In our study we use two approaches, a first one detecting topics across the collection of publications, and a second one that maps document networks into clusters of documents with an identifiable subject of research. In this Supplement we expand on the methodology and include some additional results.

**Source data and pre-processing**

The dataset includes the reference, abstract, address, and citation data for 478,006 cardiovascular publications from 2004 to 2013. These publications were published across 5537 journals, with 128 core cardiovascular journals representing 36% of all publications included in this dataset. The document set include cardiovascular publications in leading general journals in medical and life sciences (Table S1).

**Table 1. Publications from broader biomedical and multi-disciplinary journals (2004-2013).**

| Journal                                      | Number of publications |
|----------------------------------------------|------------------------|
| JOURNAL OF BIOLOGICAL CHEMISTRY             | 2055                   |
| NEW ENGLAND JOURNAL OF MEDICINE             | 1869                   |
| JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION | 1641               |
| ARCHIVES OF INTERNAL MEDICINE               | 1228                   |
| LANCET                                       | 1069                   |
| ANNALS OF INTERNAL MEDICINE                 | 712                    |
| JOURNAL OF CLINICAL INVESTIGATION           | 657                    |
| ANNALS OF THE NEW YORK ACADEMY OF SCIENCES  | 649                    |
| BMJ-BRITISH MEDICAL JOURNAL                 | 356                    |
| SCIENCE                                      | 108                    |
| CELL                                         | 107                    |
| **Total**                                   | **10451**              |

As previously described, key cardiovascular terms were searched in the Web of Science to identify the publication dataset. The Web of Science was chosen for several reasons: it has the advantage of a well-curated dataset, with extensive and structured information (addresses of all authors, indexing of included references) that allows the use of citations and cross-references. The main limitations of Web of Science is that it may not include all relevant publications because it does not include all national journals that are not published (or do not include abstracts) in English. If certain countries are focusing on very innovative work and publishing the results in their own national journals then there is indeed a risk that new and emerging research is not identified until it is included in the mainstream English language/high impact journals. This is potentially a limitation for identifying novel research (especially if it goes against current scientific status quo). On the other hand, it is now generally accepted that English has become the main vehicular language for science.

The full description of how the dataset of 478,006 cardiovascular publications was identified was described previously and the flow and processing illustrated in Figure S1, is re-iterated briefly. The approach combined a terms search (terms validated by experts) with cross-referencing, combining a core...
set of journals with journals that were identified as having a major cardiovascular component. The method went through several iterations to ensure a sufficiently wide, yet specific dataset.

**Figure S1. Developing an unbiased approach to identify topics in cardiovascular research publication output.**

Step 1-4 is the first approach resulting in 175 topics that cover all documents, with documents present in multiple topics. Step 5-6 is the second approach in which documents are uniquely assigned to clusters. Step 7 compares the content from the two approaches. Note the expert input at many stages of the process.
For building clusters, the references were also considered. We obtained the data from Clarivate Analytics Web of Science Core Collection (WoS) through a custom data license held by ECOOM, KU Leuven.

For all titles and abstracts, we extracted the noun phrases (text fragments of various lengths) using the natural language processing framework developed at Stanford. We also removed all copyright notices at the end of any abstract, all expressions containing numbers and all white spaces, and then removed the most commonly used text fragments based on the h-score, i.e. those text fragments with the highest rank based on their number of occurrences in the dataset.

**Topic modelling**

For this approach, we applied Latent Dirichlet Allocation (LDA) to the text fragments from all publications using MalletR. This approach groups text fragments to identify topics and also allocates documents to topics. The analysis provides us with the probabilities for each text fragment to belong to a topic (beta). High beta values group text fragments that potentially identify a topic. Second, the analysis provides the probabilities for each document to belong to a topic (gamma), across 200 topics. The result is that every text fragment and every publication is linked to every topic, but each text fragment and each document will have a lower or higher probability (ranging from 0 to 1) of being part of any given topic. Therefore, a document can belong to several topics.

Twelve cardiovascular experts reviewed each set of the top 40 text fragments with the highest probability (beta) of representing a topic, using an online questionnaire. The experts validated whether the text fragments identified a cardiovascular topic and were asked to suggest a name for each cardiovascular topic. All cardiovascular topics were included where at least two experts agreed that the text fragments represented a cardiovascular topic. A second round of expert review was undertaken as a discussion between three experts to agree on a suitable name for topics, where the suggested names for the topics differed between experts from the initial online questionnaire. A final review of all topics ensured naming consistency across the topics and allowed for additional expert-based classification as clinical, basic or population research. In addition, we selected a number of specific terms of interest to search for them in the text fragments, in the topics and in the documents.

Of the 200 potential topics detected by the LDA model, the cardiovascular experts agreed that 175 were cardiovascular topics and suggested labels for each of the 175 topics (see full list in Table S1). Excluded topics were related to general study protocol terms, as well as, areas of weakly linked research such as subtopics in gastroenterology or nephrology where a clear cardiovascular term was missing. Of note, general terms or terms that are used frequently across the majority of documents are filtered out as part of the methodology, resulting in groups of highly specific text fragments and, consequently, topics as illustrated here.

### Inflammation - mechanisms and mediators

NLP text fragments about experimental models to induce inflammation (LPS) and the study of cytokines.

| LPS induc | chemotax protein | bind activ |
|---|---|---|
| toll like | monocyt chemotact protein | lps stimul |
| toll like receptor | alpha interleukin | inflammatori gene |
| tumour necrosi | inflammatori mediat | tumor necroisi factor alpha interleukin |
| tumour necrosi factor | cytokin product | endotoxin induc |
| alpha level | antinflammatori properti | after lps |
| alpha il | necrosi factor alpha interleukin | dna bind |
| nf kappab | factor alpha interleukin | anti infl ammatori cytokin |
| tumour necrosi factor alpha | cytokin level | cytokin express |
| tnfalpha il | alpha express | induc inflammatori |
| tnf alpha level | inflammatori properti | alpha product |
| monocyt chemotact | beta il | nf kb |
| lipopolysaccharid induc | inflammatori activ | induc il |
Inflammation biomarkers

NLP text fragments about CRP, serum levels and identifying subgroups of subjects.

| hs crp level | inflammatori biomark | increas serum |
|-------------|----------------------|--------------|
| signific posit | corrol signific | elev serum |
| multipl linear | gender match | level did |
| multipl linear regres | level correl | multivari linear |
| crp concentr | apparr healthi | agematch healthi |
| signific negat | match healthi control | higher serum |
| signific posit corre | signific negat corre | sensi crp |
| healthi control subject | protein concentr | Independ determin |
| corre posit | level compar | signific invers |
| serum crp | ml respect | multipl logist |
| ml vs | signific relationship | elev crp |
| group consist | higher plasma | we enrol |
| agematch control | negat associ | multivari linear regres |

Coronary artery disease - CABG, techniques

NLP text fragments about vessels used and surgical methods and evaluation

| thorac arteri | myocardi re vascular | left intern thorac |
|-------------|----------------------|------------------|
| intern thorac | pump ca bg | dure coronari |
| intern thorac arteri | coroni bypass surgeri | left intern thorac arteri |
| arteri graft | left intern mammari | coronari bypass graft |
| intern mammari | pump coronari arteri bypass surgeri | elect coronari arteri |
| mammari arteri | left intern mammari arteri | patient undergo coronari arteri |
| pump coronari arteri bypass graft | undergo coronari arteri | thorac arteri graft |
| intern mammari arteri | off pump cabg | intern thorac arteri graft |
| offpump coronari arteri bypass graft | offpump coronari arteri bypass surgeri | pump group |
| left intern | undergo coronari arteri bypass | elect coronari arteri bypass |
| graft patenc | patenc rate | patient undergo coronari arteri bypass |
| beat heart | elect coronari | after off |
| saphen vein graft | coronari surgeri | pump surgeri |

Figure S2. Examples of text fragments underlying specific topics.

We counted the number of documents per topic, by identifying all documents that had greater than 10% gamma (probability) of belonging to that topic. These data underlie the graphs in Figures 1-3. We then calculated the co-occurrence of topics in each document, by counting the number of times each pair of topics occurs in the documents. This network data was then imported the VOSviewer software to undertake a network analysis and create a topic map, visualizing these topic inter-relations.

**Document clustering**

For this approach, the dataset was reduced to two time periods, and we analyzed the cardiovascular publications from 2006-2008 and those from 2011-2013, separately. For each time period, we then calculated the similarities between documents based on the noun phrase text fragments, and based on the references in the documents, using adapted cosine calculations and a hybrid document clustering algorithm, as previously described. We then applied the Louvain community detection algorithm to identify clusters of similar documents. For this method, each document is only located in one cluster. Subsequently, we applied the DrL/OpenOrd algorithm to map and visualise the documents and clusters. We used R in a high-powered cloud-based parallelized computing environment for all operations. We then identified the core documents in each of the clusters. In addition, we described the most common text fragments used in each document cluster, as well as, the most highly cited documents and the most productive authors in each cluster. These four elements were used in an expert review to describe the clusters.
Combining topic modelling and document clustering
As a next step, for each cluster we identified the most highly representative topics from the LDA topic model. To compare the results of the approaches, we limited the topic model dataset to the two time periods 2006-2008 and 2011-2013 and then linked the documents from the topic model results to the documents in the clusters using a unique identifier for each document. We then calculated the average gamma (document-topic probability) for all documents in each cluster. Thereby we identified the most highly represented topics in each of the document clusters in each time period.

Properties of the topic groups
Almost 4 million unique text fragments, from 475,593 document abstracts published from 2004 to 2013, were combined in the LDA topic model to detect 200 potential cardiovascular topics. Experts reviewed and identified 175 of the topics to be true cardiovascular topics. All topics contained at least 1700 documents and the majority contained between 1700 and 15,000 documents. The smallest topic on Lipids - cholesterol metabolism was present in 1791 documents. Seven leading topics were present in 15,000 or more documents, with the largest topic- Evidence-guided treatment being present in 49,031 documents. On average, each document contained three topics, with the majority of documents containing two to five topics.

Properties of document clusters
The hybrid clustering algorithm (based on text and references) brought the publications together into 15 clusters for 2006-2008 and into 18 clusters for 2011-2013. The size of the clusters varied between 59 and 42,000 documents. Then the algorithm was repeated separately for each of the clusters, to identify any subclusters within each cluster. The number of subclusters per cluster varied between 1 and 27, and 15 and 18 clusters per dataset had more than one subcluster. The number of publications per subcluster also varied with one-third of all the subclusters having less than 100 publications, while the largest subclusters had over 5000 publications. The process of labelling the clusters was not automatic and was therefore limited to the ten largest clusters, which included >90% of all documents in each time period and thus adequately representing the data set. Of these 20 clusters, the naming posed difficulties for one clusters, for which the content was unclear and 4 others with uncertainty whether the content was adequately described.

In a later stage clusters were linked to the LDA topics validating the naming and resolving the uncertainties. Only cluster 2 of the period 2006-2008 presents LDA topic labels that do not seem to match with the document cluster name: cell signaling, vascular function – endothelial control and MI in the LDA topics with a document cluster focus on pulmonary hypertension. Therefore, an expert reviewed the document titles of the four largest subclusters. These four subclusters seem to correlate with the LDA topics, with the expert naming the subclusters as ‘pulmonary hypertension’, ‘endothelial function and vascular tone’, ‘cell signaling for growth’, as well as, ‘ischemia and myocardial infarction’.

**Country participation in main document clusters**

We analyzed the authors’ origin in the documents within the two main clusters of the period 2011-2013. The figure represents the main contributors, covering the majority of documents in the clusters. Although the USA is the major single country, combining EU countries results in a higher fraction still. Of note is the large contribution from the PR China in the cluster ‘Gene and cell therapy and innovation’.

![Population risk factors CVD and gene & cell therapy, iPSC,..](image)

**Constraints and limitations of the methodology**

For the topic modelling we needed to define the number of topics a priori, requiring qualitative review to assess the validity, overlap and granularity of the topics. A larger number of topics could have potentially identified more specific and smaller topics. Although twenty-five topics were excluded, all publications remained in the analysis. In addition, only a small number of publications (n=6,300) contained small probabilities (<10%) across all 175 topics, meaning that all of the documents were associated to the final validated cardiovascular topics. Taken together, the topics approach was inclusive, though possibly lacking in detail. Expert review and naming of the topics required several steps. Individual experts named the topics in different ways, both in terms of writing style, and in selecting what was considered the main topic content. To check and validate the labels used and to ensure consistency, two additional rounds of expert panels were necessary. Overall, the smaller more focused topics were easier to name through linking the text fragments.

Before the final approach for document clustering was applied, other options were tested on the whole dataset, including clustering the documents based on the LDA topics identified8 and using Locality Sensitive Hashing (LSH)9, but these failed to provide adequate clustering of the large number of documents. Compared to labelling the LDA topics, the expert review of the document cluster characteristics presented a greater challenge to label and interpret the clusters. Each of the automated retrieval methods to obtain the document characteristics revealed different aspects of the clusters and only the combination brought more insight. It was only possible to make links across these data when familiar with the cardiovascular field.

This challenge has been highlighted in the scientometric literature and community with a significant project bringing partners from around the world to tackle the clustering and labelling issue on a single dataset of astronomy research10. Although several methods were presented, it was acknowledged that none were sufficiently robust to not require additional expert input and a call was made to the wider...
community to share relevant solutions. The methods available do already reduce a significant amount of work, considering the large volume of data and documents that can be processed semi-automatically.

Time lag because of the labor-intensive method is a limitation. Abstracts could be considered as a source to identify emerging topics but have several limitations. They are of a different nature than papers and the scope of a congress shapes content of selected abstracts. We complemented the literature analysis with a survey of 3000 abstracts from the 2018 congress of the European Society of Cardiology. The results in Figure S3 illustrate the strong presence of clinical research at this event, within the topics of clusters 1 and 3-7 of Table 2. Two emerging topics that could be discerned were cardio-oncology and digital health, each representing however less than 25 abstracts.

![Data from 2018 ESC congress](image)

**Figure S4.** Analysis of European Society of Cardiology 2018 abstracts. The right panel present in bar graph format the data of main Figure 4 in the manuscript.
Supplemental data

Investigating the evolution of specific terms
During the analysis, experts identified a number of terms related to recent research interests that were not identifiable in the text fragments reviewed, nor in the document cluster characteristics reviewed, such as microRNA, epigenetics, personalized medicine and Induced pluripotent stem cells (iPSC). Upon querying the text fragment, topics and document databases all terms were identified and their evolution investigated over time.
For all terms, the number of publications within the dataset was small, representing less than 0.5% of all publications (Table S2) but they showed an increase over time and could be related to identified larger topics.

miRNA is the term identified in the highest number of publications and text fragments, as well as, having over 100 publications across the largest number of topics. The number of publications are increasing steadily, with a greater increase of publications in the ‘pulmonary embolism’ and ‘cell signaling and gene transcription’ topics when compared to other topics. Epigenetics and iPSCs had similar numbers of publications identified; however, the topics where they were more highly represented differed. Epigenetics had a greater number of publications in ‘cell signaling and gene transcription’, in ‘mass spectrometry/omics & biomarker studies’ and in ‘low birth weight’ studies; whereas, the principal topic for iPSC publications was in the ‘stem cells / cardiac repair’ topic. Personalized medicine had very few text fragments identified and the 616 publications identified were most prevalent in the ‘Evidence-guided treatment’ and ‘Risk factors - genetics, GWAS studies’ topics.
To note, when searching for publications and topics with specific terms of interest, the interlinked document, text fragment and topics datasets accurately identify relevant publications; in comparison, a search of similar terms in Web of Science would bring up more publications that are irrelevant. Some terms, however, are more challenging to search and required expert input in the selection of text fragments, for example if only ‘iPS’ is searched then many text fragments and publications were identified about antipsychotics or ipsilateral or about embryonic stem cells and so the text fragments needed to be reviewed to ensure relevant results.
Table S2. All topics (ordered alphabetically by their Topic Label).

| Topic Label                                                                 | Focus of research | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|-----------------------------------------------------------------------------|-------------------|------|------|------|------|------|------|------|------|------|------|
| Acute coronary syndrome, MI - risk scoring, prognosis                      | clinical          | 546  | 696  | 685  | 739  | 929  | 949  | 1002 | 1085 | 1241 | 1390 |
| Acute coronary syndrome, MI, STEMI - PTCI, angioplasty                      | clinical          | 451  | 573  | 538  | 541  | 707  | 713  | 819  | 826  | 816  | 872  |
| Acute coronary syndromes - antiplatelet treatment                          | clinical          | 360  | 539  | 469  | 555  | 761  | 784  | 837  | 810  | 835  | 899  |
| Acute heart failure - ethnic risk                                           | population        | 378  | 428  | 466  | 446  | 563  | 525  | 601  | 582  | 609  | 719  |
| Adrenergic signalling, autonomic nervous system                            | basic             | 378  | 412  | 411  | 353  | 389  | 351  | 323  | 334  | 321  | 323  |
| Angiogenesis                                                                | basic             | 873  | 861  | 924  | 938  | 1028 | 1012 | 1079 | 1022 | 1051 | 1053 |
| Animal experiments – methodology                                          | basic             | 1020 | 1113 | 1122 | 1023 | 1090 | 1103 | 1112 | 1211 | 1190 | 1293 |
| Animal studies, pharmacology, hemodynamics, serotonin effect               | basic             | 275  | 317  | 259  | 273  | 298  | 281  | 252  | 285  | 309  | 317  |
| Anticoagulation, orthopedic surgery – NOAC                                | clinical          | 405  | 472  | 403  | 435  | 490  | 515  | 579  | 623  | 856  | 827  |
| Anticoagulation/thrombosis treatment and complications                     | clinical          | 328  | 373  | 314  | 342  | 433  | 448  | 469  | 486  | 590  | 618  |
| Aortic aneurysm - stents, repair, surgery                                  | clinical          | 445  | 560  | 555  | 575  | 712  | 703  | 724  | 747  | 718  | 830  |
| Aortic valve disease - bicuspid valve, aortic disease, Marfan syndrome     | clinical          | 332  | 399  | 410  | 470  | 504  | 564  | 582  | 649  | 687  | 789  |
| Aortic valve disease - repair, surgery                                     | clinical          | 437  | 470  | 472  | 452  | 514  | 631  | 753  | 896  | 1070 | 1208 |
| Apoptosis in the heart                                                     | basic             | 614  | 651  | 683  | 665  | 717  | 753  | 782  | 848  | 893  | 994  |
| Arrhythmias - Arrhythmogenic RV cardiomyopathy, long QT – genetics         | clinical          | 613  | 743  | 713  | 693  | 867  | 932  | 924  | 927  | 1017 | 1114 |
| Arrhythmias - conduction disorders, ECG                                    | clinical          | 585  | 642  | 648  | 642  | 912  | 830  | 806  | 818  | 898  | 954  |
| Arrhythmias - heart failure and ICD therapy                                | clinical          | 686  | 834  | 834  | 851  | 1118 | 1082 | 1051 | 1158 | 1097 | 1220 |
| Arrhythmias - ICD technology                                               | clinical          | 289  | 356  | 315  | 359  | 437  | 422  | 429  | 419  | 537  | 581  |
| Arrhythmias - mechanisms, pharmacological treatments                       | clinical / basic  | 349  | 409  | 401  | 385  | 477  | 408  | 418  | 440  | 465  | 482  |
| Arrhythmias - Torsade-de-pointes, QT prolongation, environmental risk      | clinical          | 439  | 583  | 514  | 546  | 680  | 637  | 629  | 669  | 708  | 782  |
| Topic                                                                 | Type          | Values                                                                 |
|----------------------------------------------------------------------|---------------|------------------------------------------------------------------------|
| Arrhythmias - ventricular - genetics, pathophysiology and diagnostics | clinical / basic | 143 179 187 175 207 223 221 238 247 219                               |
| Arteritis, rheumatic and autoimmune diseases                         | clinical      | 330 426 406 495 531 577 576 636 692 720                               |
| Atherosclerosis - macrophages, lipids                               | basic         | 411 450 415 502 473 514 512 536 524 562                               |
| Atherosclerosis - embolism & stroke, treatment and complications     | clinical      | 257 379 307 345 426 388 425 360 389 405                               |
| Atherosclerosis risk scoring - imaging, carotid intima thickness     | population    | 356 447 439 530 621 599 613 613 686 733                               |
| Atherosclerosis, lipids - animal models                             | basic         | 512 589 516 618 667 737 665 744 735 801                               |
| Atrial fibrillation - ablation treatment                            | clinical      | 748 877 794 841 1078 1071 1083 1080 1183 1337                         |
| Atrial fibrillation - embolic risk assessment                        | clinical      | 217 237 240 288 289 304 320 396 469 634                               |
| Atrial fibrillation – mechanisms                                     | basic         | 251 285 256 270 303 295 308 289 317 341                               |
| Atrial fibrillation - postoperative risk                            | clinical      | 199 250 257 282 292 326 321 364 406 485                               |
| Autoimmune disease, autoantibodies                                  | clinical / basic | 437 480 408 396 454 417 369 394 415 381                               |
| Autonomic nervous system - Heart rate variability                   | clinical      | 612 707 697 698 817 853 777 830 799 953                               |
| Autonomic nervous system - Renal physiology, blood pressure         | basic         | 591 630 547 554 589 620 559 570 596 624                               |
| Endothelial progenitor cells                                        | basic         | 143 196 199 247 291 305 371 350 351 381                               |
| Biomarkers - von Willebrand disease, ischemia, infarction           | clinical      | 229 300 280 267 343 325 349 396 415 465                               |
| Blood pressure - regulation, autonomic nervous system               | clinical      | 383 424 383 425 416 423 398 398 389 423                               |
| Bone mineralization, calcium metabolism, aortic calcification       | clinical / basic | 203 266 236 294 389 367 406 427 383 505                               |
| Cancer - coagulation disorders, LV outflow obstruction              | clinical      | 484 556 488 518 599 562 585 548 629 550                               |
| Cardiac arrest - resuscitation, management                          | clinical      | 207 297 322 308 443 404 472 519 534 659                               |
| Cardiac electrophysiology - action potential, conduction            | basic         | 532 590 562 577 644 619 584 638 690 643                               |
| Cardiac electrophysiology - ion channels, calcium homeostasis       | basic         | 1071 1109 1021 1099 1138 1081 1108 1058 1046 1109                      |
| Cardiac hypertrophy - animal models                                 | basic         | 696 767 763 779 892 907 1004 1036 1051 1139                         |
| Topic                                                                 | Type         | 374 | 471 | 443 | 472 | 570 | 531 | 464 | 496 | 558 | 517 |
|----------------------------------------------------------------------|--------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cardiac pacemakers – CRT                                             | clinical     |     |     |     |     |     |     |     |     |     |     |
| Cardiac surgery – cardioprotection                                   | clinical     |     |     |     |     |     |     |     |     |     |     |
| Cardiomyopathy - Chagas disease                                     | population   | 151 | 213 | 191 | 210 | 270 | 280 | 268 | 315 | 366 | 413 |
| Cardiomyopathy - fabry disease                                       | clinical     | 153 | 176 | 178 | 176 | 234 | 223 | 212 | 244 | 256 | 246 |
| Cardiopulmonary bypass - blood transfusion                          | clinical     | 378 | 384 | 399 | 377 | 429 | 456 | 379 | 468 | 477 | 462 |
| Cardiovascular development                                           | basic        | 438 | 466 | 471 | 471 | 547 | 506 | 587 | 574 | 619 | 579 |
| Catheterisation – complications                                     | clinical     | 244 | 268 | 280 | 289 | 363 | 366 | 393 | 421 | 491 | 533 |
| Cell signaling - Nitric oxide synthase, Calcium Calmodulin Kinase    | basic        | 671 | 716 | 654 | 710 | 738 | 697 | 614 | 685 | 686 | 629 |
| Cell signaling and gene transcription                               | basic        | 2449| 2685| 2375| 2549| 2827| 2715| 2749| 2692| 2868| 2810|
| Cerebrovascular disease - cognitive dysfunction, risk factors        | population   | 632 | 716 | 723 | 695 | 760 | 808 | 714 | 683 | 719 | 787 |
| Cerebrovascular disease - familial hypercholesterolemia treatment    | clinical / basic | 269 | 339 | 288 | 348 | 368 | 407 | 393 | 403 | 439 | 463 |
| Cerebrovascular disease, stroke – diagnosis                          | clinical     | 407 | 453 | 457 | 446 | 506 | 503 | 476 | 502 | 525 | 520 |
| Cholesterol, PCOS, obesity & risk                                    | population   | 698 | 809 | 842 | 983 | 1230| 1213| 1280| 1367| 1367| 1471|
| Clinical guidelines generation                                       | clinical     | 557 | 699 | 725 | 700 | 937 | 944 | 948 | 1134| 1159| 1240|
| Clinical trials - CV endpoints                                       | clinical     | 569 | 776 | 729 | 802 | 942 | 1012| 1050| 1097| 1172| 1312|
| Clinical trials - metanalysis, systematic lit review                 | clinical     | 342 | 438 | 492 | 543 | 687 | 747 | 804 | 961 | 1155| 1414|
| Clinical trials - study design and protocols                         | clinical     | 750 | 854 | 758 | 884 | 921 | 895 | 892 | 931 | 1029| 1035|
| Coagulation, hemostasis - critical illness, intensive care – measurements | clinical     | 330 | 326 | 388 | 350 | 385 | 408 | 455 | 504 | 539 | 529 |
| Congenital heart disease - anomalous pulmonary venous return        | clinical     | 222 | 263 | 251 | 261 | 289 | 289 | 255 | 255 | 244 | 213 |
| Congenital heart disease - coarctation, catheterization & complications | clinical     | 380 | 456 | 484 | 433 | 547 | 520 | 592 | 548 | 603 | 552 |
| Congenital heart disease - diagnosis, surgery, treatment            | clinical     | 739 | 944 | 1155| 962 | 1209| 1235| 1224| 1351| 1306| 1496|
| Congenital heart disease - surgical procedures                      | clinical     | 1209| 1513| 1471| 1417| 1849| 1802| 1918| 1910| 2023| 2154|
| Coronary artery disease – CABG, technique                            | clinical     | 650 | 645 | 592 | 525 | 590 | 533 | 529 | 493 | 539 | 506 |
| Coronary artery disease - CT imaging                                 | clinical     | 265 | 392 | 435 | 532 | 579 | 650 | 674 | 610 | 692 | 715 |
| Coronary artery disease - elective PTCl                              | clinical     | 127 | 148 | 150 | 195 | 252 | 251 | 299 | 311 | 293 | 343 |
| Topic                                                                 | Type         | Page Numbers |
|----------------------------------------------------------------------|--------------|--------------|
| Coronary artery disease - flow and flow reserve                      | clinical     | 471, 478, 468, 468, 489, 427, 415, 449, 452, 460 |
| Coronary artery disease - revascularization, PTCI                   | clinical     | 446, 547, 519, 618, 810, 806, 977, 1051, 986, 1207 |
| Coronary artery disease – stents DES – complications                 | clinical     | 427, 474, 482, 587, 658, 594, 752, 788, 691, 779 |
| Coronary artery disease - stenting procedures                        | clinical     | 464, 538, 494, 489, 668, 630, 704, 756, 762, 875 |
| Coronary artery disease, atherosclerosis - plaque rupture, PTCI      | clinical/bas | 416, 430, 480, 485, 608, 581, 609, 752, 788, 691 |
| Coronary artery disease, calcification - diagnosis, CT angiography   | clinical     | 429, 584, 597, 722, 809, 862, 928, 994, 969, 1122 |
| Coronary artery disease, cardiac imaging - diagnosis myocardial ischemia | clinical/bas | 670, 720, 613, 576, 713, 631, 651, 604, 578, 598 |
| Coronary artery disease, cardiac surgery – peri-operative care       | clinical     | 761, 900, 966, 939, 1125, 1180, 1310, 1412, 1503 |
| Deep vein thrombosis - complications and treatment                  | clinical     | 278, 346, 328, 306, 406, 366, 406, 378, 382, 394 |
| Diabetes - vascular complications                                    | clinical     | 584, 745, 706, 720, 998, 943, 907, 1058, 1077, 1118 |
| Diabetic cardiomyopathy - mouse models                               | basic        | 317, 330, 367, 379, 449, 392, 432, 455, 496, 552 |
| Eclampsia, peripartum cardiomyopathy, gestational diabetes           | clinical     | 320, 412, 376, 357, 490, 583, 584, 693, 722, 689 |
| Endoplasmic reticulum stress, pulmonary vein                        | basic        | 203, 259, 276, 252, 266, 330, 338, 378, 396, 375 |
| Endothelial cells – inflammation                                    | basic        | 635, 690, 643, 651, 698, 660, 703, 691, 749, 726 |
| Endothelial function, microcirculation - endothelial barrier        | basic        | 329, 337, 354, 345, 388, 371, 400, 342, 381, 386 |
| Epidemiology of CVD and risk factors                                 | population   | 1539, 1861, 1889, 2093, 2585, 2604, 2750, 2903, 3134, 3523 |
| Estrogen, gender - risk factors                                      | population   | 249, 262, 259, 341, 324, 335, 376, 352, 338, 372 |
| Evidence-guided treatment                                           | clinical     | 3442, 4194, 4102, 4117, 5397, 5486, 5276, 5338, 5739, 5940 |
| Exercise testing - cardiovascular fitness                            | population   | 728, 827, 870, 868, 1155, 1172, 1207, 1204, 1295, 1441 |
| Extracorporeal membrane oxygenation, shock management              | clinical     | 383, 435, 447, 422, 422, 469, 443, 464, 473, 502 |
| Gene delivery                                                        | basic, preclinical | 365, 375, 299, 296, 319, 305, 267, 292, 282, 314 |
| Glucose metabolism - cellular signaling                              | basic        | 509, 543, 531, 492, 550, 555, 524, 541, 545, 547 |
| Topic                                                                 | Type     | 286  | 384  | 422  | 391  | 513  | 427  | 499  | 487  | 484  | 591  |
|----------------------------------------------------------------------|----------|------|------|------|------|------|------|------|------|------|------|
| Health economics, health care policies                               | population| 286  | 384  | 422  | 391  | 513  | 427  | 499  | 487  | 484  | 591  |
| Healthcare organization, quality of care                            | clinical | 746  | 892  | 894  | 932  | 1187 | 1088 | 1291 | 1328 | 1379 | 1559 |
| Heart failure - assist devices                                      | clinical | 237  | 269  | 246  | 227  | 284  | 330  | 372  | 434  | 489  | 487  |
| Heart failure – biomarkers                                          | clinical | 354  | 428  | 450  | 507  | 603  | 568  | 537  | 519  | 508  | 528  |
| Heart failure - cancer-related, acute heart failure treatment (IABP)| clinical | 306  | 358  | 405  | 513  | 524  | 472  | 533  | 579  | 616  | 671  |
| Heart failure - clinical classification                             | clinical | 181  | 225  | 222  | 256  | 454  | 332  | 358  | 376  | 333  | 341  |
| Heart failure - transplantation - complications and therapy         | clinical | 451  | 584  | 538  | 478  | 477  | 529  | 502  | 524  | 492  | 523  |
| Heart failure - ventricular function, stem cells                    | clinical | 115  | 152  | 148  | 208  | 222  | 200  | 237  | 237  | 238  | 258  |
| Heart transplantation – techniques                                   | clinical | 203  | 248  | 224  | 267  | 306  | 249  | 288  | 293  | 303  | 306  |
| Hemodynamic measurements                                            | basic / clinical | 562  | 635  | 593  | 586  | 571  | 631  | 527  | 603  | 582  | 642  |
| Hypertension - animals models                                       | basic     | 569  | 650  | 572  | 570  | 620  | 622  | 623  | 630  | 649  | 690  |
| Hypertension - BP measurement, diagnosis                            | clinical | 718  | 841  | 814  | 861  | 1071 | 978  | 958  | 1025 | 1137 | 1256 |
| Hypertension - population studies, statistics                       | population| 364  | 510  | 502  | 460  | 659  | 579  | 634  | 651  | 677  | 650  |
| Hypertension - renovascular, treatment (denervation, angioplasty)    | clinical / basic | 151  | 204  | 208  | 188  | 268  | 271  | 265  | 273  | 306  | 442  |
| Hypertension - treatment adherence                                   | clinical | 420  | 463  | 477  | 501  | 666  | 586  | 588  | 631  | 616  | 655  |
| Hypertension - antihypertensive therapy                             | clinical | 676  | 822  | 763  | 827  | 1147 | 1032 | 972  | 960  | 978  | 995  |
| Hypertension, salt metabolism - animal models                       | basic     | 646  | 842  | 717  | 752  | 787  | 690  | 687  | 760  | 798  | 748  |
| Imaging - cardiac echocardiography technique                       | clinical | 489  | 585  | 517  | 602  | 730  | 780  | 733  | 764  | 857  | 896  |
| Imaging - echocardiography, cardiac hemodynamics                    | clinical | 522  | 626  | 678  | 757  | 974  | 947  | 948  | 969  | 1018 | 1169 |
| Imaging – MRI                                                        | clinical | 494  | 602  | 590  | 597  | 684  | 749  | 690  | 763  | 758  | 854  |
| Imaging - Optical coherence tomography, micro CT                    | clinical / basic | 452  | 497  | 506  | 458  | 598  | 631  | 657  | 679  | 783  | 823  |
| Imaging - PET, nuclear imaging techniques                           | clinical | 241  | 313  | 279  | 308  | 433  | 411  | 430  | 473  | 490  | 538  |
| Imaging - SPECT PET in diabetes                                     | clinical | 178  | 214  | 200  | 243  | 249  | 220  | 262  | 255  | 275  | 242  |
| Inflammation                                                         | basic / clinical | 951  | 1074 | 953  | 1110 | 1123 | 1215 | 1194 | 1158 | 1275 | 1304 |
| Topic                                                                 | Type    | 700 | 751 | 709 | 738 | 779 | 778 | 753 | 785 | 838 | 845 |
|----------------------------------------------------------------------|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Inflammation - mechanisms and mediators                            | basic    |     |     |     |     |     |     |     |     |     |     |
| Inflammation biomarkers                                             | clinical | 1545| 1953| 1954| 2096| 2548| 2518| 2502| 2562| 2757| 2990|
| Kidney, renal function - sodium homeostasis, aldosterone           | clinical | 528 | 637 | 580 | 574 | 748 | 678 | 713 | 733 | 793 | 831 |
| Lipids/atherosclerosis - mouse models                              | basic    | 161 | 231 | 233 | 270 | 299 | 278 | 261 | 313 | 342 | 334 |
| Lipids - cholesterol metabolism                                     | basic    | 125 | 145 | 164 | 174 | 197 | 215 | 187 | 199 | 201 | 184 |
| Lipids - cholesterol transport and lipoproteins                     | basic    | 733 | 789 | 735 | 790 | 906 | 875 | 880 | 840 | 921 | 895 |
| Lipids - population guidelines                                      | population | 271 | 400 | 493 | 664 | 744 | 725 | 696 | 695 | 697 | 761 |
| Lipids, cholesterol - statin therapy                                | clinical | 763 | 974 | 896 | 947 | 1091| 1052| 1008| 1004| 997 | 967 |
| Lipids, PPAR gamma receptors - treatment for hypercholesterolemia   | basic / clinical | 236 | 314 | 276 | 363 | 398 | 308 | 333 | 315 | 330 | 287 |
| Longitudinal studies - blood pressure                              | population | 1929| 2196| 2031| 1964| 2208| 2114| 1961| 2040| 2101| 2196|
| Low birth weight                                                    | population | 371 | 521 | 465 | 454 | 540 | 598 | 521 | 655 | 690 | 684 |
| Mass spectrometry - in omics & biomarker studies                   | basic    | 765 | 722 | 698 | 653 | 838 | 714 | 785 | 757 | 823 | 882 |
| Mental health, CVD impact                                           | population | 546 | 600 | 656 | 673 | 856 | 892 | 938 | 963 | 1074| 1150|
| Metabolic syndrome – adiponectin                                    | population | 193 | 295 | 241 | 314 | 348 | 332 | 359 | 350 | 688 | 746 |
| Metabolic syndrome - animal models                                  | basic    | 378 | 447 | 433 | 532 | 608 | 633 | 627 | 611 | 688 | 746 |
| Metabolic syndrome - obesity, diabetes                             | population | 802 | 998 | 1033| 1205| 1459| 1426| 1416| 1548| 1566| 1769|
| Mitochondrial function - oxidative stress                          | basic    | 339 | 369 | 362 | 411 | 441 | 467 | 462 | 513 | 548 | 629 |
| Myocardial infarction - animal studies                             | basic    | 517 | 597 | 634 | 633 | 701 | 662 | 786 | 813 | 769 | 851 |
| Myocardial infarction - cardiac rehabilitation                     | clinical | 277 | 366 | 337 | 354 | 430 | 463 | 461 | 444 | 462 | 543 |
| Myocardial infarction - ischemia/reperfusion injury               | basic    | 905 | 922 | 933 | 898 | 959 | 929 | 809 | 939 | 943 | 1003|
| Myocardial infarction outcomes, prognosis                          | clinical | 506 | 566 | 569 | 523 | 680 | 659 | 584 | 667 | 667 | 679 |
| Myofilaments, excitation-contraction coupling                      | basic    | 382 | 363 | 408 | 364 | 427 | 357 | 367 | 367 | 358 | 403 |
| Obstructive sleep apnea                                            | clinical | 214 | 260 | 294 | 370 | 394 | 476 | 413 | 419 | 492 | 599 |
| Outcomes, prognosis – mortality                                    | clinical | 1727| 2162| 2226| 2310| 2975| 2798| 3129| 3156| 3485| 4042|
| Oxidative stress – antioxidants                                    | basic    | 854 | 993 | 956 | 969 | 1025| 1082| 1094| 1177| 1237| 1282|
| Oxidative stress - reactive oxygen species                         | basic    | 442 | 530 | 519 | 587 | 583 | 618 | 648 | 630 | 640 | 654 |
| Pericardial disease                                                | clinical | 249 | 279 | 271 | 252 | 291 | 270 | 317 | 282 | 287 | 358 |
| Topic                                                                 | Type                        | 387 | 526 | 510 | 477 | 688 | 605 | 655 | 652 | 701 | 739 |
|----------------------------------------------------------------------|-----------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Peripheral vascular disease - diagnosis, management, surgery        | clinical                    |     |     |     |     |     |     |     |     |     |     |
| Platelet aggregation                                                 | basic / clinical            | 746 | 809 | 618 | 682 | 760 | 678 | 701 | 719 | 728 | 657 |
| Primary care setting - selfmanagement                               | clinical                    | 563 | 731 | 745 | 707 | 1053| 1017| 1084| 1188| 1261| 1413|
| Pulmonary embolism                                                   | clinical / basic            | 207 | 250 | 226 | 266 | 316 | 343 | 428 | 465 | 571 | 631 |
| Pulmonary hypertension - diagnosis, causes                          | clinical                    | 490 | 510 | 593 | 634 | 711 | 752 | 818 | 839 | 860 | 987 |
| Pulmonary hypertension - hypoxia, animal models                      | basic, preclinical          | 385 | 446 | 430 | 398 | 479 | 478 | 471 | 470 | 531 | 567 |
| Red blood cells - aggregation and rheology                           | basic                       | 212 | 235 | 200 | 190 | 203 | 220 | 225 | 200 | 238 | 240 |
| Rheumatic heart disease, left ventricular dysfunction assessment     | clinical                    | 108 | 155 | 167 | 136 | 203 | 204 | 242 | 261 | 217 | 241 |
| Risk factors - diabetes & hypertension                              | population                  | 739 | 966 | 1014| 1012| 1293| 1286| 1204| 1196| 1349| 1383|
| Risk factors - environment, psychosocial stress, depression          | population                  | 332 | 389 | 317 | 391 | 370 | 400 | 379 | 381 | 396 | 393 |
| Risk factors - genetics, GWAS studies                                | population                  | 522 | 587 | 527 | 662 | 750 | 790 | 872 | 891 | 896 | 906 |
| Risk factors - population cohort studies                             | population                  | 513 | 637 | 671 | 755 | 908 | 983 | 1032| 1114| 1227| 1268|
| Risk factors - socioeconomic, lifestyle, nutrition & activity factors| population                  | 882 | 1075| 1068| 1110| 1620| 1626| 1673| 1814| 1932| 2146|
| Risk factors - women, hormone replacement therapy                    | population                  | 493 | 550 | 470 | 524 | 563 | 548 | 499 | 557 | 523 | 564 |
| Risk factors, health - nutrition & diet                              | population                  | 570 | 713 | 699 | 689 | 844 | 863 | 885 | 945 | 987 | 1047|
| Secondary hypertension - aldosterone, complications                  | clinical                    | 180 | 236 | 243 | 245 | 305 | 312 | 285 | 287 | 315 | 314 |
| Sepsis, endocarditis                                                 | clinical                    | 339 | 395 | 392 | 410 | 512 | 486 | 478 | 475 | 560 | 586 |
| Stem cells / cardiac repair                                          | basic                       | 454 | 543 | 584 | 690 | 796 | 769 | 923 | 949 | 1042| 1174|
| Stroke - incidence, cerebrovascular disease                          | clinical                    | 368 | 384 | 412 | 425 | 518 | 605 | 478 | 535 | 578 | 615 |
| Stroke - treatment & outcome                                         | clinical                    | 283 | 334 | 302 | 327 | 370 | 423 | 411 | 447 | 546 | 576 |
| Syncope - diagnostic testing                                         | clinical                    | 250 | 306 | 271 | 295 | 307 | 347 | 312 | 345 | 345 | 346 |
| Takotsubo cardiomyopathy                                             | clinical                    | 509 | 639 | 607 | 680 | 796 | 815 | 830 | 764 | 729 | 798 |
| Thrombolysis, coagulation                                            | basic                       | 770 | 809 | 679 | 754 | 740 | 692 | 658 | 650 | 714 | 622 |
| Tissue engineering - vascular, biomechanical factors                 | basic                       | 473 | 575 | 562 | 602 | 668 | 691 | 747 | 800 | 812 | 859 |
| Condition                                             | Type          | Study 1 | Study 2 | Study 3 | Study 4 | Study 5 | Study 6 | Study 7 | Study 8 | Study 9 | Study 10 | Study 11 |
|-------------------------------------------------------|---------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Traumatic cardiac injury                             | Clinical      | 183     | 240     | 208     | 204     | 298     | 271     | 291     | 272     | 287     | 250     |
| Valvular heart disease - mitral valve                | Clinical      | 327     | 406     | 390     | 413     | 508     | 548     | 551     | 588     | 583     | 689     |
| Valvular heart disease, obesity                      | Clinical      | 143     | 195     | 217     | 182     | 215     | 286     | 240     | 303     | 272     | 312     |
| Vascular disease, arterial stiffness                 | Clinical      | 347     | 476     | 471     | 560     | 651     | 657     | 610     | 662     | 792     | 841     |
| Vascular endothelial function - diagnosis            | Clinical / Basic | 540   | 610     | 670     | 707     | 779     | 702     | 676     | 761     | 734     | 771     |
| Vascular function - endothelial control              | Basic         | 1267    | 1332    | 1137    | 1095    | 1079    | 959     | 912     | 916     | 860     | 855     |
| Vascular function & remodeling - biomechanical factors| Basic        | 580     | 628     | 604     | 585     | 738     | 721     | 724     | 790     | 837     | 878     |
| Vascular function testing – endothelial control      | Clinical      | 322     | 334     | 290     | 277     | 270     | 251     | 264     | 263     | 257     | 255     |
| Vascular smooth muscle cell physiology               | Basic         | 345     | 375     | 347     | 347     | 408     | 355     | 347     | 377     | 424     | 395     |
| Vascular smooth muscle cells - proliferation, migration| Basic      | 1182    | 1236    | 1110    | 1178    | 1182    | 1140    | 1128    | 1115    | 1116    | 1050    |
| Ventricular function assessment                      | Clinical      | 824     | 908     | 943     | 1015    | 1274    | 1197    | 1218    | 1229    | 1282    | 1464    |
Table S3. Specific terms in documents, text fragments and topics (2004-2013)

| A. miRNA                              | Total Number | Evolution - number of publications per year |
|---------------------------------------|--------------|---------------------------------------------|
| Publications with term in title or abstract | 1428         |                                             |
| Total number                          | 1099         | Number in top 200 text fragments across all topics |
| Unique text fragments                 |              | 20                                          |
| Topics                                |              | Evolution - number of publications per year for the main topics |
| Topics with 100+ publications with gamma >10% |              |                                             |
| - Pulmonary embolism                  |              |                                             |
| - Cell signaling and gene transcription|              |                                             |
| - Cardiac hypertrophy - animal models  |              |                                             |
| - Angiogenesis                        |              |                                             |
| - Cardiovascular development          |              |                                             |
| - Vascular smooth muscle cells - proliferation, migration | |                                             |
| - Arrhythmias - mechanisms, pharmacological treatments | |                                             |
|                                        |              | 0  171  15  2  165  89  148                 |
## B. Epigenetics

| Total Number | Evolution - number of publications per year |
|--------------|--------------------------------------------|
| **Publications with term in title or abstract** | ![Graph showing the evolution of publications per year.](image) |
| 652          |                                            |

| Total number | Number in top 200 text fragments across all topics |
|--------------|---------------------------------------------------|
| **Unique text fragments** | 289 | 2 |

### Topics

- **Topics with 100+ publications with gamma >10%**
  - Cell signaling and gene transcription
  - Mass spectrometry/ in omics & biomarker studies
  - Low birth weight

| Evolution - number of publications per year for the main topics |
|---------------------------------------------------------------|
| ![Graph showing the evolution of publications per year.](image) |
| 171 | 41 | 20 |
C. Induced pluripotent stem cells (iPSC)

| Total Number | Evolution - number of publications per year |
|--------------|---------------------------------------------|
| Publications with text fragments in title or abstract | 685 |
| Total number | Number in top 200 text fragments across all topics |
| Unique text fragments | 582 |
| Topics | Evolution - number of publications per year for the main topics |
| Topics with 100+ publications with gamma >10% | 148-Stem cells / cardiac repair |

![Graph showing the evolution of number of publications per year for iPSC over years 2004 to 2013.](image)
### D. Personalized medicine

| Total Number | Evolution - number of publications per year |
|--------------|---------------------------------------------|
| Publications with term in title or abstract | 616 |

| Total number | Number in top 200 text fragments across all topics |
|--------------|---------------------------------------------------|
| Unique text fragments | 11 |
| Topics | |

| Topics with 100+ publications with gamma >10% | Evolution - number of publications per year for the main topics |
|---------------------------------------------|---------------------------------------------------------------|
| 123-Evidence-guided treatment | |
| 168- Risk factors - genetics, GWAS studies | |
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