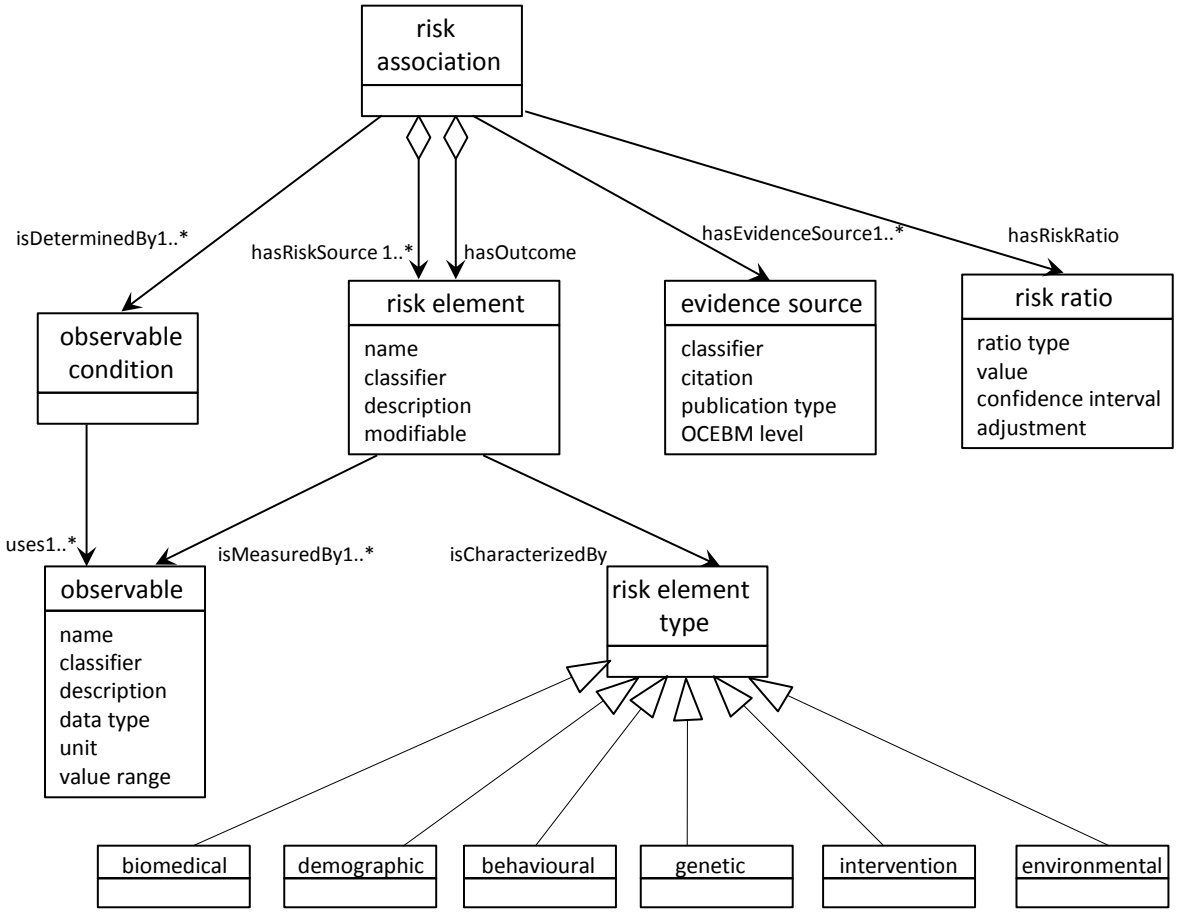

Figure 5. Risk factor class diagram.

4.4. Medical Controlled Vocabularies

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

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

Table 6. Related medical controlled vocabularies and ontologies

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

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

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

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

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

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

5. Functional Requirements

The system shall have the functional components:

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

5.1. Functional Requirements of System Functional Units

5.1.1. Patient Application

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

5.1.2. Medical Expert Application

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

5.1.3. Data Harvesting and Interlinking

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

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

5.1.4. Comorbidities model visualization

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

5.1.5. Patient Empowerment and Decision Support Services

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

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

5.2. Consolidated Functional Requirements

Table 13. Consolidated functional requirements

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

5.3. CARRE Security Requirements

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

Annex 1
CARRE Risk Model Semantic Data Entry System

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

We have developed a web-based system for clinicians to use to enter this data. 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.

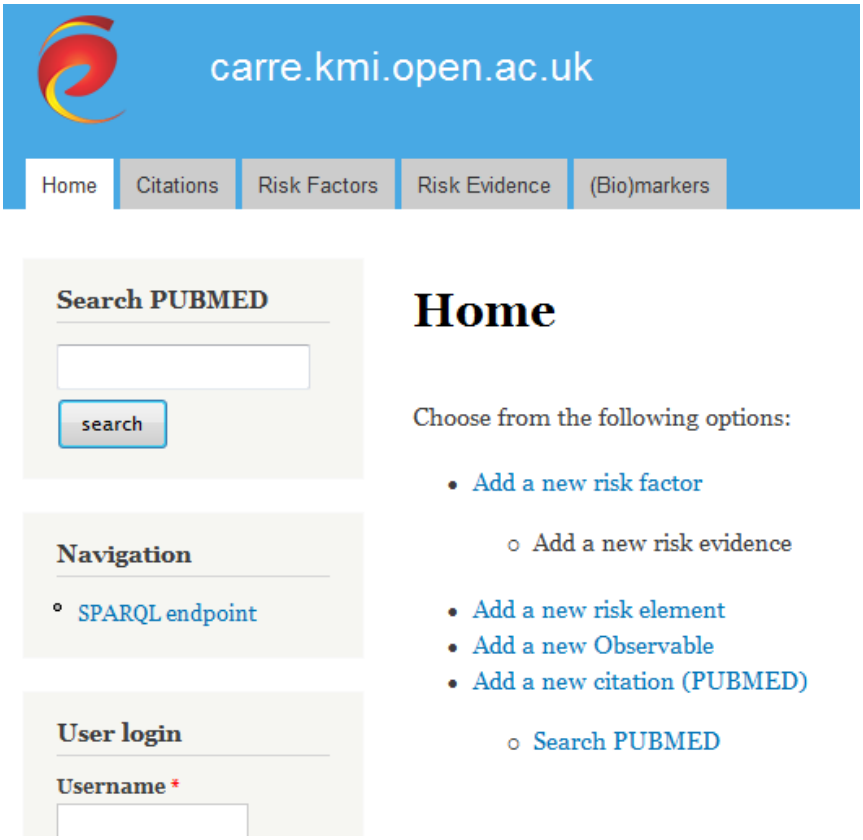

Figure 6. Home page of Drupal-based semantic data entry system.

[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

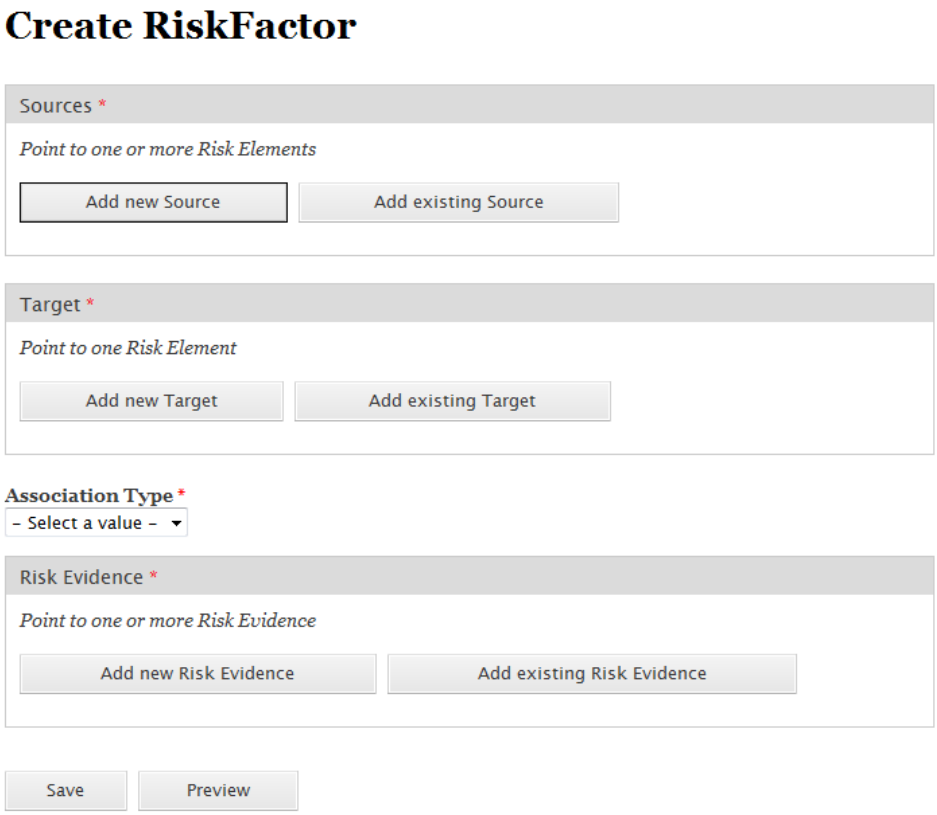

Figure 7. Create a new Risk Association

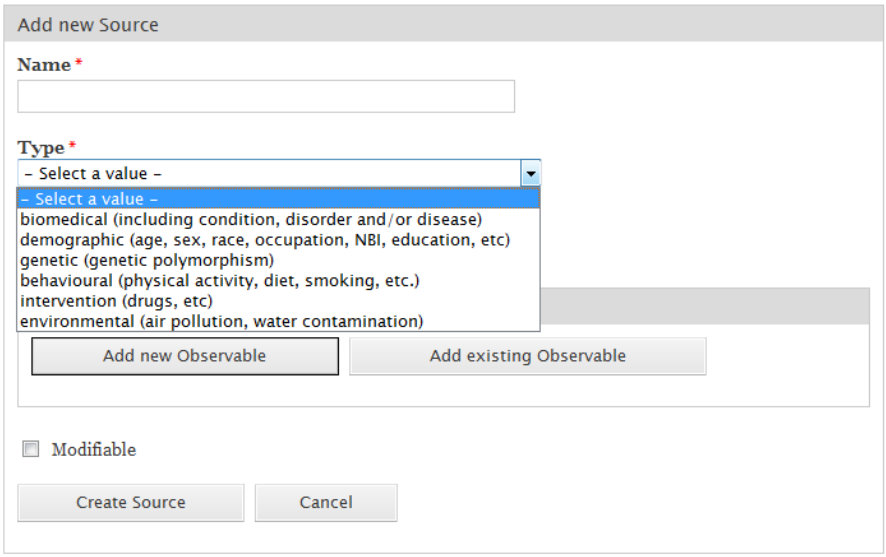

Figure 8. Create a new source Risk Element

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.

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 109 different risk factors with their respective risk associations (total of 291). The involved risk elements attributes tables are presented in Section 3. Finally, Section 4 presents the attributes tables for the sources of evidence mentioned in risk association descriptions.

2. Risk Associations

2.1. Acute myocardial infarction – Atrial Fibrillation

Risk Association	
Risk Source:	Acute myocardial infarction
Risk Target:	Atrial fibrilllation
Association Type:	complicates
Risk Evidence ID:	REID1 – REID5
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Killip class IV
Observable Condition:	individuals in cardiogenic shock or hypotension (systolic blood pressure < 90 mmHg), and evidence of peripheral vasoconstriction (oliguria, cyanosis or sweating)
Ratio Type:	Odds ratio
Ratio Value:	1.58
Confidence Interval:	1.45-1.73
Adjusted for:	
Evidence source PMID:	19109347 10704162
Author	Neringa

Risk Evidence ID2	
RiskID:	2
Observable:	Killip class III
Observable Condition:	Acute pulmonary edema
Ratio Type:	Odds ratio
Ratio Value:	1.46
Confidence Interval:	1.41 - 1.51
Adjusted for:	-
Evidence source PMID	10704162
Author	Neringa

Risk Evidence ID3	
RiskID:	3
Observable:	Age of 78.6

Observable Condition:	Age (78.6) + 5 years increments
Ratio Type:	Odds ratio
Ratio Value:	1.17
Confidence Interval:	1.16 – 1.18
Adjusted for:	
Evidence source PMID	19109347 10704162
Author	Neringa

Risk Evidence ID4	
RiskID:	4
Observable:	Heart rate
Observable Condition:	Heart rate (90 beats/min) + 10 beats increments
Ratio Type:	Odds ratio
Ratio Value:	1.13
Confidence Interval:	1.16 – 1.18
Adjusted for:	
Evidence source PMID	19109347 10704162
Author	Neringa

Risk Evidence ID5	
RiskID:	5
Observable:	Cerebrovascular disease existence
Observable Condition:	Cerebrovascular disease = diagnosed
Ratio Type:	Odds ratio
Ratio Value:	1.18
Confidence Interval:	1.14 – 1.23
Adjusted for:	
Evidence source PMID	10704162
Author	Neringa

2.2. Acute kidney injury – Chronic Kidney Disease

Risk Association	
Risk Source:	Acute kidney injury
Risk Target:	Chronic kidney disease
Association Type:	Is an issue in

RiskID:	REID1
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	Serum creatinine
Observable Condition:	-
Ratio Type:	HR
Ratio Value:	8.8
Confidence Interval:	3.1 – 25.5
Adjusted for:	-
Evidence source PMID	22113526
Author	Laurynas

2.3. Age – Coronary Heart Disease Incidence

Risk Association	
Risk Source:	Age
Risk Target:	Coronary heart disease incidence
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Age in years 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

Risk Evidence ID2	
RiskID:	2

Observables:	Age in years 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

Risk Evidence ID3	
RiskID:	3
Observables:	Age in years 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

Risk Evidence ID4	
RiskID:	4
Observables:	Age in years 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

2.4. Age – Coronary Heart Disease Death

Risk Association	
Risk Source:	Age
Risk Target:	Coronary heart disease death
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Age in years AND Sex
Observable Condition:	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

Risk Evidence ID2	
RiskID:	2
Observables:	Age in years Sex
Observable Condition:	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

Risk Evidence ID3	
RiskID:	3

Observables:	Age in years Sex
Observable Condition:	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

Risk Evidence ID4	
RiskID:	4
Observables:	Age, sex
Observable Condition:	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

2.5. Age – Peripheral arterial disease

Risk Association	
Risk Source:	Age
Risk Target:	Peripheral arterial disease
Association Type:	causes
RiskID:	REID1
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	age
Observable Condition:	age = every 10 years increase
Ratio Type:	Odds ratio
Ratio Value:	2.9

Confidence Interval:	2.3 – 3.7
Adjusted for:	sex and age
Evidence source PMID	12075249
Author	Kalliopi

2.6. Age – Stroke

Risk Association	
Risk Source:	Age
Risk Target:	Stroke
Association Type:	is an issue in
RiskID:	REID1
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	Age
Observable Condition:	Age per year
Ratio Type:	Hazard ratio
Ratio Value:	1.09
Confidence Interval:	1.09 – 1.10
Adjusted for:	Cardiovascular disease at baseline
Evidence source PMID	19520994
Author	Kalliopi

2.7. Anemia AND Acute Coronary Syndromes (ACS) – Death

Risk Association	
Risk Source:	Anemia AND Acute Coronary Syndromes
Risk Target:	Death
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Hemoglobin (Hb) level AND Acute Coronary Syndrome

	AND Time after Acute Coronary Syndrome
Observable Condition:	Hb<12.5 g/dL AND Acute Coronary Syndromes = diagnosed AND Time after Acute Coronary Syndrome = 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 heart failure, revascularization, treatment with thrombolysis, Killip class on presentation, and renal function
Evidence source PMID	23351816
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Hemoglobin (Hb) level AND Acute Coronary Syndrome AND Time after Acute Coronary Syndrome
Observable Condition:	Hb <12.5 g/dL AND Acute Coronary Syndromes = diagnosed AND Time after Acute Coronary Syndrome = 1 year
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 heart failure, revascularization, treatment with thrombolysis, Killip class on presentation, and renal function
Evidence source PMID	23351816
Author	Gintare

2.8. Atherosclerosis – Heart Failure

Risk Association	
Risk Source:	Atherosclerosis
Risk Target:	Heart failure
Association Type:	is an issue in
RiskID:	REID1 – REID6
Author	Gintare

Risk Evidence ID1

RiskID:	1
Observable:	High-density lipoprotein cholesterol (HDL-C)
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

Risk Evidence ID2	
RiskID:	2
Observable:	High-density lipoprotein cholesterol (HDL-C)
Observable Condition:	50 ≤ HDL-C ≤ 64 mg/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

Risk Evidence ID3	
RiskID:	3
Observable:	non–HDL-C (HDL-C subtracted from total cholesterol)
Observable Condition:	160 ≤ non–HDL-C ≤ 189 mg/dL
Ratio Type:	Hazard ratio (Long-Term Follow-Up)
Ratio Value:	1.04
Confidence Interval:	0.85 – 1.26
Adjusted for:	Age, sex, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, and smoking
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 PMID	19933936
Evidence source type:	Cohort study
Author	Gintare

Risk Evidence ID4	
RiskID:	4
Observable:	High-density lipoprotein cholesterol (HDL-C) 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

Risk Evidence ID5	
RiskID:	5
Observable:	High-density lipoprotein cholesterol (HDL-C)
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

Risk Evidence ID6	
RiskID:	6
Observable:	non–HDL-C (HDL-C subtracted from total cholesterol)
Observable Condition:	non–HDL-C ≥ 190 mg/dL
Ratio Type:	Hazard ratio
Ratio Value:	1.29
Confidence Interval:	1.08 – 1.55
Adjusted for:	Age, sex, body mass index, systolic blood pressure, hypertension treatment, diabetes mellitus, and smoking
Evidence source PMID	19933936
Author	Gintare

2.9. CKD – Death

Risk Association	
Risk Source:	CKD
Risk Target:	Death
Association Type:	causes
RiskID:	REID1 – REID4
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	eGFR
Observable Condition:	stage 2: $45 \leq eGFR \leq 59$
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 coronary 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

Risk Evidence ID2	
RiskID:	2
Observable:	eGFR
Observable Condition:	stage 3: $30 \leq eGFR \leq 44$
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 coronary 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

Risk Evidence ID3

RiskID:	3
Observable:	eGFR
Observable Condition:	stage 4: 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 coronary 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

Risk Evidence ID4	
RiskID:	4
Observable:	eGFR
Observable Condition:	eGFR < 15
Ratio Type:	HR
Ratio Value:	5.9
Confidence Interval:	5.4 – 6.5
Adjusted for:	age, sex, income, education, use or no use of dialysis, presence or absence of prior coronary 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

2.10. CKD – Death: all cause

Risk Association	
Risk Source:	CKD
Risk Target:	All cause mortality
Association Type:	Is an issue in
RiskID:	REID1
Author	Laurynas

Risk Evidence ID1

RiskID:	1
Observable:	eGFR, CrCl
Observable Condition:	CrCl or GFR 60 ml/min (with or without standardization to body surface area) or when SCr was >120 mkmol/L when data from estimating equations were unavailable
Ratio Type:	RR
Ratio Value:	1.77
Confidence Interval:	1.33 – 2.34
Adjusted for:	-
Evidence source PMID	16738019
Author	Laurynas

2.11. CKD – Death from Cardiovascular Disease

Risk Association	
Risk Source:	CKD
Risk Target:	Cardiovascular mortality
Association Type:	Is an issue in
RiskID:	REID1
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	eGFR, CrCl
Observable Condition:	CrCl or GFR 60 ml/min (with or without standardization to body surface area) or when SCr was >120 mkmol/L when data from estimating equations were unavailable
Ratio Type:	RR
Ratio Value:	2.47
Confidence Interval:	1.42 – 4.30
Adjusted for:	-
Evidence source PMID	16738019
Author	Laurynas

2.12. CKD – Cardiovascular events

Risk Association	
Risk Source:	CKD
Risk Target:	Cardiovascular events

Association Type:	causes
RiskID:	REID1 – REID4
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	eGFR
Observable Condition:	stage 2: 45 ≤ eGFR ≤ 59
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 coronary 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

Risk Evidence ID2	
RiskID:	2
Observable:	eGFR
Observable Condition:	30 ≤ eGFR ≤ 44
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 coronary 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

Risk Evidence ID3	
RiskID:	3
Observable:	eGFR
Observable Condition:	stage 4: 15 ≤ eGFR ≤ 29
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 coronary 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

Risk Evidence ID4	
RiskID:	4
Observable:	eGFR
Observable Condition:	stage 5: eGFR < 15
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 coronary 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

2.13. CKD – Hospitalization

Risk Association	
Risk Source:	CKD
Risk Target:	Hospitalization
Association Type:	causes
RiskID:	REID1 – REID4
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	eGFR
Observable Condition:	stage 2: $45 \leq eGFR \leq 59$
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 coronary 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

Risk Evidence ID2	
RiskID:	2
Observable:	eGFR
Observable Condition:	stage 3: $30 \leq eGFR \leq 44$
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 coronary 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

Risk Evidence ID3	
RiskID:	3
Observable:	eGFR
Observable Condition:	stage 4: $15 \leq eGFR \leq 29$
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 coronary 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

Risk Evidence ID4	
RiskID:	4
Observable:	eGFR
Observable Condition:	stage 5: eGFR < 15
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 coronary 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

2.14. CKD – Peripheral Arterial Disease (PAD)

Risk Association	
Risk Source:	CKD
Risk Target:	Peripheral Arterial Disease (PAD)
Association Type:	causes
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Ankle-Branchial index
Observable Condition:	Ankle-Branchial index < 0.9
Ratio Type:	OR
Ratio Value:	2.5
Confidence Interval:	1.2-5.1
Adjusted for:	age, diabetes, hypertension, coronary artery disease, stroke history, and hypercholesterolemia
Evidence source PMID	14732743
Author:	Stefanos

2.15. CKD – Sudden Sensorineural Hearing Loss (SSHL)

Risk Association

Risk Source:	CKD
Risk Target:	Sudden Sensorineural Hearing Loss (SSHL)
Association Type:	Causes
RiskID:	REID1 – REID4
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Hearing test
Observable Condition:	loss of greater than 30 dB in three contiguous frequencies in less than 3 days
Ratio Type:	HR
Ratio Value:	1.45
Confidence Interval:	1.194 – 1.787
Adjusted for:	Age, gender, comorbidities (Stroke, Diabetes, Hypertension, Gout, Hyperlipidemia)
Evidence source PMID	22927011
Author:	Stefanos
Reviewed:	

Risk Evidence ID2	
RiskID:	2
Observable:	Hearing test, age
Observable Condition:	Loss of greater than 30 dB in three contiguous frequencies in less than 3 days AND 35 ≤ age ≤ 49
Ratio Type:	HR
Ratio Value:	2.01
Confidence Interval:	1.328 – 3.033
Adjusted for:	Gender, comorbidities (Stroke, Diabetes, Hypertension, Gout, Hyperlipidemia)
Evidence source PMID	22927011
Author:	Stefanos

Risk Evidence ID3	
RiskID:	3
Observable:	Hearing test, age
Observable Condition:	Loss of greater than 30 dB in three contiguous frequencies in less than 3 days AND 50 ≤ age ≤ 64
Ratio Type:	HR
Ratio Value:	3.178

Confidence Interval:	2.139 – 4.721
Adjusted for:	Gender, comorbidities (Stroke, Diabetes, Hypertension, Gout, Hyperlipidemia)
Evidence source PMID	22927011
Author:	Stefanos

Risk Evidence ID4	
RiskID:	4
Observable:	Hearing test, age
Observable Condition:	Loss of greater than 30 dB in three contiguous frequencies in less than 3 days AND age ≥ 65
Ratio Type:	HR
Ratio Value:	2.285
Confidence Interval:	1.312 – 3.454
Adjusted for:	Gender, comorbidities (Stroke, Diabetes, Hypertension, Gout, Hyperlipidemia)
Evidence source PMID	22927011
Author:	Stefanos

2.16. CKD during Myocardial Infarction – Death (survival 1 month after MI)

Risk Association	
Risk Source:	Renal function during myocardial infarction
Risk Target:	Death
Association Type:	Affects
RiskID:	REID1 – REID4
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observables:	Creatinine /creatinine clearance
Observable Condition:	From 1.5 to 2.4 mg/dL (132 to 212 µmol/L) / 33–55 mL/min (0.55–0.92 mL/sec)
Ratio Type:	HR
Ratio Value:	1.68
Confidence Interval:	1.63–1.73
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic

	reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Creatinine /creatinine clearance
Observable Condition:	From 1.5 to 2.4 mg/dL (132 to 212 µmol/L) / 33–55 mL/min (0.55–0.92 mL/sec)
Ratio Type:	HR
Ratio Value:	1.61
Confidence Interval:	1.54–1.69
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Creatinine/creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	2.35

Confidence Interval:	2.26–2.45
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID4	
RiskID:	4
Observables:	Creatinine/creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	2.76
Confidence Interval:	2.64–2.89
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

2.17. CKD during Myocardial Infraction – Death (survival 2-3 months after MI)

Risk Association	
Risk Source:	Renal function during myocardial infarction
Risk Target:	Death
Association Type:	Affects
RiskID:	REID1 – REID4
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 1.5 to 2.4 mg/dL (132 to 212 µmol/L) / 33–55 mL/min (0.55–0.92 mL/sec)
Ratio Type:	HR
Ratio Value:	1.24
Confidence Interval:	1.17–1.31
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 1.5 to 2.4 mg/dL (132 to 212 µmol/L) / 33–55 mL/min (0.55–0.92 mL/sec)
Ratio Type:	HR
Ratio Value:	1.11
Confidence Interval:	1.02–1.21

Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Creatinine /creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	1.63
Confidence Interval:	1.50–1.78
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID4

RiskID:	4
Observables:	Creatinine /creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	1.41
Confidence Interval:	1.30–1.54
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

2.18. CKD during Myocardial Infraction – Death (survival 4-6 months after MI)

Risk Association	
Risk Source:	Renal function during myocardial infarction
Risk Target:	Death
Association Type:	Affects
RiskID:	REID1, REID2
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	1.26
Confidence Interval:	1.14–1.40
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or

	urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	1.24
Confidence Interval:	1.13–1.36
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

2.19. CKD during Myocardial Infraction – Death (survival 1 year after MI)

Risk Association	
Risk Source:	Renal function during myocardial infarction
Risk Target:	Death
Association Type:	Affects
RiskID:	REID1 – REID4
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 1.5 to 2.4 mg/dL (132 to 212 µmol/L) / 33–55 mL/min (0.55–0.92 mL/sec)
Ratio Type:	HR
Ratio Value:	1.03
Confidence Interval:	0.98–1.09
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 1.5 to 2.4 mg/dL (132 to 212 µmol/L) / 33–55 mL/min (0.55–0.92 mL/sec)
Ratio Type:	HR
Ratio Value:	1.01
Confidence Interval:	0.94–1.08

Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID3	
RiskID:	3
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	1.05
Confidence Interval:	0.96–1.15
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

Risk Evidence ID4

RiskID:	4
Observables:	Creatinine / creatinine clearance
Observable Condition:	From 2.5 to 3.9 mg/dL (221 to 345 µmol/L) / 10–33 mL/min (0.17–0.54 mL/sec)
Ratio Type:	HR
Ratio Value:	1.07
Confidence Interval:	0.99–1.16
Adjusted for:	Adjusted for: demographic and geographic characteristics (age, sex, race, rural or urban location, and nearest metropolitan area); comorbid conditions (history of diabetes, hypertension, tobacco use, chronic obstructive pulmonary disease, heart failure, stroke, angina, peripheral vascular disease, dementia; previous myocardial infarction, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, and other cardiac surgery; history of peptic ulcer disease, surgical procedure, trauma, bleeding disorder, and allergic reaction; incontinence, terminal illness, and ambulatory status); severity of presentation (ability to respond to verbal commands; heart rate; temperature; mean arterial blood pressure; respiratory rate; height; body mass index; presence of S3 gallop, conduction disorder, clinical heart failure on examination, and cardiomegaly on chest radiography; hematocrit; platelet count; and electrocardiogram findings); and treatment (in-hospital use of aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, intravenous nitroglycerin, heparin, thrombolytic therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery; discharge prescriptions for aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists).
Evidence source PMID	12353942
Author	Gintare

2.20. Cardiovascular disease – Death

Risk Association	
Risk Source:	Cardiovascular disease
Risk Target:	Death
Association Type:	cause
RiskID:	REID1
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Hyperkalemia
Observable Condition:	Serum potassium > 5.0 mEq/L
Ratio Type:	Odds ratio
Ratio Value:	1.56
Confidence Interval:	1.30-1.88
Adjusted for:	-

Evidence source PMID	22342847
Author	Neringa

2.21. Cardiovascular disease – Hyperkalemia

Risk Association	
Risk Source:	Cardiovascular disease
Risk Target:	Hyperkalemia
Association Type:	Issue in
RiskID:	REID1 – REID8
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Advanced chronic kidney disease
Observable Condition:	chronic kidney disease stage 3-5 (patients with estimated glomerular filtration rates (eGFRs) <60 ml/min/1.73m^2 (estimated by the 4-variable Modification of Diet in Renal Disease [MDRD] equation)
Ratio Type:	Odds ratio
Ratio Value:	2.14
Confidence Interval:	2.02-2.28
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID2	
RiskID:	2
Observable:	Diabetes mellitus
Observable Condition:	based on definition on the International Classification of Disease, Ninth Revision
Ratio Type:	Odds ratio
Ratio Value:	1.59
Confidence Interval:	1.47-1.72
Adjusted for:	
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID3	
RiskID:	3

Observable:	Diabetes mellitus Advanced chronic kidney disease
Observable Condition:	based on definition on the International Classification of Disease, Ninth Revision AND chronic kidney disease stage 3-5 (patients with estimated glomerular filtration rates (eGFRs) <60 ml/min/1.73m^2 (estimated by the 4-variable Modification of Diet in Renal Disease [MDRD] equation)
Ratio Type:	Odds ratio
Ratio Value:	1. 36
Confidence Interval:	1.08-1.71
Adjusted for:	
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID4	
RiskID:	4
Observable:	Periferal vascular disease
Observable Condition:	based on definition on the International Classification of Disease, Ninth Revision
Ratio Type:	Odds ratio
Ratio Value:	1.55
Confidence Interval:	1.36-1.77
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID5	
RiskID:	5
Observable:	Periferal vascular disease Advanced chronic kidney disease
Observable Condition:	based on definition on the International Classification of Disease, Ninth Revision AND chronic kidney disease stage 3-5 (patients with estimated glomerular filtration rates (eGFRs) <60 ml/min/1.73m^2 (estimated by the 4-variable Modification of Diet in Renal Disease [MDRD] equation)
Ratio Type:	Odds ratio
Ratio Value:	1.72
Confidence Interval:	1.15-2.58
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID6

RiskID:	6
Observable:	Coronary artery disease
Observable Condition:	based on definition on the International Classification of Disease, Ninth Revision
Ratio Type:	Odds ratio
Ratio Value:	1.32
Confidence Interval:	1.21 -1.43
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID7	
RiskID:	7
Observable:	Potassiun-sparing diuretics
Observable Condition:	Use of potassiun-sparing diuretics
Ratio Type:	Odds ratio
Ratio Value:	1.25
Confidence Interval:	0.98 -1.59
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID8	
RiskID:	8
Observable:	Potassiun-sparing diuretics Advanced chronic kidney disease
Observable Condition:	AND chronic kidney disease stage 3-5 (patients with estimated glomerular filtration rates (eGFRs) <60 ml/min/1.73m^2 (estimated by the 4-variable Modification of Diet in Renal Disease [MDRD] equation)
Ratio Type:	Odds ratio
Ratio Value:	1.72
Confidence Interval:	1.15-2.58
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

2.22. Cardiovascular disease – Peripheral vascular disease

Risk Association

Risk Source:	Cardiovascular disease
Risk Target:	Peripheral vascular disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	History of other cardiovascular disease such as coronary heart disease (CHD) or stroke
Observable Condition:	Yes
Ratio Type:	Odds ratio
Ratio Value:	2.27
Confidence Interval:	1.98–2.59
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare

2.23. Cardiovascular disease AND advanced CKD – Death

Risk Association	
Risk Source:	Cardiovascular disease AND advanced CKD
Risk Target:	death
Association Type:	cause
RiskID:	REID1, REID2
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	hyperkalemia
Observable Condition:	Serum potassium > 5.0 mEq/L
Ratio Type:	Odds ratio
Ratio Value:	1.63
Confidence Interval:	1.04-2.55
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

Risk Evidence ID2	
RiskID:	2
Observable:	Cororary artery disease
Observable Condition:	Cororary artery disease = diagnosed
Ratio Type:	Odds ratio
Ratio Value:	1.66
Confidence Interval:	1.05 -2.63
Adjusted for:	-
Evidence source PMID	22342847
Author	Neringa

2.24. Chronic obstructive pulmonary disease (COPD) – Death: Cardiovascular

Risk Association	
Risk Source:	Chronic obstructive pulmonary disease (COPD)
Risk Target:	Death due to Cardiovascular event
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Spirometry
Observable Condition:	
Ratio Type:	Hazard ratio
Ratio Value:	1.28
Confidence Interval:	1.01–1.57
Adjusted for:	gender, body mass index, 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 coronary artery disease, left main coronary artery disease, age, and triple vessel disease
Evidence source PMID	19368979
Author	Gintare

2.25. Depression – Stroke

Risk Association

Risk Source:	Depression
Risk Target:	Stroke
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Depression scale, depression index
Observable Condition:	
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

2.26. Depression – Coronary heart disease

Risk Association	
Risk Source:	Depression
Risk Target:	Coronary heart disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk evidence ID1	
RiskID:	1
Observable	Fatal CHD, incident MI (fatal and non-fatal, mortality from all causes or from coronary disease, after MI, angiographic coronary disease, unspecified cardiac patients
Observable Condition:	
Ratio Type:	Relative risk
Ratio Value:	Aetiological studies
	1.90
Confidence Interval:	1.49–2.42
Adjusted for:	age, sex, marital status, smoking, alcohol, physical activity, cholesterol, blood pressure, obesity/BMI, diabetes, CHD severity—previous history, number of

	affected vessels, dyspnoea, left ventricular (LV) function (ejection fraction, Killip class, or pulmonary oedema on X-ray)
Evidence source PMID	17082208
Author	Gintare

2.27. Diabetes – Cardiovascular Disease

Risk Association	
Risk Source:	Diabetes
Risk Target:	Cardiovascular disease
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observable	Plasma glucose
Observable Condition:	Fasting plasma glucose ≥7.0mmol/l
Ratio Type:	Hazard ratio
Ratio Value:	2.48
Confidence Interval:	1.84 – 3.34
Adjusted for:	Age and sex,
Evidence source PMID	15562129
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observable	Plasma glucose
Observable Condition:	2–h plasma glucose ≥11.1mmol/l
Ratio Type:	Hazard ratio
Ratio Value:	1.96
Confidence Interval:	1.44-2.66
Evidence source:	Fox CS, Coady S, Sorlie PD, Levy D, Meigs JB, D'Agostino RB, Wilson PW, Savage PJ Trends in cardiovascular complications of diabetes. JAMA 2004 Nov 24;292(20):2495-9.
Evidence source PMID	15562129
Author	Kalliopi

2.28. Diabetes – Coronary heart disease

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

Risk Evidence ID1	
RiskID1:	1
Observables:	diabetes, sex
Observable Condition:	diabetes = diagnose AND sex=female
Ratio Type:	RR
Ratio Value:	2.82
Confidence Interval:	2.35 – 3.38
Adjusted for:	
Evidence source PMID	24859435
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	sex
Observable Condition:	diabetes = 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

2.29. Diabetes – Death (sudden cardiac death)

Risk Association	
Risk Source:	Diabetes
Risk Target:	Sudden cardiac death

Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Diabetes and sex
Observable Condition:	diabetes = diagnosed AND sex =female
Ratio Type:	Relative Risk
Ratio Value:	2.93
Confidence Interval:	2.13 – 4.04
Adjusted for:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare

2.30. Diabetes – Heart failure

Risk Association	
Risk Source:	Diabetes
Risk Target:	Heart failure
Association Type:	issue in
RiskID:	REID1 – REID5
Author	Zydrune

Risk Evidence ID1	
RiskID:	1
Observable:	HbA1c
Observable Condition:	7.0 - < 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	22912709
Author	Zydrune

Risk Evidence ID2	
RiskID:	2

Observable:	HbA1c
Observable Condition:	8.0 - < 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	22912709
Author	Zydrune

Risk Evidence ID3	
RiskID:	3
Observable:	HbA1c
Observable Condition:	9.0 - < 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	22912709
Author	Zydrune

Risk Evidence ID4	
RiskID:	4
Observable:	HbA1c
Observable Condition:	≥ 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	22912709
Author	Zydrune

Risk Evidence ID5	
RiskID:	5
Observable:	HbA1c
Observable Condition:	Increase by 1.0%
Ratio Type:	Pooled relative risk
Ratio Value:	1.11
Confidence Interval:	1.05 - 1.18

Adjusted for:	
Evidence source PMID	22912709
Author	Zydrune

2.31. Diabetes – Peripheral Vascular Disease

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

Risk Evidence ID1	
RiskID:	REID1
Observable:	Fasting glucose or diabetes medication or doctor's diagnosis
Observable Condition:	Fasting glucose >7 mmol/L; diabetes medication: yes/no; doctor's diagnosis: diabetes/no diabetes
Ratio Type:	Odds ratio
Ratio Value:	1.68
Confidence Interval:	1.53–1.84
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare

2.32. Diabetes AND CKD – Sudden Sensorineural Hearing Loss (SSHL)

Risk Association	
Risk Source:	Diabetes mellitus in CKD
Risk Target:	Sudden Sensorineural Hearing Loss (SSHL)
Association Type:	causes
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Hearing test
Observable Condition:	loss of greater than 30 dB in three contiguous frequencies in less than 3 days

Ratio Type:	HR
Ratio Value:	1.31
Confidence Interval:	1.003-1.711
Adjusted for:	Age, gender, comorbitities (Stroke, Hypertension, Gout, Hyperlipidemia)
Evidence source PMID	22927011
Author:	Stefanos

2.33. Diabetic nephropathy – Cardiovascular Disease

Risk Association	
Risk Source:	Diabetic nephropathy
Risk Target:	Cardiovascular disease CVD
Association Type:	issue in
RiskID:	REID1 – REID18
Author	Zydrune

Risk Evidence ID1	
RiskID:	1
Observable:	eGFR (ml/min/1.73 m^2)
Observable Condition:	$60 \leq$ eGFR ≤ 89
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	16310551
Author	Zydrune

Risk Evidence ID2	
RiskID:	2
Observable:	eGFR (ml/min/1.73 m^2)
Observable Condition:	$30 \leq$ eGFR ≤ 69
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

Risk Evidence ID3	
RiskID:	3
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	60≤ eGFR ≤ 89 AND UACR <2.5 mg/mmol AND sex=male
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

Risk Evidence ID4	
RiskID:	4
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	60 ≤ eGFR ≤ 89 AND UACR <3.5 mg/mmol AND sex=female
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

Risk Evidence ID5

RiskID:	5
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	30 ≤ eGFR ≤ 59 AND UACR <2.5 mg/mmol AND sex=male
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

Risk Evidence ID6	
RiskID:	6
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	30 ≤ eGFR ≤ 59 AND UACR <3.5 mg/mmol AND sex=female
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

Risk Evidence ID7	
RiskID:	7
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	eGFR >90 ml/min/1.73 m^2 AND UACR >2.5 mg/mmol AND sex=male

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

Risk Evidence ID8	
RiskID:	8
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	eGFR >90 ml/min/1.73 m^2 AND UACR >3.5 mg/mmol AND sex=female
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

Risk Evidence ID9	
RiskID:	9
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	$60 \leq$ eGFR ≤ 89 AND UACR >2.5 mg/mmol AND sex=male
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

Risk Evidence ID10	
RiskID:	10
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	60 ≤ eGFR ≤ 89 AND UACR >3.5 mg/mmol AND sex=women
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

Risk Evidence ID11	
RiskID:	11
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	30 ≤ eGFR ≤ 59 AND UACR >2.5 mg/mmol AND sex=male
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

Risk Evidence ID12	
RiskID:	12
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex

Observable Condition:	30 ≤ eGFR ≤ 59 AND UACR >3.5 mg/mmol AND sex=female
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

Risk Evidence ID13	
RiskID:	13
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	eGFR >90 AND UACR >25 mg/mmol AND sex=male
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

Risk Evidence ID14	
RiskID:	14
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	eGFR >90 AND UACR >35 mg/mmol AND sex=female
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

Risk Evidence ID15	
RiskID:	15
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	60 ≤ eGFR ≤ 89 AND UACR >25 mg/mmol AND sex=male
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

Risk Evidence ID16	
RiskID:	16
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	60 ≤ eGFR ≤ 89 AND UACR >35 mg/mmol AND sex=female
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

Risk Evidence ID17	
RiskID:	17
Observable:	eGFR

	AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	30 ≤ eGFR ≤ 59 AND UACR >25 mg/mmol AND sex=male
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

Risk Evidence ID18	
RiskID:	18
Observable:	eGFR AND albuminuria (defined as urine albumin to creatinine ratio –UACR) AND sex
Observable Condition:	30 ≤ eGFR ≤ 59 AND UACR >35 mg/mmol AND sex=female
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

2.34. Drugs: Contrast agents – Renal Disease

Risk Association	
Risk Source:	contrast agents
Risk Target:	renal disease
Association Type:	causes
RiskID:	REID1, REID2
Author:	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Contrast agents
Observable Condition:	IV administration
Ratio Type:	RR
Ratio Value:	0.79
Confidence Interval:	0.62 - 1.02
Adjusted for:	contrast medium type, diagnostic criteria for AKI, presence of of diabetes mellitus or renal insufficiency
Evidence source:	McDonald JS, McDonald RJ, Comin J, Williamson EE, Katzberg RW, Murad MH, Kallmes DF. Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. Radiology 2013; 267(1):119-28
Evidence source PMID	23319662
Evidence source type:	systematic review and meta-analysis
Author:	Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Contrast agents
Observable Condition:	IV administration for Coronary Angiography
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

2.35. Dyslipidemia – Coronary heart disease (CHD)

Risk Association	
Risk Source:	Dyslipidemia (hypercholesterolemia)
Risk Target:	Cardiovascular disease (coronary heart disease (CHD))
Association Type:	is an issue in
RiskID:	REID1 – REID6
Author	Gintare

Risk Evidence ID1	
RiskID:	1

Observable:	Total cholesterol (TC)
Observable Condition:	TC ≥ 240 mg/dL
Ratio Type:	Relative risk
Ratio Value:	1.97
Confidence Interval:	1.42-2.73
Adjusted for:	Age, sex, and remaining risk factors (hypertension, diabetes, smoking)
Evidence source PMID	18082090
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Total cholesterol (TC) Age
Observable Condition:	TC ≥ 240 mg/dL AND age = Middle-age and above
Ratio Type:	Relative risk
Ratio Value:	1.28
Confidence Interval:	1.17–1.39
Adjusted for:	
Evidence source PMID	15380802
Author	Gintare

Risk Evidence ID3	
RiskID:	3
Observable:	Total cholesterol (TC) Age
Observable Condition:	TC ≥ 240 mg/dL AND age = 65 and above
Ratio Type:	Relative risk
	1.24
Confidence Interval:	1.11–1.37
Adjusted for:	
Evidence source PMID	15380802
Author	Gintare

Risk Evidence ID4	
RiskID:	4
Observable:	Total cholesterol (TC)

Observable Condition:	TC ≥ 6.7 mmol/L Age = Middle-age and above
Ratio Type:	Relative risk
	1.54
Confidence Interval:	1.27–1.88
Adjusted for:	
Evidence source PMID	15380802
Author	Gintare

Risk Evidence ID5	
RiskID:	5
Observable:	Total cholesterol (TC)
Observable Condition:	TC ≥ 6.7 mmol/L Age = 65 years and above
Ratio Type:	Relative risk
	1.22
Confidence Interval:	1.15–1.28
Adjusted for:	
Evidence source PMID	15380802
Author	Gintare

Risk Evidence ID6	
RiskID:	6
Observable:	Total cholesterol (TC)
Observable Condition:	1.0 mmol/L increase in total cholesterol
Ratio Type:	Relative risk
Ratio Value:	1.04
Confidence Interval:	0.85–1.23
Adjusted for:	
Evidence source PMID	15380802
Author	Gintare

2.36. Dyslipidemia – Peripheral vascular disease

Risk Association	
Risk Source:	Dyslipidemia
Risk Target:	Peripheral vascular disease
Association Type:	is an issue in

RiskID:	REID1 – REID4
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Total cholesterol (TC)
Observable Condition:	>240 mg/dL or >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

Risk Evidence ID2	
RiskID:	2
Observable:	Low-density lipoprotein cholesterol (LDL-C)
Observable Condition:	>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

Risk Evidence ID3	
RiskID:	3
Observable:	High-density lipoprotein cholesterol (HDL-C)
Observable Condition:	Binary (<40 mg/dL) or continuous (per 5 mg/dL increase in HDL)
Ratio Type:	Odds ratio
Ratio Value:	0.92
Confidence Interval:	0.83–1.01
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare

Risk Evidence ID4	
RiskID:	4

Observable:	Triglycerides (TG)
Observable Condition:	>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

2.37. Early referral to nephrologist – Presence of depressive symptoms in ESRD

Risk Association	
Risk Source:	Early referral to nephrologist
Risk Target:	Presence of depressive symptoms in ESRD
Association Type:	Is issue in
RiskID:	REID1
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	Depression scales
Observable Condition:	Not specified
Ratio Type:	HR
Ratio Value:	1.45
Confidence Interval:	1.27-1.65
Adjusted for:	Adjusting for potential publication bias
Evidence source PMID	24183836
Author	Laurynas

2.38. Exercise AND CKD – Arterial stiffness

Risk Association	
Risk Source:	Exercise in CKD
Risk Target:	Arterial stiffness
Association Type:	improves
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Long term exercise training
Observable Condition:	30minutes, 5 times per week
Ratio Type:	OR
Ratio Value:	–11.7
Confidence Interval:	–18.79 to –4.61
Adjusted for:	
Evidence source PMID	20842429
Author:	Stefanos

2.39. Exercise AND CKD – Physical activity

Risk Association	
Risk Source:	Exercise in CKD
Risk Target:	Physical activity
Association Type:	improves
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Long term exercise training
Observable Condition:	30 minutes, 5 times per week
Ratio Type:	OR
Ratio Value:	10.97
Confidence Interval:	4.94 – 17.59
Adjusted for:	
Evidence source PMID	20842429
Author:	Stefanos

2.40. Exercise AND CKD – Quality of Life (QOL)

Risk Association	
Risk Source:	Exercise in CKD
Risk Target:	Quality of Life (QOL)
Association Type:	improves

RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Long term exercise training
Observable Condition:	30minutes, 5 times per week
Ratio Type:	Questionnaires
Ratio Value:	Positive correlation
Confidence Interval:	
Adjusted for:	
Evidence source PMID	20842429
Author:	Stefanos

2.41. Exercise AND CKD – Systolic Blood Pressure

Risk Association	
Risk Source:	Exercise in CKD
Risk Target:	Systolic Blood Pressure
Association Type:	reduces
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Long term exercise training
Observable Condition:	30minutes, 5 times per week for at least 8 weeks
Ratio Type:	OR
Ratio Value:	1.57
Confidence Interval:	0.09 - 3.05
Adjusted for:	
Evidence source PMID	24913219
Author:	Stefanos

2.42. Heart failure – Death

Risk Association

Risk Source:	Heart failure
Risk Target:	Mortality rate
Association Type:	causes
RiskID:	REID1 – REID7
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Hypertension
Observable Condition:	as the only explanation of HF
Ratio Type:	Hazard ratio
Ratio Value:	1.0 (ref.)
Confidence Interval:	
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

Risk Evidence ID2	
RiskID:	2
Observable:	Ischemic heart disease
Observable Condition:	Ischemic heart disease, when LVEF < 30
Ratio Type:	Hazard ratio
Ratio Value:	2.1
Confidence Interval:	1.7-2.7
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

Risk Evidence ID3	
RiskID:	3
Observable:	Ischemic heart disease
Observable Condition:	Ischemic heart disease, when LVEF ≥30%
Ratio Type:	Hazard ratio
Ratio Value:	1.3
Confidence Interval:	1.0-1.5
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

Risk Evidence ID4	
RiskID:	4
Observable:	Ischemic heart disease
Observable Condition:	Ischemic heart disease, when LVEF ≥30%
Ratio Type:	Hazard ratio
Ratio Value:	1.3
Confidence Interval:	1.0-1.5
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

Risk Evidence ID5	
RiskID:	5
Observable:	Valvular heart disease
Observable Condition:	Patients with severe aortic valve stenosis, severe aortic regurgitation, severe organic mitral valve regurgitation on echocardiography, patients operated for mitral or aortic valve disease with signs of left ventricle dysfunction
Ratio Type:	Hazard ratio
Ratio Value:	1.7
Confidence Interval:	1.3-2.2
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

Risk Evidence ID6	
RiskID:	6
Observable:	Dilated cardiomypathy
Observable Condition:	patients with dilatation of the left ventricle when another distinct etiology had not been found
Ratio Type:	Hazard ratio
Ratio Value:	1.7
Confidence Interval:	1.2-2.3
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

Risk Evidence ID7	
RiskID:	7

Observable:	Unknown or mixed etiology
Observable Condition:	All the patients, for whom one single etiology could not be ascertained
Ratio Type:	Hazard ratio
Ratio Value:	1.4
Confidence Interval:	1.1-2.7
Adjusted for:	
Evidence source PMID	20193969
Author	Neringa

2.43. High haemoglobin in CKD – Hypertension

Risk Association	
Risk Source:	High haemoglobin in CKD
Risk Target:	Hypertension
Association Type:	Causes
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Hb
Observable Condition:	> 13 **g/dL.**
Ratio Type:	Relative Risk
Ratio Value:	1.27
Confidence Interval:	1.08 - 1.50
Adjusted for:	
Evidence source PMID	17276778
Author:	Stefanos

2.44. High haemoglobin in CKD – Death

Risk Association	
Risk Source:	High haemoglobin in CKD
Risk Target:	Death
Association Type:	Causes
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Hb
Observable Condition:	> 13 g/dL
Ratio Type:	Relative Risk
Ratio Value:	1.17
Confidence Interval:	1.01- 1.35
Adjusted for:	
Evidence source PMID	17276778
Author:	Stefanos

2.45. High haemoglobin in CKD – Arteriovenous acess thrombosis

Risk Association	
Risk Source:	High haemoglobin in CKD
Risk Target:	Arteriovenous acess thrombosis
Association Type:	Causes
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Hb
Observable Condition:	> 13 g/dL
Ratio Type:	Relative Risk
Ratio Value:	1.34
Confidence Interval:	
Adjusted for:	1.16- 1.54
Evidence source PMID	17276778
Author:	Stefanos

2.46. History of Myocardial Infarction (maternal/paternal) – Cardiovascular disease

Risk Association	
Risk Source:	Maternal and paternal history of Myocardial Infarction
Risk Target:	Cardiovascular disease events (CVD): myocardial infarction (MI), coronary artery bypass grafting *(CABG), p*ercutaneous transluminal coronary angioplasty (PTCA), stroke, cardiovascular death

Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	MI, CABG, PTCA, stroke, cardiovascular death
Observable Condition:	Yes/no
Ratio Type:	Relative risk
Ratio Value:	1.85
Confidence Interval:	1.56–2.19
Adjusted for:	Age, BMI, smoking status, exercise, and alcohol intake
Evidence source PMID	11468199
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	MI, CABG, PTCA, stroke, cardiovascular death
Observable Condition:	Yes/no
Ratio Type:	Relative risk
Ratio Value:	2.05
Confidence Interval:	1.51–2.79
Adjusted for:	Age, BMI, smoking status, exercise, and alcohol intake
Evidence source PMID	11468199
Author	Gintare

2.47. History of Myocardial Infarction (maternal/paternal history) – Myocardial infarction

Risk Association	
Risk Source:	Maternal and paternal history of MI
Risk Target:	Myocardial infarction
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare

Risk Evidence ID1	
RiskID:	1

Observable:	World Health Organization criteria
Observable Condition:	Yes/no 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
Evidence source PMID	11468199
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	World Health Organization criteria
Observable Condition:	Yes/no 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
Evidence source PMID	11468199
Author	Gintare

2.48. History of Myocardial Infraction (maternal/paternal) – Stroke

Risk Association	
Risk Source:	Maternal and paternal history of MI
Risk Target:	Stroke
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Typical neurological deficit (sudden or rapid in onset, lasting >24 hours)
Observable Condition:	Yes
Ratio Type:	Relative risk
Ratio Value:	1.03
Confidence Interval:	0.67–1.60

Adjusted for:	Age, BMI, smoking status, exercise, and alcohol intake
Evidence source PMID	11468199
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Typical neurological deficit (sudden or rapid in onset, lasting >24 hours)
Observable Condition:	Yes
Ratio Type:	Relative risk
Ratio Value:	1.45
Confidence Interval:	0.80–2.62
Adjusted for:	Age, BMI, smoking status, exercise, and alcohol intake
Evidence source PMID	11468199
Author	Gintare

2.49. Hypertension – Death from Cardiovascular Disease

Risk Association	
Risk Source:	Hypertension
Risk Target:	Cardiovascular disease death
Association Type:	Causes
RiskID:	REID1
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure (BP)
Observable Condition:	Systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or taking antihypertensive treatment
Ratio Type:	Hazard ratio
Ratio Value:	2.10
Confidence Interval:	1.83 - 2.41
Adjusted for:	Adjusted for age, gender
Evidence source PMID	24886432
Author	Gintare

2.50. Hypertension – CKD

Risk Association	
Risk Source:	Hypertension
Risk Target:	CKD
Association Type:	Causes
RiskID:	REID1
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	Systolic blood pressure
Observable Condition:	NCEP-ATP III criteria, modified NCEP-ATP III criteria, IDF definition, WHO criteria
Ratio Type:	Odds ratio
Ratio Value:	1.61
Confidence Interval:	1.21 – 2.01
Adjusted for:	Adjusted in the multivariate analyses of the included studies
Evidence source PMID	21852664
Author	Laurynas

2.51. Hyperphosphatemia in CKD – Death (all cause)

Risk Association	
Risk Source:	Hyperphosphatemia in CKD
Risk Target:	All cause mortality
Association Type:	is an issue in
RiskID:	REID1
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	Serum level of phosphorus
Observable Condition:	≥5.5 mg/dL
Ratio Type:	Relative risk
Ratio Value:	1.35
Confidence Interval:	1.16-1.57
Adjusted for:	age, race, time receiving dialysis [or estimated glomerular filtration rate], cardiovascular disease, and diabetes mellitus

Evidence source PMID	21406649
Author	Laurynas

2.52. Hypertension – Diabetes

Risk Association	
Risk Source:	Hypertension
Risk Target:	Diabetes
Association Type:	issue in
RiskID:	REID1
Author	Zydrune

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure (BP)
Observable Condition:	systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg or reported use of a medication for hypertension
Ratio Type:	Relative risk (RR) (after 6 years of FUP)
Ratio Value:	2.43
Confidence Interval:	2.16 - 2.73
Adjusted for:	
Evidence source PMID	10979786
Author	Zydrune

2.53. Hypertension – Heart Failure

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

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure (BP)
Observable Condition:	Systolic BP (SBP) ≥140 mm Hg, diastolic BP (DBP) ≥ 90 mm Hg, or current use

	of antihypertensive medication
Ratio Type:	Hazard ratio
Ratio Value:	1.58
Confidence Interval:	1.26–1.9
Adjusted for:	Multivariable-Adjusted
Evidence source PMID	23271790
Author	Gintare

2.54. Hypertension – Peripheral vascular disease

Risk Association	
Risk Source:	Hypertension
Risk Target:	Peripheral vascular disease
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Blood pressure (BP)
Observable Condition:	≥140/90 mm Hg
Ratio Type:	Odds ratio
Ratio Value:	1.47
Confidence Interval:	1.37–1.57
Adjusted for:	
Evidence source PMID	23915883
Author	Gintare

2.55. Hypertension – Death (sudden cardiac)

Risk Association	
Risk Source:	Hypertension
Risk Target:	Sudden cardiac death
Association Type:	is an issue in
RiskID:	REID1
Author	Gintare

Risk Evidence ID1

RiskID:	1
Observable:	Death sex
Observable Condition:	Death sex = female
Ratio Type:	Relative Risk
Ratio Value:	2.49
Confidence Interval:	1.87-3.32
Adjusted for:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare

2.56. Hyperuricemia – Stroke

Risk Association	
Risk Source:	Hyperuricemia
Risk Target:	Stroke
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Larynas

Risk Evidence ID1	
RiskID:	1
Observables:	Uric acid serum concentration
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

Risk Evidence ID2	
RiskID:	2
Observables:	Uric acid serum concentration
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

2.57. Intensive Blood Glucose Control – Diabetic Nephropathy

Risk Association	
Risk Source:	Intensive Blood Glucose Control
Risk Target:	Diabetic Nephropathy
Association Type:	Associated with, reduces
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	HbA1c
Observable Condition:	6.5 vs 7.3
Ratio Type:	Hazard Ratio
Ratio Value:	0.79
Confidence Interval:	0.66-0.93
Adjusted for:	
Evidence source PMID	18539916
Author:	Stefanos

2.58. Intensive Blood Glucose Control – Hypoglycemia

Risk Association	
Risk Source:	Intensive Blood Glucose Control
Risk Target:	Hypoglycemia
Association Type:	Associated with
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1

RiskID:	1
Observable:	HbA1c
Observable Condition:	6.5 vs 7.3
Ratio Type:	Hazard Ratio
Ratio Value:	1.86
Confidence Interval:	1.42- 2.40
Adjusted for:	
Evidence source PMID	18539916
Author:	Stefanos

2.59. Intensive Blood Glucose Control – Death

Risk Association	
Risk Source:	Intensive Blood Glucose Control
Risk Target:	Death
Association Type:	NOT associated with
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	HbA1c
Observable Condition:	6.5 vs 7.3
Ratio Type:	Hazard Ratio
Ratio Value:	0.93
Confidence Interval:	0.83- 1.06
Adjusted for:	
Evidence source PMID	18539916
Author:	Stefanos

2.60. Intensive Blood Glucose Control – Death due to cardiovascular disease

Risk Association	
Risk Source:	Intensive Blood Glucose Control
Risk Target:	Death due to cardiovascular disease
Association Type:	NOT associated with
RiskID:	REID1

Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	HbA1c
Observable Condition:	6.5 vs 7.3
Ratio Type:	Hazard Ratio
Ratio Value:	0.88
Confidence Interval:	0.74- 1.04
Adjusted for:	
Evidence source PMID	18539916
Author:	Stefanos

2.61. Lack of physical activity in CKD – Death

Risk Association	
Risk Source:	Lack of physical activity in CKD
Risk Target:	Death
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	Interview about physical active
Observable Condition:	Moderately active
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

Risk Evidence ID2	
RiskID:	2
Observable:	Interview about physical active
Observable Condition:	Very active
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

2.62. Left ventricular hypertrophy – Cardiovascular disease

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Any cardiovascular disease event
Association Type:	issue in
RiskID:	REID1, REID2
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observables:	Electrocardiographic changes Sex
Observable Condition:	Sokolow - Lyon criteria (sum of S wave in V1 and R wave in V5 or V6 ≥3.5 mV (35 mm) and/or R wave in aVL ≥1.1 mV (11 mm) 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

Risk Evidence ID2	
RiskID:	2
Observable:	Electrocardiographic changes Sex
Observable Condition:	Sokolow - Lyon criteria (sum of S wave in V1 and R wave in V5 or V6 ≥3.5 mV (35 mm) and/or R wave in aVL ≥1.1 mV (11 mm) 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

2.63. Left ventricular hypertrophy – Heart failure (as a 1st CVD event)

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Heart failure
Association Type:	Issue in
RiskID:	REID1, REID2
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Left ventricular hypertrophy Sex
Observable Condition:	Sokolow- Lyon criteria 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

Risk Evidence ID2	
RiskID:	2
Observable:	Left ventricular hypertrophy Sex
Observable Condition:	Sokolow- Lyon criteria 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

2.64. Left ventricular hypertrophy – Stroke (as a 1st CVD event)

Risk Assocation	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Stroke
Association Type:	Issue in
RiskID:	REID1, REID2
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Left ventricular hypertrophy Sex
Observable Condition:	Sokolow- Lyon criteria 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

Risk Evidence ID2	
RiskID:	2
Observable:	Left ventricular hypertrophy Sex
Observable Condition:	Sokolow-Lyon criteria 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

2.65. Left Ventricular hypertrophy – Hypertension

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	Hypertension
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Left ventricular mass index
Observable Condition:	26.5 g/m increase in indexed left ventricular mass (1-SD increment)
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	8025994
Author	Neringa

Risk Evidence ID2	
RiskID:	2
Observable:	left ventricular wall thickness
Observable Condition:	increment in left ventricular wall thickness (1-SD increment)
Ratio Type:	Odds ratio
Ratio Value:	1,16
Confidence Interval:	1.02 – 1.33
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	8025994
Author	Neringa

2.66. Left ventricular hypertrophy – Death due to cardiovascular disease

Risk Association	
Risk Source:	Left ventricular hypertrophy
Risk Target:	cardiovascular mortality

Association Type:	issue in
RiskID:	REID1, REID2
Author	Neringa

Risk Evidence ID1	
RiskID:	1
Observable:	Electrocardiographic changes Sex
Observable Condition:	Cornell product of [(SV3+RaVL) x QRS duration] >244 μV · s AND sex=male
Ratio Type:	Hazard ratio
Ratio Value:	2.10
Confidence Interval:	0.67-6.62
Adjusted for:	LVMI, other ECG-LVH methods; Insulin sensitivity index, proinsulin, LDL cholesterol, HDL cholesterol, Triglycerides, waist circumference, hypertension, smoking, previous ischemic heart disease
Evidence source PMID	11352882
Author	Neringa

Risk Evidence ID2	
RiskID:	2
Observable:	Echocardiographic changes Sex
Observable Condition:	left ventricular mass index (LVMI) 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

2.67. Low protein diet in CKD – End stage renal disease (ESRD)

Risk Association	
Risk Source:	Low protein intake (diet) in CKD
Risk Target:	ESRD (end stage renal disease)
Association Type:	Cause

RiskID:	REID1
Author	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Low protein diet
Observable Condition:	0.8 g/kg/day
Ratio Type:	RR
Ratio Value:	1.62
Confidence Interval:	0.62-4.21
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos

2.68. Low protein diet in CKD – Death

Risk Association	
Risk Source:	Low protein intake (diet) in CKD
Risk Target:	mortality
Association Type	DO NOT cause
RiskID:	REID1
Author	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Low protein diet
Observable Condition:	0.8 g/kg/day
Ratio Type:	RR
Ratio Value:	0.58
Confidence Interval:	0.29-1.16
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos

2.69. Menopause – Death due to coronary heart disease

Risk Association

Risk Source:	Menopause
Risk Target:	Mortality from coronary heart disease
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	ICD-9 (International Classification of Diseases, Ninth Revision) codes 410.0–414.9, ICD-10 (Tenth Revision) codes I20.0–I25 Age (in years)
Observable Condition:	Menopause AND 40 ≤ age ≤ 44
Ratio Type:	Rate ratio
Ratio Value:	1.09
Confidence Interval:	1.00 – 1.18
Adjusted for:	Age, race, marital status, body mass index, age at menarche, parity, education, alcohol consumption, oral contraceptive use, and exercise
Evidence source PMID	16221806
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	ICD-9 (International Classification of Diseases, Ninth Revision) codes 410.0–414.9, ICD-10 (Tenth Revision) codes I20.0–I25 Age (in years)
Observable Condition:	Menopause AND 45 ≤ age ≤ 49
Ratio Type:	Rate ratio
Ratio Value:	0.98
Confidence Interval:	0.92 – 1.04
Adjusted for:	Age, race, marital status, body mass index, age at menarche, parity, education, alcohol consumption, oral contraceptive use, and exercise
Evidence source PMID	16221806
Author	Gintare

2.70. Obesity – Asthma

Risk Association	
Risk Source:	Obesity

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

Risk Evidence ID1	
RiskID1:	1
Observables:	BMI, sex
Observable Condition:	25-30, sex=male
Ratio Type:	Relative Risk
Ratio Value:	1.20
Confidence Interval:	1.08 – 1.33
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi

Risk Evidence ID2	
RiskID2:	2
Observables:	BMI, 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	PMID:24360912
Author	Kalliopi

Risk Evidence ID3	
RiskID3:	3
Observables:	BMI, sex
Observable Condition:	$25 \leq BMI \leq 30$ 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

Risk Evidence ID4	
RiskID4:	4
Observables:	BMI, 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

2.71. Obesity – Atrial Fibrillation

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

Risk Evidence ID1	
RiskID:	1
Observables:	BMI, sex
Observable Condition:	$25 \leq BMI \leq 30$ 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

Risk Evidence ID2

RiskID2:	2
Observables:	BMI, 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
Evidence source type:	prospective, community- based observational study
Author	Kalliopi

Risk Evidence ID3	
RiskID:	3
Observables:	BMI, 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

Risk Evidence ID4	
RiskID:	4
Observables:	BMI, 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

2.72. Obesity – Cancer: diffuse large B-cell lemphoma

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: diffuse large B-cell lemphoma
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	$25 \leq BMI \leq 30$
Ratio Type:	Relative Risk
Ratio Value:	1.14
Confidence Interval:	1.04 – 1.24
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI > 30
Ratio Type:	Relative Risk
Ratio Value:	1.29
Confidence Interval:	1.16 – 1.43
Adjusted for:	-
Evidence source PMID	24360912
Author	Kalliopi

2.73. Obesity – Cancer: gastric cardia cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: gastric cardia cancer
Association Type:	is an issue in
RiskID:	REID1, REID2

Author	Kalliopi

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

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

2.74. Obesity – Cancer: colorectal cancer

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

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	>30

Ratio Type:	Relative Risk
Ratio Value:	1.334
Confidence Interval:	1.253 – 1.420
Adjusted for:	-
Evidence source PMID	23349764
Author	Kalliopi

2.75. Obesity – Cancer: post-menopausal breast cancer

Risk Association	
Risk Source:	Obesity
Risk Target:	Cancer: post-menopausal breast cancer
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	25 ≤ BMI ≤ 30
Ratio Type:	Relative Risk
Ratio Value:	1.08
Confidence Interval:	1.03 – 1.14
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI > 30
Ratio Type:	Relative Risk
Ratio Value:	1.13
Confidence Interval:	1.05 – 1.22)
Adjusted for:	-
Evidence source PMID	19320986
Evidence source type:	Systematic review and meta-analysis

Author	Kalliopi

2.76. 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

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	$25 \leq BMI \leq 30$
Ratio Type:	Relative Risk
Ratio Value:	1.28
Confidence Interval:	0.94 – 1.75
Adjusted for:	-
Evidence source PMID	19320986
Author	Kalliopi

Risk Evidence ID2	
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

2.77. Obesity – CVD: Heart Failure

Risk Association	
Risk Source:	Obesity

Risk Target:	Cardiovascular disease
Association Type:	Is an issue in
RiskID:	REID1 – REID7
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	BMI, 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

Risk Evidence ID2	
RiskID:	2
Observables:	BMI, 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

Risk Evidence ID3	
RiskID:	3
Observables:	BMI, 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

Risk Evidence ID4	
RiskID:	4
Observables:	BMI, 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

Risk Evidence ID5	
RiskID5:	5
Observables:	BMI, sex
Observable Condition:	$25 \leq BMI \leq 30$ 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

Risk Evidence ID6

RiskID:	6
Observables:	BMI, 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

Risk Evidence ID7	
RiskID:	7
Observables:	BMI, 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

2.78. Obesity – CVD: Ischemic stroke

Risk Association	
Risk Source:	Obesity
Risk Target:	Cardiovascular disease: ischemic stroke
Association Type:	Is an issue in
RiskID:	REID1, REID2
Author	Kalliopi

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

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	PMID: 20299666
Author	Kalliopi

2.79. Obesity – CVD: Haemorrhagic stroke

Risk Association	
Risk Source:	Obesity
Risk Target:	Cardiovascular disease: haemorrhagic stroke
Association Type:	Is an issue in
RiskID:	REID1, REID2
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	BMI
Observable Condition:	25 ≤ BMI ≤ 30
Ratio Type:	Risk ratio
Ratio Value:	1.01
Confidence Interval:	0.88 – 1.17
Adjusted for:	-

Evidence source PMID	20299666
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	BMI
Observable Condition:	BMI >30
Ratio Type:	Risk ratio
Ratio Value:	1.24
Confidence Interval:	0.99 – 1.54
Adjusted for:	-
Evidence source PMID	20299666
Evidence source type:	Systematic review
Author	Kalliopi

2.80. Obesity – CVD: Coronary arterial disease

Risk Association	
Risk Source:	Obesity
Risk Target:	Cardiovascular disease: Coronary arterial disease
Association Type:	Is an issue in
RiskID:	REID1 – REID8
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	BMI, 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

Risk Evidence ID2	
RiskID:	2

Observables:	BMI, 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

Risk Evidence ID3	
RiskID:	3
Observables:	WC, 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

Risk Evidence ID4	
RiskID:	4
Observables:	WC, 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

Risk Evidence ID5	
RiskID:	5
Observables:	WC, 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

Risk Evidence ID6	
RiskID:	6
Observables:	WC, 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

Risk Evidence ID7	
RiskID:	7
Observables:	BMI, 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

Risk Evidence ID8	
RiskID19:	8
Observables:	BMI, 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

2.81. Obesity – Gallbladder disease

Risk Association	
Risk Source:	Obesity
Risk Target:	Gallbladder disease
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	BMI, 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

Risk Evidence ID2	
RiskID:	2
Observables:	BMI, 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

Risk Evidence ID3	
RiskID:	3
Observables:	BMI, 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

Risk Evidence ID4	
RiskID:	4
Observables:	BMI, 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

2.82. Obesity – Diabetes

Risk Association	
Risk Source:	obesity
Risk Target:	type 2 diabetes
Association Type:	causes
RiskID:	REID1 – REID4
Author	Kalliopi

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

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

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

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

2.83. Obesity – Osteoarthritis

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

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

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

2.84. Obesity – Progression of CKD

Risk Association

Risk Source:	Obesity
Risk Target:	Progression of CKD
Association Type:	is an issue in
RiskID:	REID1
Author	Laurynas

Risk Evidence ID1	
RiskID:	1
Observable:	BMI
Observable Condition:	BMI ≥ 25.5
Ratio Type:	Odds ratio
Ratio Value:	1.483
Confidence Interval:	1.083–2.031
Adjusted for:	age, systolic blood pressure, proteinuria
Evidence source PMID	15086929
Author	Laurynas

2.85. Obesity – Death: sudden cardiac death

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

Risk Evidence ID1	
RiskID:	1
Observable:	BMI, 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:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare

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:	Multivariate-adjusted
Evidence source PMID	12695299
Author	Gintare

2.86. Obesity central – Cardiovascular disease

Risk Association	
Risk Source:	Central obesity
Risk Target:	cardiovascular disease
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	waist circumference (WC), sex
Observable Condition:	94≤ WC ≤102 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	1
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	waist circumference (WC), sex
Observable Condition:	WC >102 AND sex=male

Ratio Type:	Odds ratio
Ratio Value:	2.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

Risk Evidence ID4	
RiskID:	4
Observables:	waist circumference (WC), sex
Observable Condition:	Wc >88 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	1.5
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

2.87. Obesity central – Diabetes

Risk Association	
Risk Source:	Central obesity
Risk Target:	Type 2 diabetes
Association Type:	causes
RiskID:	REID1 – REID8
Author	Kalliopi

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

Risk Evidence ID2	
RiskID:	2
Observables:	waist circumference (WC), sex
Observable Condition:	94.3 ≤ WC ≤ 99.3 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	3.9
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	PMID:19705980
Evidence source type:	prospective, national, population based study.
Author	Kalliopi

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

Risk Evidence ID4	
RiskID:	4
Observables:	waist circumference (WC), sex
Observable Condition:	WC > 106.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	1.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

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

Risk Evidence ID7	
RiskID:	7

Observables:	waist circumference (WC), sex
Observable Condition:	87.1 ≤ WC ≤ 96.2 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	4
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID8	
RiskID:	8
Observables:	waist circumference (WC), sex
Observable Condition:	WC >96.2 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	6
Confidence Interval:	95%
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

2.88. Obesity central – Dyslipidemia: low HDL cholosterol levels

Risk Association	
Risk Source:	Central obesity
Risk Target:	dyslipidemia: low HDLcholosterol levels
Association Type:	Is an issue in
RiskID:	REID1 – REID8
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	waist circumference (WC), sex
Observable Condition:	88.2 ≤ WC ≤ 94.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	2

Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

Risk Evidence ID3	
RiskID:	3
Observables:	waist circumference (WC), sex
Observable Condition:	99.4 ≤ WC ≤ 106.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	4
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID4	
RiskID	4
Observables:	waist circumference (WC) and sex=male
Observable Condition:	WC >106.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	

Adjusted for:	age and smoking status
Evidence source PMID	1970598
Author	Kalliopi

Risk Evidence ID5	
RiskID5:	5
Observables:	waist circumference (WC), sex
Observable Condition:	73.7 ≤ WC ≤ 80.2 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	1.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID6	
RiskID:	6
Observables:	waist circumference (WC), sex
Observable Condition:	80.4 ≤ WC ≤ 87 and sex=female
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

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

2.89. Obesity central – Dyslipidemia: high triglyceride levels

Risk Association	
Risk Source:	Central obesity
Risk Target:	dyslipidemia: low HDLcholosterol levels
Association Type:	Is an issue in
RiskID:	REID1 – REID8
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	waist circumference (WC), sex
Observable Condition:	88.2 ≤ WC ≤ 94.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	2
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	waist circumference (WC), sex
Observable Condition:	94.3 ≤ WC ≤ 99.3

	AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	3.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

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

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

Ratio Value:	3
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

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

Risk Evidence ID8	
RiskID:	8
Observables:	waist circumference (WC), sex
Observable Condition:	WC > 96.2 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	8

Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

2.90. Obesity central – Dyslipidemia: elevated ocidized LDL levels

Risk Association	
Risk Source:	Central obesity
Risk Target:	dyslipidemia: elevated ocidized LDL levels
Association Type:	Is an issue in
RiskID:	REID1 – REID6
Author	Kalliopi

Risk Evidence ID1	
RiskID:	1
Observables:	waist circumference (WC), sex
Observable Condition:	88≤ WC ≤ 94 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	1.29
Confidence Interval:	0.72 – 2.32
Adjusted for:	sex, age, energy consumption, educational level, leisure-time physical activity, smoking and alcohol drinking status, and dietary intakes of vitamin C, vitamin E, β-carotene, and polyunsaturated fatty acids, diabetes, HDL cholesterol (categorical: 0 = >40 mg/dL for men or >50 mg/dL for women and 1 = <40 mg/dL for men and <50 mg/dL for women), and LDL cholesterol (categorical: 0 = <160 mg/dL and 1 = >160 mg/dL)
Evidence source PMID	16400046
Author	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	waist circumference (WC), sex
Observable Condition:	73 ≤ WC ≤ 81.9 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	1.29
Confidence Interval:	0.72 – 2.32
Adjusted for:	sex, age, energy consumption, educational level, leisure-time physical activity,

	smoking and alcohol drinking status, and dietary intakes of vitamin C, vitamin E, β-carotene, and polyunsaturated fatty acids, diabetes, HDL cholesterol (categorical: 0 = >40 mg/dL for men or >50 mg/dL for women and 1 = <40 mg/dL for men and <50 mg/dL for women), and LDL cholesterol (categorical: 0 = <160 mg/dL and 1 = >160 mg/dL)
Evidence source PMID	16400046
Author	Kalliopi

Risk Evidence ID3	
RiskID:	3
Observables:	waist circumference (WC), sex
Observable Condition:	95 ≤ WC ≤ 102.7 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	1.08
Confidence Interval:	0.68 – 1.93
Adjusted for:	sex, age, energy consumption, educational level, leisure-time physical activity, smoking and alcohol drinking status, and dietary intakes of vitamin C, vitamin E, β-carotene, and polyunsaturated fatty acids, diabetes, HDL cholesterol (categorical: 0 = >40 mg/dL for men or >50 mg/dL for women and 1 = <40 mg/dL for men and <50 mg/dL for women), and LDL cholesterol (categorical: 0 = <160 mg/dL and 1 = >160 mg/dL)
Evidence source PMID	16400046
Author	Kalliopi

Risk Evidence ID4	
RiskID:	4
Observables:	waist circumference (WC), sex
Observable Condition:	82 ≤ WC ≤ 91.9 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	1.08
Confidence Interval:	0.68 – 1.93
Adjusted for:	sex, age, energy consumption, educational level, leisure-time physical activity, smoking and alcohol drinking status, and dietary intakes of vitamin C, vitamin E, β-carotene, and polyunsaturated fatty acids, diabetes, HDL cholesterol (categorical: 0 = >40 mg/dL for men or >50 mg/dL for women and 1 = <40 mg/dL for men and <50 mg/dL for women), and LDL cholesterol (categorical: 0 = <160 mg/dL and 1 = >160 mg/dL)
Evidence source PMID	16400046
Author	Kalliopi

Risk Evidence ID5

RiskID:	5
Observables:	waist circumference (WC), sex
Observable Condition:	WC>103 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	2.15
Confidence Interval:	1.16 – 3.98
Adjusted for:	sex, age, energy consumption, educational level, leisure-time physical activity, smoking and alcohol drinking status, and dietary intakes of vitamin C, vitamin E, β-carotene, and polyunsaturated fatty acids, diabetes, HDL cholesterol (categorical: 0 = >40 mg/dL for men or >50 mg/dL for women and 1 = <40 mg/dL for men and <50 mg/dL for women), and LDL cholesterol (categorical: 0 = <160 mg/dL and 1 = >160 mg/dL)
Evidence source PMID	16400046
Author	Kalliopi

Risk Evidence ID6	
RiskID:	6
Observables:	waist circumference (WC), sex
Observable Condition:	WC>92 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	2.15
Confidence Interval:	1.16 – 3.98
Adjusted for:	sex, age, energy consumption, educational level, leisure-time physical activity, smoking and alcohol drinking status, and dietary intakes of vitamin C, vitamin E, β-carotene, and polyunsaturated fatty acids, diabetes, HDL cholesterol (categorical: 0 = >40 mg/dL for men or >50 mg/dL for women and 1 = <40 mg/dL for men and <50 mg/dL for women), and LDL cholesterol (categorical: 0 = <160 mg/dL and 1 = >160 mg/dL)
Evidence source PMID	16400046
Author	Kalliopi

2.91. Obesity central – Hypertension

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

Risk Evidence ID1	
RiskID:	1
Observables:	waist circumference (WC), sex
Observable Condition:	88.2 ≤ WC ≤ 94.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	1.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

Risk Evidence ID3	
RiskID:	3
Observables:	waist circumference (WC), sex
Observable Condition:	99.4 ≤ WC ≤ 106.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	2.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID4	
RiskID:	4

Observables:	waist circumference (WC), sex
Observable Condition:	WC>106.2 AND sex=male
Ratio Type:	Odds ratio
Ratio Value:	3.5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

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

Risk Evidence ID6	
RiskID:	6
Observables:	waist circumference (WC), sex
Observable Condition:	80.4 ≤ WC ≤ 87 AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	2
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID7	
RiskID:	7
Observables:	waist circumference (WC), sex
Observable Condition:	87.1 ≤ WC ≤ 96.2

	AND sex=female
Ratio Type:	Odds ratio
Ratio Value:	3
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

Risk Evidence ID8	
RiskID:	8
Observables:	waist circumference (WC), sex
Observable Condition:	WC>96.2 and sex=female
Ratio Type:	Odds ratio
Ratio Value:	5
Confidence Interval:	
Adjusted for:	age and smoking status
Evidence source PMID	19705980
Author	Kalliopi

2.92. Obstructive sleep apnoea (OSA) – Death due to Cardiovascular disease

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

Risk Evidence ID1	
RiskID:	1
Observable:	Apnoea– hypopnoea index (AHI)
Observable Condition:	Ranges of AHI were given in individual studies. In meta-analysis they used the midpoint of the range (see table 2 in excerpts)
Ratio Type:	Hazard ratio
Ratio Value:	2.09
Confidence Interval:	1.20–3.65
Adjusted for:	multivariate
Evidence source PMID	22828826

Author	Gintare

2.93. Obstructive sleep apnoea (OSA) – Diabetes

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

Risk Evidence ID1	
RiskID:	1
Observable:	Apnoea– hypopnoea index (AHI), oxygen desaturation index (ODI)
Observable Condition:	AHI ≥ 15 but <30 (moderate OSA) and AHI ≥ 30 (severe OSA) or 3% ODI of ≥15 per hour (moderate-severe OSA)
Ratio Type:	Hazard ratio
Ratio Value:	1.63
Confidence Interval:	1.09–2.45
Adjusted for:	multivariate
Evidence source PMID	22988888
Author	Gintare

Risk Evidence ID2	
RiskID:	2
Observable:	Apnoea– hypopnoea index (AHI), oxygen desaturation index (ODI)
Observable Condition:	5 ≤ AHI <15 (mild OSA) OR 3% ODI of 5 to <15 per hour (mild OSA)
Ratio Type:	Hazard ratio
Ratio Value:	1.22
Confidence Interval:	0.91–1.6
Adjusted for:	multivariate
Evidence source PMID	22988888
Author	Gintare

2.94. Obstructive sleep apnoea (OSA) – Hypertension

Risk Association

Risk Source:	Obstructive sleep apnea (OSA)
Risk Target:	Hypertension
Association Type:	is an issue in
RiskID:	REID1 – REID8
Author	Gintare

Risk Evidence ID1	
RiskID:	1
Observable:	Apnoea–hypopnoea index (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

Risk Evidence ID2	
RiskID:	2
Observable:	Apnoea–hypopnoea index (AHI)
Observable Condition:	5 ≤ AHI < 14.9
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

Risk Evidence ID3	
RiskID:	3
Observable:	Apnoea– hypopnoea index (AHI)
Observable Condition:	15 ≤ AHI < 29.9
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

Risk Evidence ID4	
RiskID:	4
Observable:	Apnoea–hypopnoea index (AHI)
Observable Condition:	AHI ≥ 30
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

Risk Evidence ID5	
RiskID:	5
Observable:	Percentage of sleep time < 90% of oxygen saturation
Observable Condition:	0.05-0.49
Ratio Type:	Odds ratio
Ratio Value:	1.10
Confidence Interval:	0.94-1.29
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare

Risk Evidence ID6	
RiskID:	6
Observable:	Percentage of sleep time < 90% of oxygen saturation
Observable Condition:	0.50-3.9
Ratio Type:	Odds ratio
Ratio Value:	1.24
Confidence Interval:	1.05-1.46
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare

Risk Evidence ID7	
RiskID:	7
Observable:	Percentage of sleep time < 90% of oxygen saturation
Observable Condition:	4.0-11.9

Ratio Type:	Odds ratio
Ratio Value:	1.13
Confidence Interval:	0.90-1.42
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare

Risk Evidence ID8	
RiskID:	8
Observable:	Percentage of sleep time < 90% of oxygen saturation
Observable Condition:	≥12
Ratio Type:	Odds ratio
Ratio Value:	1.45
Confidence Interval:	1.12-1.88
Adjusted for:	Adjusted for demographics, BMI, neck, wait-to-hip ratio, alcohol use, smoking
Evidence source PMID	10770144
Author	Gintare

2.95. Obstructive sleep apnoea (OSA) – 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

Risk Evidence ID1	
RiskID:	1
Observable:	Apnoea–hypopnoea index (AHI)
Observable Condition:	Ranges of AHI were given in individual studies. In meta-analysis they used the midpoint of the range (see table 2 in excerpts)
Ratio Type:	Hazard ratio
Ratio Value:	1.92
Confidence Interval:	1.06–3.48
Adjusted for:	See table 1 in excerpts
Evidence source PMID	22828826
Author	Gintare

2.96. Obstructive sleep apnoea (OSA) – Stroke

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

Risk Evidence ID1	
RiskID:	1
Observable:	Apnoea–hypopnoea index (AHI)
Observable Condition:	Ranges of AHI were given in individual studies. In meta-analysis they used the midpoint of the range (see table 2 in excerpts)
Ratio Type:	Hazard ratio
Ratio Value:	2.24
Confidence Interval:	1.57–3.19
Adjusted for:	See table 2 in excerpts
Evidence source PMID	22828826
Author	Gintare

2.97. Physical Exercise – Cardiovascular Disease

Risk Association	
Risk Source:	Physical exercise
Risk Target:	Cardiovascular disease
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	MET
Observable Condition:	>10 MET h/week AND sex=male
Ratio Type:	RR
Ratio Value:	0.76
Confidence Interval:	0.70-0.82

Adjusted for:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	MET
Observable Condition:	>10 MET h/week AND sex=female
Ratio Type:	RR
Ratio Value:	0.73
Confidence Interval:	0.68-0.78
Adjusted for:	Age, smoking
Evidence source PMID	22470299
Author	Dimitris

2.98. Physical Exercise – Diabetes

Risk Association	
Risk Source:	Physical exercise
Risk Target:	Diabetes type 2
Association Type:	is an issue in
RiskID:	REID1
Author	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	MET (h/week)
Observable Condition:	MET >10
Ratio Type:	RR
Ratio Value:	0.83
Confidence Interval:	0.75–0.91
Adjusted for:	BMI
Evidence source PMID	17327354
Author	Dimitris

2.99. Serum Lipid levels – Cancer (obesity related)

Risk Association	
Risk Source:	Serum Lipid levels
Risk Target:	Cancer (which is obesity related)
Association Type:	is an issue in
RiskID:	REID1 – REID3
Author:	Kalliopi

Risk Evidence ID1	
RiskID1:	1
Observables:	Total cholesterol
Observable Condition:	>/=6,5 mmol/l
Ratio Type:	Relative Risk
Ratio Value:	1.18
Confidence Interval:	1.08 – 1.29
Adjusted for:	-
Evidence source PMID	24360912
Author:	Kalliopi

Risk Evidence ID2	
RiskID:	2
Observables:	Triglycerides
Observable Condition:	>/=1,71 mmol/l
Ratio Type:	Relative Risk
Ratio Value:	1.20
Confidence Interval:	1.07 – 1.35
Adjusted for:	-
Evidence source PMID	24360912
Author:	Kalliopi

Risk Evidence ID3	
RiskID:	3
Observables:	High Density Lipoprotein
Observable Condition:	>/=1,03 mmol/l
Ratio Type:	Relative Risk
Ratio Value:	1.15
Confidence Interval:	1.01 – 1.32

Adjusted for:	-
Evidence source PMID	24360912
Author:	Kalliopi

2.100. Smoking – Chronic Kidney Disease

Risk Association	
Risk Source:	Smoking
Risk Target:	Chronic kidney disease
Association Type:	Issues in
RiskID:	REID1, REID2
Author	Dimitris, Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking
Observables Condition:	Current smoking 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

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking amount
Observable Condition:	>20 cigarettes per day
Ratio Type:	Relative Risk
Ratio Value:	3.26
Confidence Interval:	1.66 - 6.80
Adjusted for:	
Evidence source PMID	18003763
Author:	Stefanos

2.101. Smoking – Death: sudden cardiac death

Risk Factor	
Risk Source:	Smoking
Risk Target:	Sudden cardiac death
Association Type:	is an issue in
RiskID:	REID1 – REID4
Author	Gintare

Risk Evidence ID1	
RiskID:	REID1
Observable:	Smoking status and amount sex
Observable Condition:	status = Past 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

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status and amount sex
Observable Condition:	status=Current AND amount = 1 to 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

Risk Evidence ID3	
RiskID:	3
Observable:	Smoking status and amount

	sex
Observable Condition:	status=Current AND amount = 15 to 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

Risk Evidence ID4	
RiskID:	4
Observable:	Smoking status and amount sex
Observable Condition:	status=Current AND amount ≥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

2.102. Smoking – Myocardial Infraction

Risk Association	
Risk Source:	Smoking
Risk Target:	Myocardial infarction
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Dimitris

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status sex
Observable Condition:	Current smoking

	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	9552903
Author	Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status sex
Observable Condition:	Current smoking 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	9552903
Author	Dimitris

2.103. 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

Risk Evidence ID1	
RiskID:	1
Observable:	Smoking status
Observable Condition:	Current smoking
Ratio Type:	Relative risk
Ratio Value:	2.71

Confidence Interval:	2.28 - 3.21
Adjusted for:	-
Evidence source PMID	23922053
Author	Dimitris

Risk Evidence ID2	
RiskID:	2
Observable:	Smoking status
Observable Condition:	Ex-smokers
Ratio Type:	Relative risk
Ratio Value:	1.67
Confidence Interval:	1.54 to 1.81
Adjusted for:	-
Evidence source PMID	23922053
Author	Dimitris

2.104. Smoking – Stroke

Risk Association	
Risk Source:	Smoking
Risk Target:	Stroke
Association Type:	is an issue in
RiskID:	REID1, REID2
Author	Dimitris

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

Risk Evidence ID2	
RiskID:	2

Observable:	Smoking status
Observable Condition:	Ex-smokers
Ratio Type:	Relative risk
Ratio Value:	1.17
Confidence Interval:	1.05 to 1.30
Adjusted for:	-
Evidence source PMID	2496858
Author	Dimitris

2.105. Statins in CKD 1 to 3 – ESRD

Risk Association	
Risk Source:	Use of statins in CKD 1-3
Risk Target:	ESRD
Association Type:	Reduces risk of
RiskID:	REID1
Author	Stefanos

Risk Evidence ID1	
RiskID:	REID1
Observable:	Use of statins
Observable Condition:	
Ratio Type:	RR
Ratio Value:	0.98
Confidence Interval:	0.62-1.56
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos

2.106. Statins in CKD 1 to 3 – Myocardial Infraction

Risk Association	
Risk Source:	Use of statins in CKD 1-3
Risk Target:	MI (myocardial infarction)
Association Type:	Reduces risk of
RiskID:	REID1
Author	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Use of statins
Observable Condition:	
Ratio Type:	RR
Ratio Value:	0.73
Confidence Interval:	0.54-0.98
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos

2.107. Statins in CKD 1 to 3 – Stroke

Risk Association	
Risk Source:	Use of statins in CKD 1-3
Risk Target:	Stroke
Association Type:	Reduces
RiskID:	REID1
Author	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Use of statins
Observable Condition:	
Ratio Type:	RR
Ratio Value:	0.61
Confidence Interval:	0.41-0.91
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos

2.108. Statins in CKD 1 to 3 – Death

Risk Association	
Risk Source:	Use of statins in CKD 1-3
Risk Target:	Death
Association Type:	Reduces

RiskID:	REID1
Author	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	Use of statins
Observable Condition:	
Ratio Type:	RR
Ratio Value:	0.81
Confidence Interval:	0.71-0.94
Adjusted for:	
Evidence source PMID	22508734
Author	Stefanos

2.109. Weight loss in CKD – Urine protein excretion, albuminuria

Risk Association	
Risk Source:	Weight loss in CKD
Risk Target:	Urine protein excretion- albuminuria
Association Type:	Associated with (reduces)
RiskID:	REID1
Author:	Stefanos

Risk Evidence ID1	
RiskID:	1
Observable:	body weight in CKD
Observable Condition:	Loss , reduction
Ratio Type:	
Ratio Value:	14mg
Confidence Interval:	11-17
Adjusted for:	
Evidence source PMID	19945950
Author:	Stefanos

3. Risk Elements

3.1. Acute kidney injury

Risk Element	
Name	Acute Kidney Injury
Type	biomedical
Modifiable	yes
Observables	serum creatinine, eGFR
Author	Stefanos

3.2. Age

Risk Element	
Name	Age
Type	demographic
Modifiable	no
Observables	Age per year
Author	

3.3. Anemia

Risk Element	
Name	Anemia
Type	Biomedical
Modifiable	Yes
Observables	Hemoglobin level
Author	Gintare

3.4. Arterial stiffness

Risk Element	
Name	Arterial stiffness
Type	biomedical
Modifiable	yes
Observables	PWV- AI (augmentation index)
Author	Stefanos

3.5. Arteriovenous access thrombosis

Risk Element	
Name	Arteriovenous access thrombosis
Type	clinical
Modifiable	yes
Observables	fistula flow , AV graft flow
Author	Stefanos

3.6. Asthma

Risk Element	
Name	asthma
Type	Biomedical
Modifiable	yes
Observables	FEV1/FVC
Author	Kalliopi

3.7. Atherosclerosis

Risk Element	
Name	Atherosclerosis
Type	Biomedical
Modifiable	Yes
Observables	Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), pulse wave velocity (PWV)
Author	Gintare

3.8. Atrial fibrillation

Risk Element	
Name	Atrial fibrillation
Type	biomedical
Modifiable	yes
Observables	ECG
Author	Neringa

3.9. Cancer

Risk Element	
Name	cancer
Type	Biomedical, genetic, environmental
Modifiable	no
Observables	BRCA1 / BRCA2 (Breast/Ovarian Cancer), BRAF V600E (Melanoma/Colorectal Cancer), CA19.9 (Pancreatic Cancer), CEA (Colorectal Cancer), HER-2 (Breast Cancer), Gastric(HER-2/neu)
Author	Kalliopi

3.10. Cardiovascuar disease

Risk Element	
Name	Cardiovascular disease
Type	biomedical
Modifiable	yes, no
Observables	cardiovascular disease group defined as patients with hypertension and heart failure (Observables are already listed)
Author	Neringa, Gintare

3.11. Cardiovascular event

Risk Element	
Name	Cardiovascular event
Type	biomedical
Modifiable	yes
Observables	coronary heart disease heart failure non-fatal myocardial infarction transient ischemic attack
Author	Neringa

3.12. Chronic Kidney Disease

Risk Element	
Name	CKD
Type	Biomedical
Modifiable	Yes

Observables	glomerular filtration rate [GFR] or albuminuria
Author	Stefanos

3.13. Chronic obstructive pulmonary disease (COPD)

Risk Element	
Name	Chronic obstructive pulmonary disease (COPD)
Type	Biomedical
Modifiable	Yes
Observables	Spirometry
Author	Gintare

3.14. Coronary and carotid revascularisation

Risk Element	
Name	Coronary and carotid revascularisation
Type	clinical
Modifiable	yes
Observables	Diagnosis reported by investigator - criteria not defined
Author	Zydrune

3.15. Coronary Heart Disease (CHD)

Risk Element	
Name	Coronary heart disease (CHD)
Type	Biomedical
Modifiable	No
Observables	
Author	Gintare, Stefanos

3.16. Death

Risk Element	
Name	Death
Type	biomedical
Modifiable	no
Observables	Death criteria

Author	Gintare

3.17. Depression

Risk Element	
Name	Depression
Type	Biomedical
Modifiable	Yes
Observables	Depression scale
Author	Gintare

3.18. Diabetic nephropathy

Risk Element	
Name	Diabetic nephropathy
Type	biomedical
Modifiable	yes
Observables	eGFR, albuminuria, serum creatinine, the need for renal-replacement therapy
Author	Zydrune

3.19. Diabetes

Risk Element	
Name	Diabetes
Type	biomedical
Modifiable	no
Observables	Plasma glucose, use of insulin or an oral hypoglycemic drug, or a physician's diagnosis of diabetes mellitus fasting plasma glucose levels, HbA1c, glucose at two hours after oral glucose tolerance test fasting plasma glucose levels, HbA1c, glucose at two hours after oral glucose tolerance test, diabetes medication, doctor's diagnosis of diabetes
Author	Zydrune, Gintare, Kalliopi

3.20. Drugs: Contrast agents

Risk Element	
Name	Contrast agents

Type	intervention
Modifiable	yes
Observables	IV administration of contrast agents
Author	Dimitris

3.21. Dyslipidemia

Risk Element	
Name	Dyslipidemia
Type	Biomedical
Modifiable	Yes
Observables	Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG)
Author	Gintare

3.22. End stage renal disease

Risk Element	
Name	ESRD
Type	Biomedical/condition
Modifiable	no
Observables	eGFR
Author	Stefanos

3.23. Gallbladder disease

Risk Element	
Name	Gallbladder disease
Type	Biomedical
Modifiable	no
Observables	X-Ray
Author	Kalliopi

3.24. Heart Failure

Risk Element	
Name	Heart failure

Type	Biomedical
Modifiable	yes
Observables	Brain-type natriuretic peptide (BNP), ejection fraction (EF), fluid balance, Plasma B-type natriuretic peptide (BNP)
Author	Gintare, Zydrune

3.25. Hyperkalemia

Risk Element	
Name	hyperkalemia
Type	biomedical
Modifiable	yes
Observables	Serum potassium, ECG, symptoms (nausea, fatigue, malaise, palpitations and muscle weakness)
Author	Neringa

3.26. Hyperuricemia

Risk Element	
Name	hyperuricemia
Type	biomedical
Modifiable	yes
Observables	Uric acid serum concentration
Author	Laurynas

3.27. Hypertension

Risk Element	
Name	hypertension
Type	biomedical
Modifiable	yes
Observables	Blood pressure (BP), reported use of a medication for hypertension left ventricular hypertrophy (LVH) current use of antihypertensive medication
Author	Neringa, Gintare, Zydrune

3.28. Hypoglycaemia

Risk Element	
Name	Hypoglycaemia
Type	clinical
Modifiable	yes
Observables	Fasting Plasma Glucose
Author	Stefanos

3.29. Ischemic heart disease

Risk Element	
Name	Ischemic heart disease
Type	Biomedical
Modifiable	No
Observables	
Author	Gintare

3.30. Left ventricular hypertrophy

Risk Element	
Name	Left ventricular hypertrophy
Type	biomedical
Modifiable	yes
Observables	ECG, echocardiography, magnetic resonance imaging
Author	Neringa

3.31. Maternal and paternal history of MI

Risk Element	
Name	Maternal and paternal history of MI
Type	Genetic
Modifiable	No
Observables	
Author	Gintare

3.32. Menopause

Risk Element	
Name	Menopause
Type	Biomedical
Modifiable	No
Observables	1 year without menses
Author	Gintare

3.33. Myocardial Infarction

Risk Element	
Name	MI
Type	Biomedical
Modifiable	Yes
Observables	ECG findings (Electrocardiogram), cardiac enzymes, Cardiac troponin (cTn) (I and T), symptoms of ischemia, diagnosis reported by investigator – criteria not defined
Author	Stefanos, Zydrune, Dimitris, Gintare

3.34. Obesity

Risk Element	
Name	obesity
Type	behavioral
Modifiable	yes
Observables	BMI, waist circumference, waist to hip ratio, waist to height ratio, body fat percentage
Author	Kalliopi

3.35. Obesity Central

Risk Element	
Name	Central obesity
Type	behavioural
Modifiable	yes
Observables	waist circumference, waist to hip ratio
Author	Kalliopi

3.36. Obstructive Sleep Apnoea

Risk Element	
Name	Obstructive sleep apnea (OSA)
Type	Biomedical
Modifiable	Yes
Observables	Apnoea–hypopnoea index (AHI), oxygen desaturation index (ODI)
Author	Gintare

3.37. Osteoarthritis

Risk Element	
Name	osteoarthritis
Type	Biomedical
Modifiable	no
Observables	X- Ray
Author	Kalliopi

3.38. Peripheral Arterial/Vascular Disease

Risk Element	
Name	Peripheral arterial disease
Type	Biomedical, behavioural
Modifiable	yes
Observables	ankle-branchial index
Author	Dimitris, Kalliopi

3.39. Physical activity (fitness)

Risk Element	
Name	Physical activity
Type	clinical
Modifiable	yes
Observables	Endurance time
Author	Stefanos

3.40. Physical exercise

Risk Element	
Name	Physical exercise
Type	behavioral
Modifiable	yes
Observables	MET h/week
Author	Dimitris

3.41. Quality of Life

Risk Element	
Name	QOL (Quality Of Life)
Type	clinical
Modifiable	yes
Observables	EQ-5D , SF-36 questionnaires
Author	Stefanos

3.42. Renal Function

Risk Element	
Name	Renal function during myocardial infarction
Type	Biomedical
Modifiable	Yes
Observables	Glomerular filtration rate (GFR)
Author	Gintare

3.43. Smoking

Risk Element	
Name	Smoking
Type	behavioral
Modifiable	yes
Observables	smoking status, smoking amount
Author	Dimitris

3.44. Stroke

Risk Element	
Name	Stroke
Type	biomedical
Modifiable	no
Observables	imaging, diagnosis reported by investigator - criteria not defined
Author	Dimitris, Stefanos, Gintare

3.45. Sudden Sensorineural Hearing Loss (SSHL)

Risk Element	
Name	Sudden Sensorineural Hearing Loss (SSHL)
Type	clinical
Modifiable	yes
Observables	Hearing test
Author	Stefanos

3.46. Urine protein excretion

Risk Element	
Name	Urine protein excretion
Type	Clinical
Modifiable	yes
Observables	albuminuria
Author	Stefanos

4. Observables

4.1. Age

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

4.2. Albuminuria

Observable	
Name	Albuminuria
Type	Clinical
Data type	Real
Unit	mg/24hours or mg/mmol
Values/range	Normal: < 10mg/g (<1mg/mmol) Normal to mildly increased: <30 mg/24 hours or <3 mg/mmol <30 mg/g Moderately increased: 30-300 mg/24 hours or 3-30 mg/mmol or 30-300 mg/g Severely increased: >300 mg/24 hours or >30 mg/mmol or >300 mg/g
Author	Stefanos, Zydrune

4.3. Ankle – branchial index

Observable	
Name	Ankle- branchial index
Type	clinical
Data type	real
Unit	-
Values/range	Normal: 1.0 to 1.4 Borderline abnormal: < 0.9 – Abnormal: 0.91 to 0.99
Author	Kalliopi, Dimitris, Gintare

4.4. Apnoea – hypopnoea index (AHI)

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
Author	Gintare

4.5. Arteriovenous fistula flow (AVF)

Observable	
Name	Arteriovenous fistula (AVF) flow
Type	clinical
Data type	integer
Unit	ml/min
Values/range	Normal: >500 Abnormal: <500 or drop >20% from baseline
Author	Stefanos

4.6. Arteriovenous graft flow (AVG)

Observable	
Name	Arteriovenous graft (AVG) flow
Type	clinical
Data type	integer
Unit	ml/min
Values/range	Normal: > 650 Abnormal: <650 or drop >20% from baseline
Author	Stefanos

4.7. Blood Pressure

Observable	
Name	Blood pressure (BP)

Type	clinical
Data type	real
Unit	mmHg
Values/range	Category — Systolic — Diastolic High normal — 130–139 and/or 85–89 Grade 1 hypertension — 140–159 and/or 90–99 Grade 2 hypertension — 160–179 and/or 100–109 Grade 3 hypertension — ≥180 and/or ≥110 Isolated systolic hypertension — ≥140 and <90
Author	Zydrune

4.8. 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
Author	Kalliopi

4.9. 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
Author	Zydrune

4.10. Blood pressure

Observable	
Name	Blood pressure (BP)
Type	clinical

Data type	real
Unit	mmHg
Values/range	Normal: systolic pressure ≤140 mm Hg and/or diastolic pressure ≤90 mm Hg Optimal: SBP<120 and DBP<80; normal BP: SBP 120-129 and/or DBP 80-84; high normal BP: SBP 130-139 and/or DBP 85-89 Category — Systolic — Diastolic High normal — 130–139 and/or 85–89 Grade 1 hypertension — 140–159 and/or 90–99 Grade 2 hypertension — 160–179 and/or 100–109 Grade 3 hypertension — ≥180 and/or ≥110 Isolated systolic hypertension — ≥140 and <90
Author	Neringa, Gintare, Zydrune

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%+
Author	Kalliopi		

4.12. Body Mass Index (BMI)

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)
Author	Kalliopi	

4.13. Brain-type natriuretic peptide (BNP)

Observable	
Name	Brain-type natriuretic peptide (BNP)
Type	Clinically measured
Data type	Real
Unit	pg/mL
Values/range	Normal <200 pg/mL: likely compensated congestive heart failure (CHF) Abnormal >or =200 to < or =400 pg/mL: likely moderate CHF >400 pg/mL: likely moderate-to-severe CHF
Author	Gintare

4.14. Cardiac troponin (cTn)

Observable	
Name	Cardiac troponin (cTn) (I and T)
Type	Clinically measured
Data type	Real
Unit	µg/L or ng/mL
Values/range	NormL: Troponin I : <10 µg/L or <0.01 ng/ml; troponin T : 0–0.1 µg/L (normal value ranges may vary slightly among different laboratories) Abnormal: Value exceeding the 99th percentile of a normal reference (upper reference limit (URL))
Author	Gintare

4.15. Chronic kidney disease stage 3-5

Observable

name:	chronic kidney disease stage 3-5
type:	biomedical
Data type:	yes/no
Unit:	N/A
Normal values	N/A
abnormal values/range	patients with estimated glomerular filtration rates (eGFRs) < 60 ml/min/1.73m^2(estimated by the 4-variable Modification of Diet in Renal Disease [MDRD] equation)
Author	Neringa

4.16. Cholesterol Total

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)
Author	Gintare

4.17. Creatine kinase MB fraction

Observable	
Name	Creatine kinase MB fraction (CK-MB)
Type	clinical
Data type	real
Unit	U/l
Values/range	Normal: 0-5 Abnormal: >5
Author	Zydrune

4.18. Current use of antihypertensive medication

Observable	
Name	current use of antihypertensive medications
Type	personal
Data type	Yes/no

Unit	N/A
Values/range	N/A
Author	Neringa

4.19. Dilated cardiomyopathy

Observable	
Name	Dilated cardiomyopathy
Type	clinical
Data type	Yes/no
Unit	
Values/range	DCM requires evidence of dilatation (LV diastolic diameter <5,3 cm for female; LV diastolic diameter <5.9 cm for male) and impaired contraction of the left ventricle or both ventricles (eg, left ventricular ejection fraction <40 percent or fractional shortening less than 25 percent).
Author	Neringa

4.20. Diabetes Medication

Observable	
Name	Doctor's diagnosis of diabetes
Type	Pacient history
Data type	Date from doctor's diagnosis
Unit	-
Values/range	
Author	Gintare

4.21. Drug intake: insulin or an oral hypoglycemic drug

Observable	
Name	Use of insulin or an oral hypoglycemic drug
Type	personal
Data type	Yes/No
Unit	
Values/range	
Author	Zydrune

4.22. Drug intake: medication for hypertension

Observable	
Name	Reported use of a medication for hypertension
Type	Patients medical history
Data type	Yes/No
Unit	
Values/range	
Author	Zydrune

4.23. ECG

Observable	
Name	ECG
Type	Biomedical
Data type	2D signal
Unit	
Values/range	Abnormal: Hyperacute T wave changes - increased T wave amplitude and width; may also see ST elevation Marked ST elevation with hyperacute T wave changes (transmural injury) Pathologic Q waves, less ST elevation, terminal T wave inversion (necrosis) (Pathologic Q waves are usually defined as duration ≥ 0.04 s or ≥ 25% of R-wave amplitude) Pathologic Q waves, T wave inversion (necrosis and fibrosis) Pathologic Q waves, upright T waves (fibrosis)
Author	Stefanos

4.24. ECG: Q waves

Observable	
Name	Pathologic Q waves on ECG
Type	biomedical
Data type	
Unit	S and mm (mV)
Values/range	Normal: <0.04 s and <1/4 of R amplitude in mm (mV) Abnormal: ≥0.04 s and ≥1/4 of R amplitude in mm (mV)
Author	Zydrune

4.25. ECG: ST Elevation

Observable	
Name	ST elevation on ECG
Type	biomedical
Data type	
Unit	mm (mV)
Values/range	Normal < 1 mm (0.1 mV) elevation in the limb leads (I, II, III) < 2 mm (0.2 mV) in the precordial leads (V1-V6) Abnormal ≥1 mm (0.1 mV) elevation in the limb leads (I, II, III) ≥2 mm (0.2 mV) elevation in the precordial leads (V1-V6)
Author	Zydrune

4.26. 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
Author	Steafnos, Gintare, Zydrune

4.27. Ejection fraction

Observable	
Name	Ejection fraction (EF)
Type	Clinically measured by echocardiograhy
Data type	Real
Unit	%
Values/range	Normal: 55-70% Abnormal: <55%
Author	Gintare

4.28. Electrocardiographic changes

Observable	
Name	Electrocardiographic changes
Type	clinical
Data type	integer
Unit	µV · s
Values/range	normal: [(SV3+RaVL)xQRS duration] <244 abnormal: [(SV3+RaVL)xQRS duration] >244
Author	Neringa

4.29. Endurance time

Observable	
Name	Endurance time
Type	behavioural
Data type	integer
Unit	minutes
Values/range	< 5
Author	Stefanos

4.30. EQ-5D , SF-36 questionnaires

Observable	
Name	EQ-5D , SF-36 questionnaires
Type	behavioural
Data type	answers
Unit	-
Values/range	-
Author	Stefanos

4.31. FEV1/FVC

Observable	
Name	FEV1/FVC
Type	clinical
Data type	real
Unit	-

Values/range	Normal: >0.70 Abnomral: <0.70
Author	Kalliopi

4.32. Fluid balance

Observable	
Name	Fluid balance
Type	Clinically measured, personal
Data type	Calculated, state signs (peripheral edema, increased body weight, pulmonary edema, and elevated central venous pressure with or without a significant level of hyponatremia), assessed by bioimpedence vector analysis
Unit	Hypervolemia signs (peripheral edema, increased body weight, dyspnea)
Values/range	
Author	Gintare

4.33. Haemoglobin (Hb)

Observable	
Name	Haemoglobin (Hb)
Type	biomedical
Data type	integer
Unit	**g/dL**
Values/range	Normal: >13 for men, >12g/dL for women Abnormal: <13 g/dL for men, <12g/dL for women
Author	Stefanos, Gintare

4.34. HbA1c

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

4.35. Hearing test

Observable	
Name	Hearing test
Type	biomedical
Data type	
Unit	dB
Values/range	Abnormal: loss of greater than 30 dB in three contiguous frequencies in less than 3 days
Author	Stefanos

4.36. Heart rate (90 beats/min) + 10 beats increments

Observable	
Name	Heart rate
Type	personal
Data type	integer
Unit	beats/min
Values/range	Normal: >90 Abnormal: 90 beats/min + 10 beats increments
Author	Neringa

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

Observable	
Name	High-density lipoprotein cholesterol (HDL-C)
Type	Clinically measured
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
Author	Gintare

4.38. History of coronary heart disease (CHD) or stroke

Observable	
Name	History of coronary heart disease (CHD) or stroke

Type	Pacient history
Data type	Data from pacient history
Unit	-
Values/range	
Author	Gintare

4.39. Hyperkalemia

Observable	
Name	hyperkalemia
Type	clinical
Data type	real
Unit	mEq/L
Values/range	Normal: 3.5-5.3 mEq/L Moderate hyperkalemia: serum potassium values in the 5.0 to 6.0 mEq/liter (5.0-6.0 mmol/L) range Significant hyperkalemia: a serum potassium value >6.0 mEq/liter (>6.0 mmol/L).
Author	Neringa

4.40. Intracoronary thrombus by angiography

Observable	
Name	An intracoronary thrombus by angiography
Type	clinical
Data type	integer
Unit	
Values/range	
Author	Zydrune

4.41. Ischemic heart disease, when LVEF ≥30%

Observable	
Name	Ischemic heart disease, when LVEF ≥30%
Type	clinical
Data type	yes/no
Unit	
Values/range	Normal: LVEF >55% Abnormal: LVEF ≥30%

Author	Neringa

4.42. Killip class III

Observable	
Name	Killip class III
Type	clinical
Data type	Yes/no
Unit	
Values/range	Abnormal: Acute pulmonary edema, a history of an acute cardiac event; physical examination shows: a low-flow state, an S_3 gallop, jugular venous distention, crackles on auscultation.
Author	Neringa

4.43. Killip class IV

Observable	
Name	Killip class IV
Type	clinical
Data type	yes/no
Unit	N/A
Values/range	
Author	Neringa

4.44. Left ventricular hypertrophy

Observable			
Name	Left ventricular hypertrophy (LVH)		
Type	Clinically measured (ECG, echocardiography)		
Data type	Electrocardiographic changes	Electrocardiographic changes	
Unit	integer	integer	
Values/range	Millivolt or millimetres	µV · s	g/m^2
Author	Normal sum of S wave in V1 and R wave in V5 or V6 ≤3.5 mV (35 mm) and/or R wave in aVL ≤1.1 mV (11 mm)	[(SV3+RaVL)xQRS duration] <244	<150

	Abnormal sum of S wave in V1 and R wave in V5 or V6 ≥3.5 mV (35 mm) and/or R wave in aVL ≥1.1 mV (11 mm)	[(SV3+RaVL)xQRS duration] >244	>150

4.45. Left ventricular mass index

Observable	
Name	Left ventricular mass index (echocardiographic parameter, left ventricular mass (g)=1.04 [(LVID+VST+PWT)3-(LVID)3]- 13.6, where LVID is left ventricular internal dimension, VST is ventricular septal thickness, and PWT is posterior left ventricular wall thickness.)
Type	clinical
Data type	real
Unit	g/m
Values/range	
Author	Neringa

4.46. Left ventricular wall thickness

Observable	
Name	left ventricular wall thickness (echocardiographic parameter, sum of VST and PWT, VST is ventricular septal thickness, and PWT is posterior left ventricular wall thickness)
Type	clinical
Data type	real
Unit	mm
Values/range	
Author	Neringa

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

Observable	
Name	Low-density lipoprotein cholesterol (LDL-C)
Type	Clinically measured
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
Author	Gintare

4.48. Metabolic Equivalent (MET)

Observable	
Name	Metabolic equivalent
Type	personal
Data type	real
Unit	hours of activity/week
Values/range	> 0
Author	Dimitris

4.49. New loss of viable myocardium or a new regional wall motion abnormality

Observable	
Name	An intracoronary thrombus by angiography
Type	clinical
Data type	integer
Unit	
Values/range	
Author	Zydrune

4.50. Oxidized LDL levels

Observable	
Name	Oxidized LDL levels
Type	clinical
Data type	integer
Unit	U/L
Values/range	Normal Men</=74, women</=69,4 Abnormal Men>74, women>69,4
Author	Kalliopi

4.51. Oxygen desaturation index (ODI)

Observable	
Name	Oxygen desaturation index (ODI)
Type	clinical
Data type	integer
Unit	the number of times per hour of sleep that the blood's oxygen level drops by 3 percent or more from baseline
Values/range	Normal: 3% ODI < 5 per hour Mild OSA: 3% ODI of 5 to <15 per hour; Moderate-severe OSA: 3% ODI of ≥15 per hour
Author	Gintare

4.52. Physical Exercise

Observable	
Name	physical exercise
Type	personal
Data type	integer
Unit	Minutes of exercise
Values/range	suggested: 30minutes, 5 times per week
Author	Stefanos

4.53. Plasma B-type natriuretic peptide

Observable	
Name	Plasma B-type natriuretic peptide (BNP)
Type	clinical
Data type	integer
Unit	pg/mL
Values/range	Normal: <200 pg/mL: likely compensated congestive heart failure (CHF) Abnormal ≥200 to ≤400 pg/mL: likely moderate CHF >400 pg/mL: likely moderate-to-severe CHF
Author	Zydrune

4.54. Potassium – sparing diuretics

Observable

Name	Potassiun-sparing diuretics
Type	intervention
Data type	Yes/no
Unit	
Values/range	
Author	Neringa

4.55. Prior cerebrovascular disease

Observable	
Name	Prior cerebrovascular disease
Type	personal
Data type	Yes/no
Unit	
Values/range	
Author	Neringa

4.56. Pulse wave velocity (PWV)

Observable	
Name	Pulse wave velocity (PWV)
Type	Clinically measured
Data type	Calculated from measurements of pulse transit time and the distance traveled by the pulse between two recording sites: PWV=Distance (meters)/Transit Time (seconds)
Unit	m/s
Values/range	
Author	Gintare

4.57. Salt intake

Observable	
Name	Salt intake
Type	behavioural
Data type	integer
Unit	gr/day
Values/range	Normal: 0-5 Abnormal: > 5 (5-10)

Author	Stefanos

4.58. 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
Author	Stefanos

4.59. Smoking Amount

Observable	
Name	Smoking amount
Type	Personal
Data type	Integer
Unit	Cigarettes/day
Values/range	No cigarettes 1 and more cigarettes
Author	Gintare

4.60. Smoking Status

Observable	
Name:	Smoking status
Type:	Personal
Data type:	From pacient history
Unit:	-
Abnormal values/range	Never smoker Ex-smoker (past) Current smoker
Author	Dimitris, Gintare

4.61. Sokolow – Lyon criteria

Observable	
Name	Sokolow – Lyon criteria
Type	clinical
Data type	integer
Unit	Millivolt or millimetres
Values/range	Normal sum of S wave in V1 and R wave in V5 or V6 ≤3.5 mV (35 mm) and/or R wave in aVL ≤1.1 mV (11 mm) Abnormal sum of S wave in V1 and R wave in V5 or V6 ≥3.5 mV (35 mm) and/or R wave in aVL ≥1.1 mV (11 mm)
Author	Neringa

4.62. Spirometry

Observable	
Name	Spirometry
Type	Clinically measured
Data type	Real
Unit	%
Values/range	The lower limit of normal for FEV1/FVC – 70-75% (the exact limit depends on age, sex, height) and FEV1 80-120% predicted Stage I (mild COPD): FEV1/FVC<0.70; FEV_1≥ 80% predicted. Stage II (moderate COPD): FEV1/FVC<0.70; FEV_1 50-79% predicted. Stage III (severe COPD): FEV1/FVC<0.70; FEV_1 30-49% predicted. Stage IV (very severe COPD): FEV1/FVC<0.70; FEV_1 <30% predicted, or <50% normal with chronic respiratory failure present. (Based on post-bronchodilator FEV1)
Author	Gintare

4.63. Triglycerides (TG)

Observable	
Name	Triglycerides (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)
Author	Gintare

4.64. 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%
Author	Larynas

4.65. 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
Author	Kalliopi

4.66. 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
Author	Kalliopi

4.67. 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
Author	Kalliopi

4.68. Valvular heart disease

Observable	
Name	Valvular heart disease
Type	clinical
Data type	Yes/no
Unit	
Values/range	
Author	Neringa

5. Evidence Sources

5.1. PMID = 02496858

Evidence source PMID	2496858
Evidence source	Shinton R, Beevers G. Meta-analysis of relation between cigarette smoking and stroke. BMJ. 1989;298(6676):789-94.
Evidence source type	Meta-analysis
OCEBM Level	
Author	Dimitris

5.2. PMID = 08025994

Evidence source	8025994
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	
OCEBM Level	III
Author	Neringa

5.3. PMID = 09552903

Evidence source PMID	9552903
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	
Author	Dimitris

5.4. 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	
Author	Kalliopi

5.5. PMID = 10209001

Evidence source PMID	10209001
Evidence source	Jouven X, Desnos M, Guerot C, Ducimetière P. Predicting Sudden Death in the Population: The Paris Prospective Study I. Circulation. 1999;99:1978-1983
Evidence source type	Prospective study
OCEBM Level	
Author	Gintare

5.6. PMID = 10704162

Evidence source	Rathore SS, Berger AK, Weinfurt KP, Schulman KA, Oetgen WJ, Gersh BJ, Solomon AJ. Acute myocardial infarction complicated by atrial fibrillation in the elderly: prevalence and outcomes.Circulation. 2000 Mar 7;101(9):969-74.
Evidence source PMID	10704162
Evidence source type	Cohort study
OCEBM Level	III?
Author	Neringa

5.7. 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	
Author:	Gintare

5.8. PMID = 10979786

Evidence source PMID	10979786
Evidence source	Bell DS. Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. N Engl J Med. 2000 Aug 24;343(8):580.
Evidence source type	Prospective cohort studies
OCEBM Level	
Author:	

5.9. PMID = 11352882

Evidence source PMID	11352882
Evidence source	Sundström J, Lind L, Arnlöv J, Zethelius B, Andrén B, Lithell HO. Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men. Circulation. 2001 May 15;103(19):2346-51.
Evidence source type	Comparative Study
OCEBM Level	III
Author:	

5.10. 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	
Author	Gintare

5.11. PMID = 12075249

Evidence source PMID	12075249
Evidence source	Murabito JM, Evans JC, Nieto K, Larson MG, Levy D, Wilson PW. Prevalence and clinical correlates of peripheral arterial disease in the Framingham Offspring Study. Am Heart J. 2002 Jun;143(6):961-5.
Evidence source type	Cohort study
OCEBM Level	
Author	Kalliopi

5.12. PMID = 12151467

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

5.13. PMID = 12353942

Evidence source PMID	12353942
Evidence source:	Shlipak MG, Heidenreich PA, Noguchi H, Chertow GM, Browner WS, McClellan MB. Association of renal insufficiency with treatment and outcomes after myocardial infarction in elderly patients. Ann Intern Med. 2002 Oct 1;137(7):555-62
Evidence source type:	Cohorts study
OCEBM Level	
Author	Gintare

5.14. 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	
Author	Gintare

5.15. 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	
Author	Laurynas

5.16. 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	
Author	Stefanos

5.17. PMID = 15086929

Evidence source PMID	15086929
Evidence source:	Iseki K, Ikemyia Y, Kinjo K, Inoue T, Iseki Ch, Takisita Sh, Body mass index and the risk of development of end-stage renal disease in a screened cohort. Kidney Int 2004;65:1870–1876.
Evidence source type:	Cohort study
OCEBM Level	
Author	Laurynas

5.18. PMID = 15380802

Evidence source PMID	15380802
Evidence source:	Anum EA, Adera T. Hypercholesterolemia and Coronary Heart Disease in the Elderly: A Meta-analysis. Ann Epidemiol. 2004 Oct;14(9):705-21
Evidence source type:	Meta-analysis
OCEBM Level	
Author	Gintare

5.19. 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	
Author	Stefanos

5.20. 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	
OCEBM Level	
Author	Kalliopi

5.21. PMID = 15562129

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

5.22. PMID = 16221806

Evidence source PMID	16221806
Evidence source:	Mondul AM, Rodriguez C, Jacobs EJ, Calle EE. Age at Natural Menopause and Cause-specific Mortality. Am J Epidemiol 2005;162:1089–1097
Evidence source type:	Prospective cohort study
OCEBM Level	
Author	Gintare

5.23. 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	OCEBM Level I
Author	Gintare

5.24. PMID = 16400046

Evidence source PMID	16400046
Evidence source	Weinbrenner T, Schröder H, Escurriol V, Fito M, Elosua R, Vila J, Marrugat J, Covas MI. Circulating oxidized LDL is associated with increased waist circumference independent of body mass index in men and women. Am J Clin Nutr. 2006 Jan;83(1):30-5; quiz 181-2.
Evidence source type	cross-sectional study
OCEBM Level	
Author	Kalliopi

5.25. 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	
Author	Laurynas

5.26. 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	
Author	Gintare

5.27. PMID = 17276778

Evidence source PMID	17327354
Evidence source	Phrommintikul A, Haas SJ, Elsik M, Krum H. Mortality and target haemoglobin concentrations in anaemic patients with chronic kidney disease treated witherythropoietin: a meta-analysis. Lancet. 2007 Feb 3;369(9559):381-8.
Evidence source type	Meta-analysis
OCEBM Level	
Author	Stefanos

5.28. 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	
Author	Dimitris

5.29. 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	
Author	Dimitris

5.30. PMID = 18003763

Evidence source PMID	18003763
Evidence source:	Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality inrenal patients--absence of evidence or evidence of absence? Clin J Am Soc Nephrol. 2008 Jan;3(1):226-36. Epub 2007 Nov 14.
Evidence source type:	Review
OCEBM Level	
Author	Stefanos

5.31. PMID = 18082090

Evidence source PMID	18082090
Evidence source:	Medrano MJ, Pastor-Barriuso R, Boix R. del Barrio JL, Damián J, Álvarez R, Marínc A, on behalf of the ZACARIS study research group. Coronary Disease Risk Attributable to Cardiovascular Risk Factors in the Spanish Population. Rev Esp Cardiol. 2007;60(12):1250-6
Evidence source type:	Cohort study
OCEBM Level	
Author	Gintare

5.32. PMID = 18539916

Evidence source PMID	18539916
Evidence source	ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompoint S, de Galan BE, Joshi R, Travert F. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008 Jun 12;358(24):2560-72. doi: 10.1056/NEJMoa0802987. Epub 2008 Jun 6.
Evidence source type	Multi-center, randomized, controlled trial
OCEBM Level	

Author	Stefanos

5.33. PMID = 19109347

Evidence source PMID	19109347
Evidence source	Schmitt J, Duray G, Gersh BJ, Hohnloser SH. Atrial fibrillation in acute myocardial infarction: a systematic review of the incidence, clinical features and prognostic implications. Eur Heart J.2009 May;30(9):1038-45. doi: 10.1093/eurheartj/ehn579. Epub 2008 Dec 24.
Evidence source type	Systematic review
OCEBM Level	I
Author	Neringa

5.34. 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	
Author	Kalliopi

5.35. 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	
Author	Gintare

5.36. PMID = 19520994

Evidence source PMID	19520994
Evidence source	Asplund K, Karvanen J, Giampaoli S, Jousilahti P, Niemelä M, Broda G, Cesana G, Dallongeville J, Ducimetriere P, Evans A, Ferrières J, Haas B, Jorgensen T,

	Tamosiunas A, Vanuzzo D, Wiklund PG, Yarnell J, Kuulasmaa K, Kulathinal S; MORGAM Project. Relative risks for stroke by age, sex, and population based on follow-up of 18 European populations in the MORGAM Project. Stroke. 2009 Jul;40(7):2319-26.
Evidence source type	Prospective stroke study
OCEBM Level	
Author	Kalliopi

5.37. 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	
Author	Kalliopi

5.38. 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	
Author	Gintare

5.39. PMID = 19945950

Evidence source PMID	19945950
Evidence source	Afshinnia F, Wilt TJ, Duval S, Esmaeili A, Ibrahim HN. Weight loss and proteinuria: systematic review of clinical trials and comparative cohorts. Nephrol Dial Transplant. 2010 Apr;25(4):1173-83. doi: 10.1093/ndt/gfp640. Epub 2009 Nov 27.
Evidence source type	systematic review of clinical trials and comparative cohorts
OCEBM Level	
Author	Stefanos

5.40. PMID = 20193969

Evidence source PMID	20193969
Evidence source	Pecini R, Møller DV, Torp-Pedersen C, Hassager C, Køber Heart failure etiology impacts survival of patients with heart failure. L.Int J Cardiol. 2011 Jun 2;149(2):211-5. doi: 10.1016/j.ijcard.2010.01.011. Epub 2010 Mar 2.
Evidence source type	Clinical Trial; Comparative Multicenter Study
OCEBM Level	
Author	Neringa

5.41. 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
OCEBM Level	
Author	Kalliopi

5.42. PMID = 20842429

Evidence source PMID	20842429
Evidence source:	Mustata S, Groeneveld S, Davidson W et al Effects of exercise training on physical impairment, arterial stiffness and health-related quality of life in patients with chronic kidney disease: a pilot study.. Int Urol Nephrol 201
Evidence source type:	Prospective randomized controlled pilot study
OCEBM Level	
Author	Stefanos

5.43. PMID = 21406649

Evidence source PMID	21406649
Evidence source:	Palmer S.C., Hayen A., Macaskill P., Pellegrini F., Craig J.C., Elder G.J., Strippoli G.F.M. Serum Levels of Phosphorus, Parathyroid Hormone, and Calcium and Risks of Death and Cardiovascular Disease in Individuals With Chronic Kidney Disease: A Systematic Review and Meta-analysis, JAMA. 2011;305(11):1119-1127.
Evidence source type:	Systematic Review and Meta-analysis
OCEBM Level	
Author	Laurynas

5.44. 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	II-III
Author	Laurynas

5.45. 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	
Author	Gintare

5.46. 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	
Author	Laurynas

5.47. 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	III
Author	Neringa

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Evidence source PMID	22232539
Evidence source	Harel Z, Gilbert C, Wald R, Bell C, Perl J, Juurlink D, Beyene J, Shah PS. The effect of combination treatment with aliskiren and blockers of the renin-angiotensin system on hyperkalaemia and acute kidney injury: systematic review and meta-analysis. BMJ. 2012 Jan 9; 344:e42.
Evidence source type	Systematic review and meta-analysis
OCEBM Level	
Author	Laurynas

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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	
Author	Neringa

5.50. 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	
Author	Dimitris

5.51. 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	Meta-analysis
OCEBM Level	

Author	Stefanos

5.52. 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:	Meta-analysis
OCEBM Level	
Author	Gintare

5.53. PMID = 22912709

Evidence source PMID	22912709
Evidence source	Zhang Y, Hu G, Yuan Z, Chen L. Glycosylated hemoglobin in relationship to cardiovascular outcomes and death in patients with type 2 diabetes: a systematic review and meta-analysis. PLoS One. 2012;7(8):e42551. doi: 10.1371/journal.pone.0042551.
Evidence source type	meta-analysis of prospective cohort studies
OCEBM Level	OCEBM Level I
Author	Zydrune

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Evidence source PMID	22927011
Evidence source	Lin C, Hsu HT, Lin YS, Weng SF. Increased risk of getting sudden sensorineural hearing loss in patients with chronic kidney disease: a population-based cohort study. Laryngoscope. 2013 Mar;123(3):767-73. doi: 10.1002/lary.23669. Epub 2012 Aug 24.
Evidence source type	retrospective cohort study
OCEBM Level	
Author	Stefanos

5.55. 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	
Author	Gintare

5.56. 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	
Author	Kalliopi

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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:	Cohorts study
OCEBM Level	
Author	Gintare

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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	
Author	Kalliopi

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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	
Author	Dimitris

5.60. PMID = 23351816

Evidence source PMID	23319662
Evidence source:	McDonald JS, McDonald RJ, Comin J, Williamson EE, Katzberg RW, Murad MH, Kallmes DF. Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. Radiology 2013; 267(1):119-28
Evidence source type:	systematic review and meta-analysis
OCEBM Level	
Author	Dimitris, Gintare

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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	
Author	Laurynas

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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	
Author	

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Evidence source PMID	23766260
Evidence source:	Isaacs A, Willems SM, Bos D, Dehghan A, Hofman A, Arfan Ikram M, Uitterlinden AG, Oostra BA, Franco OH, Witteman JC, van Duijn CM. Risk Scores of Common Genetic Variants for Lipid Levels Influence Atherosclerosis and Incident Coronary Heart Disease. Arterioscler Thromb Vasc Biol 2013;33:2233-2239. doi:10.1161/ATVBAHA.113.301236
Evidence source type:	Cohorts study
OCEBM Level	
Author	Gintare

5.64. 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:	A systematic review and analysis
OCEBM Level	
Author	Gintare

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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	
Author	Dimitris

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Evidence source	Farrokhi F, Abedi N, Beyene J, Kurdyak P, Jassal SV. Association between depression and mortality in patients receiving long-term dialysis: a systematic review and meta-analysis. Am J Kidney Dis. 2014 Apr;63(4):623-35.
Evidence source type	Systematic review and meta-analysis
OCEBM Level	
Author	Laurynas

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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	
Author	Kalliopi

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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
OCEBM Level	
Author	Laurynas

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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	
Author	Kalliopi

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Evidence source PMID	24886432
Evidence source:	Batty GD, Russ TC, Starr JM, Stamatakis E, Kivimäki M. Modifiable cardiovascular disease risk factors as predictors of dementia death: pooling of ten general population-based cohort studies. J Negat Results Biomed. 2014 May 23;13:8. doi: 10.1186/1477-5751-13-8
Evidence source type:	Population-based cohort studies
OCEBM Level	
Author	Gintare

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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	
Author	Stefanos