**Appendix – 1**

**Top 91 Intervention** (Death trials#>=5)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Index** | **Intervention** | **All Trials(#)** | **Death Trials(#)** | **Death Trials/All Trials** | **Average Incidence** |
| 1 | filgrastim | 44 | 10 | 23% | 47.74% |
| 2 | cyclosporine | 26 | 7 | 27% | 44.90% |
| 3 | busulfan | 17 | 7 | 41% | 34.51% |
| 4 | mycophenolate\_mofetil | 31 | 7 | 23% | 31.52% |
| 5 | stem\_cell\_infusion | 7 | 5 | 71% | 30.65% |
| 6 | tacrolimus | 51 | 13 | 25% | 25.50% |
| 7 | imatinib\_mesylate | 34 | 12 | 35% | 22.70% |
| 8 | saracatinib | 13 | 5 | 38% | 22.37% |
| 9 | methotrexate | 102 | 25 | 25% | 22.36% |
| 10 | vincristine | 30 | 8 | 27% | 21.90% |
| 11 | melphalan | 40 | 16 | 40% | 20.55% |
| 12 | fludarabine\_phosphate | 34 | 10 | 29% | 17.94% |
| 13 | fludarabine | 44 | 14 | 32% | 17.85% |
| 14 | decitabine | 20 | 8 | 40% | 16.65% |
| 15 | doxorubicin | 43 | 7 | 16% | 15.71% |
| 16 | cyclophosphamide | 161 | 43 | 27% | 15.57% |
| 17 | radiation\_therapy | 102 | 28 | 27% | 13.99% |
| 18 | etoposide | 66 | 22 | 33% | 14.92% |
| 19 | g-csf | 9 | 5 | 56% | 14.44% |
| 20 | polymorphism\_analysis | 8 | 6 | 75% | 14.41% |
| 21 | stem\_cell\_transplant | 9 | 5 | 56% | 14.00% |
| 22 | vorinostat | 50 | 14 | 28% | 13.27% |
| 23 | alemtuzumab | 27 | 5 | 19% | 12.56% |
| 24 | cytarabine | 50 | 25 | 50% | 12.33% |
| 25 | irinotecan\_hydrochloride | 18 | 10 | 56% | 12.09% |
| 26 | methylprednisolone | 32 | 8 | 25% | 12.03% |
| 27 | pharmacological\_study | 49 | 12 | 24% | 12.00% |
| 28 | cixutumumab | 11 | 7 | 64% | 10.87% |
| 29 | thalidomide | 31 | 10 | 32% | 10.60% |
| 30 | immunohistochemistry\_staining\_method | 13 | 8 | 62% | 10.49% |
| 31 | rituximab | 122 | 32 | 26% | 10.48% |
| 32 | gene\_expression\_analysis | 15 | 6 | 40% | 10.42% |
| 33 | sargramostim | 24 | 5 | 21% | 10.34% |
| 34 | temsirolimus | 21 | 10 | 48% | 9.83% |
| 35 | ara-c | 9 | 6 | 67% | 9.75% |
| 36 | gemcitabine\_hydrochloride | 25 | 5 | 20% | 9.68% |
| 37 | sunitinib\_malate | 31 | 15 | 48% | 9.54% |
| 38 | vincristine\_sulfate | 26 | 10 | 38% | 8.58% |
| 39 | erlotinib | 58 | 23 | 40% | 8.02% |
| 40 | lapatinib | 31 | 7 | 23% | 7.98% |
| 41 | pegfilgrastim | 18 | 6 | 33% | 7.84% |
| 42 | sirolimus | 34 | 7 | 21% | 7.76% |
| 43 | erlotinib\_hydrochloride | 23 | 10 | 43% | 7.66% |
| 44 | clofarabine | 18 | 8 | 44% | 7.38% |
| 45 | dasatinib | 64 | 24 | 38% | 7.00% |
| 46 | cetuximab | 84 | 39 | 46% | 6.74% |
| 47 | bibw\_2992 | 23 | 8 | 35% | 6.25% |
| 48 | bortezomib | 76 | 21 | 28% | 6.25% |
| 49 | sorafenib | 33 | 13 | 39% | 5.51% |
| 50 | ofatumumab | 18 | 5 | 28% | 5.16% |
| 51 | gemcitabine | 121 | 39 | 32% | 5.06% |
| 52 | radiotherapy | 22 | 6 | 27% | 5.05% |
| 53 | dexamethasone | 106 | 34 | 32% | 4.88% |
| 54 | oxaliplatin | 79 | 28 | 35% | 4.57% |
| 55 | capecitabine | 92 | 31 | 34% | 4.55% |
| 56 | pemetrexed\_disodium | 12 | 5 | 42% | 4.54% |
| 57 | ixabepilone | 28 | 8 | 29% | 4.51% |
| 58 | irinotecan | 31 | 9 | 29% | 4.43% |
| 59 | prednisone | 96 | 31 | 32% | 4.35% |
| 60 | basiliximab | 12 | 5 | 42% | 4.21% |
| 61 | bevacizumab | 201 | 81 | 40% | 4.14% |
| 62 | sorafenib\_tosylate | 29 | 9 | 31% | 4.09% |
| 63 | docetaxel | 138 | 40 | 29% | 3.53% |
| 64 | temozolomide | 51 | 18 | 35% | 3.45% |
| 65 | gemtuzumab\_ozogamicin | 7 | 5 | 71% | 3.33% |
| 66 | cisplatin | 151 | 42 | 28% | 3.29% |
| 67 | lenalidomide | 64 | 23 | 36% | 3.13% |
| 68 | carboplatin | 157 | 53 | 34% | 3.10% |
| 69 | azacitidine | 23 | 8 | 35% | 3.00% |
| 70 | pemetrexed | 89 | 39 | 44% | 2.88% |
| 71 | ranibizumab | 29 | 13 | 45% | 2.21% |
| 72 | peginesatide | 21 | 13 | 62% | 2.18% |
| 73 | 5-fluorouracil | 26 | 6 | 23% | 1.92% |
| 74 | paclitaxel | 151 | 43 | 28% | 1.89% |
| 75 | doxorubicin\_hydrochloride | 30 | 8 | 27% | 1.70% |
| 76 | everolimus | 43 | 17 | 40% | 1.67% |
| 77 | placebo | 2286 | 368 | 16% | 1.66% |
| 78 | trastuzumab | 47 | 11 | 23% | 1.61% |
| 79 | metformin | 101 | 18 | 18% | 1.38% |
| 80 | fluorouracil | 29 | 10 | 34% | 0.95% |
| 81 | abatacept | 33 | 5 | 15% | 0.95% |
| 82 | leucovorin\_calcium | 24 | 11 | 46% | 0.94% |
| 83 | saxagliptin | 32 | 10 | 31% | 0.71% |
| 84 | zoledronic\_acid | 32 | 10 | 31% | 0.66% |
| 85 | degarelix | 55 | 8 | 15% | 0.61% |
| 86 | adalimumab | 58 | 14 | 24% | 0.45% |
| 87 | albiglutide | 8 | 5 | 63% | 0.37% |
| 88 | tiotropium | 38 | 13 | 34% | 0.28% |
| 89 | warfarin | 17 | 9 | 53% | 0.26% |
| 90 | 13-valent\_pneumococcal\_conjugate\_vaccine | 32 | 5 | 16% | 0.21% |
| 91 | apixaban | 12 | 9 | 75% | 0.11% |

**Appendix – 2**

**Top 142 conditions** (Death trials#>=5)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Index** | **Condition** | **All Trials(#)** | **Death Trials(#)** | **Death Trials/All Trials** | **Average Incidence** |
| 1 | leukemia | 106 | 45 | 42.45% | 19.36% |
| 2 | breast\_cancer | 212 | 40 | 18.87% | 3.74% |
| 3 | non-small\_cell\_lung\_cancer | 101 | 36 | 35.64% | 1.64% |
| 4 | hiv\_infections | 137 | 35 | 25.55% | 1.45% |
| 5 | rheumatoid\_arthritis | 210 | 33 | 15.71% | 0.53% |
| 6 | lung\_cancer | 86 | 32 | 37.21% | 6.38% |
| 7 | pulmonary\_disease\_chronic\_obstructive | 103 | 31 | 30.10% | 0.44% |
| 8 | multiple\_myeloma | 110 | 31 | 28.18% | 7.07% |
| 9 | diabetes\_mellitus\_type\_2 | 191 | 31 | 16.23% | 0.40% |
| 10 | lymphoma | 91 | 26 | 28.57% | 27.93% |
| 11 | prostate\_cancer | 142 | 25 | 17.61% | 2.48% |
| 12 | carcinoma\_non-small-cell\_lung | 51 | 24 | 47.06% | 2.94% |
| 13 | myelodysplastic\_syndrome | 39 | 20 | 51.28% | 11.75% |
| 14 | atrial\_fibrillation | 55 | 20 | 36.36% | 1.24% |
| 15 | coronary\_artery\_disease | 62 | 20 | 32.26% | 0.65% |
| 16 | heart\_failure | 43 | 19 | 44.19% | 3.50% |
| 17 | colorectal\_cancer | 75 | 19 | 25.33% | 2.43% |
| 18 | chronic\_kidney\_disease | 43 | 17 | 39.53% | 1.42% |
| 19 | stroke | 32 | 16 | 50.00% | 1.90% |
| 20 | cancer | 68 | 16 | 23.53% | 3.98% |
| 21 | gliosarcoma | 22 | 15 | 68.18% | 7.12% |
| 22 | glioblastoma | 28 | 15 | 53.57% | 7.99% |
| 23 | anemia | 59 | 15 | 25.42% | 1.78% |
| 24 | type\_2\_diabetes\_mellitus | 126 | 15 | 11.90% | 3.66% |
| 25 | diabetes\_mellitus | 44 | 14 | 31.82% | 2.56% |
| 26 | melanoma | 45 | 14 | 31.11% | 7.93% |
| 27 | myelodysplastic\_syndromes | 48 | 13 | 27.08% | 32.02% |
| 28 | stage\_iv\_non-small\_cell\_lung\_cancer | 19 | 12 | 63.16% | 4.34% |
| 29 | acute\_coronary\_syndrome | 22 | 12 | 54.55% | 0.62% |
| 30 | carcinoma\_renal\_cell | 29 | 12 | 41.38% | 3.06% |
| 31 | pancreatic\_cancer | 45 | 12 | 26.67% | 6.83% |
| 32 | breast\_neoplasms | 45 | 12 | 26.67% | 1.54% |
| 33 | alzheimer's\_disease | 49 | 12 | 24.49% | 1.94% |
| 34 | chronic\_obstructive\_pulmonary\_disease | 53 | 12 | 22.64% | 0.26% |
| 35 | hypertension | 132 | 12 | 9.09% | 0.50% |
| 36 | schizophrenia | 142 | 12 | 8.45% | 0.42% |
| 37 | recurrent\_non-small\_cell\_lung\_cancer | 17 | 11 | 64.71% | 4.00% |
| 38 | esophageal\_cancer | 27 | 11 | 40.74% | 6.13% |
| 39 | chronic\_obstructive\_pulmonary\_disease\_(copd) | 39 | 11 | 28.21% | 0.83% |
| 40 | osteoarthritis | 54 | 11 | 20.37% | 1.31% |
| 41 | hepatitis\_c\_chronic | 72 | 11 | 15.28% | 0.32% |
| 42 | pain | 91 | 11 | 12.09% | 3.75% |
| 43 | myocardial\_infarction | 20 | 10 | 50.00% | 1.53% |
| 44 | glioblastoma\_multiforme | 21 | 10 | 47.62% | 3.94% |
| 45 | prostatic\_neoplasms | 22 | 10 | 45.45% | 3.84% |
| 46 | metastatic\_colorectal\_cancer | 22 | 10 | 45.45% | 1.79% |
| 47 | acute\_myeloid\_leukemia | 23 | 10 | 43.48% | 8.05% |
| 48 | acute\_myelogenous\_leukemia | 24 | 10 | 41.67% | 12.09% |
| 49 | pulmonary\_arterial\_hypertension | 28 | 10 | 35.71% | 1.24% |
| 50 | epilepsy | 63 | 10 | 15.87% | 6.30% |
| 51 | ischemic\_stroke | 15 | 9 | 60.00% | 10.62% |
| 52 | stage\_iiib\_non-small\_cell\_lung\_cancer | 16 | 9 | 56.25% | 3.43% |
| 53 | cardiovascular\_diseases | 19 | 9 | 47.37% | 5.01% |
| 54 | gastric\_cancer | 26 | 9 | 34.62% | 3.51% |
| 55 | non-hodgkin's\_lymphoma | 36 | 9 | 25.00% | 16.21% |
| 56 | fallopian\_tube\_cancer | 39 | 9 | 23.08% | 6.69% |
| 57 | osteoporosis | 45 | 9 | 20.00% | 0.89% |
| 58 | ovarian\_cancer | 73 | 9 | 12.33% | 9.72% |
| 59 | hepatitis\_c | 79 | 9 | 11.39% | 2.26% |
| 60 | carcinoma\_hepatocellular | 15 | 8 | 53.33% | 5.84% |
| 61 | cardiovascular\_disease | 15 | 8 | 53.33% | 0.64% |
| 62 | recurrent\_ovarian\_epithelial\_cancer | 16 | 8 | 50.00% | 4.86% |
| 63 | heart\_diseases | 16 | 8 | 50.00% | 4.52% |
| 64 | secondary\_acute\_myeloid\_leukemia | 18 | 8 | 44.44% | 6.23% |
| 65 | non\_small\_cell\_lung\_cancer | 27 | 8 | 29.63% | 2.81% |
| 66 | parkinson's\_disease | 44 | 8 | 18.18% | 0.54% |
| 67 | diabetes | 57 | 8 | 14.04% | 1.60% |
| 68 | adult\_acute\_monoblastic\_leukemia\_(m5a) | 11 | 7 | 63.64% | 7.07% |
| 69 | adult\_acute\_monocytic\_leukemia\_(m5b) | 11 | 7 | 63.64% | 7.07% |
| 70 | adult\_acute\_myeloblastic\_leukemia\_with\_maturation\_(m2) | 11 | 7 | 63.64% | 7.07% |
| 71 | adult\_acute\_myeloblastic\_leukemia\_without\_maturation\_(m1) | 11 | 7 | 63.64% | 7.07% |
| 72 | adult\_acute\_myelomonocytic\_leukemia\_(m4) | 11 | 7 | 63.64% | 7.07% |
| 73 | smoking | 12 | 7 | 58.33% | 1.36% |
| 74 | primary\_peritoneal\_cavity\_cancer | 14 | 7 | 50.00% | 3.66% |
| 75 | adult\_acute\_myeloid\_leukemia\_with\_11q23\_(mll)\_abnormalities | 16 | 7 | 43.75% | 7.07% |
| 76 | adult\_acute\_myeloid\_leukemia\_with\_t(16;16)(p13;q22) | 16 | 7 | 43.75% | 7.07% |
| 77 | heart\_failure\_congestive | 17 | 7 | 41.18% | 4.46% |
| 78 | sarcoma | 22 | 7 | 31.82% | 8.15% |
| 79 | secondary\_hyperparathyroidism | 22 | 7 | 31.82% | 1.62% |
| 80 | multiple\_myeloma\_and\_plasma\_cell\_neoplasm | 24 | 7 | 29.17% | 43.74% |
| 81 | stage\_iv\_breast\_cancer | 27 | 7 | 25.93% | 13.66% |
| 82 | smoking\_cessation | 27 | 7 | 25.93% | 0.55% |
| 83 | diabetic\_macular\_edema | 28 | 7 | 25.00% | 1.06% |
| 84 | parkinson\_disease | 33 | 7 | 21.21% | 1.00% |
| 85 | neoplasms | 34 | 7 | 20.59% | 8.81% |
| 86 | bipolar\_disorder | 40 | 7 | 17.50% | 2.09% |
| 87 | metastatic\_breast\_cancer | 46 | 7 | 15.22% | 0.99% |
| 88 | recurrent\_endometrial\_carcinoma | 7 | 6 | 85.71% | 3.68% |
| 89 | lymphocytic\_leukemia\_chronic | 8 | 6 | 75.00% | 1.32% |
| 90 | small\_cell\_lung\_cancer | 9 | 6 | 66.67% | 2.60% |
| 91 | recurrent\_small\_cell\_lung\_cancer | 10 | 6 | 60.00% | 9.42% |
| 92 | adult\_acute\_megakaryoblastic\_leukemia\_(m7) | 10 | 6 | 60.00% | 7.27% |
| 93 | adult\_acute\_minimally\_differentiated\_myeloid\_leukemia\_(m0) | 10 | 6 | 60.00% | 7.27% |
| 94 | chronic\_renal\_failure | 10 | 6 | 60.00% | 1.87% |
| 95 | extensive\_stage\_small\_cell\_lung\_cancer | 11 | 6 | 54.55% | 7.30% |
| 96 | head\_and\_neck\_neoplasms | 11 | 6 | 54.55% | 1.85% |
| 97 | tuberculosis | 12 | 6 | 50.00% | 0.85% |
| 98 | stage\_iv\_pancreatic\_cancer | 13 | 6 | 46.15% | 9.55% |
| 99 | recurrent\_adult\_acute\_myeloid\_leukemia | 13 | 6 | 46.15% | 5.79% |
| 100 | adult\_acute\_myeloid\_leukemia\_with\_inv(16)(p13;q22) | 15 | 6 | 40.00% | 7.27% |
| 101 | adult\_acute\_myeloid\_leukemia\_with\_t(8;21)(q22;q22) | 15 | 6 | 40.00% | 7.27% |
| 102 | untreated\_adult\_acute\_myeloid\_leukemia | 15 | 6 | 40.00% | 5.14% |
| 103 | bladder\_cancer | 15 | 6 | 40.00% | 4.86% |
| 104 | brain\_and\_central\_nervous\_system\_tumors | 15 | 6 | 40.00% | 2.54% |
| 105 | acute\_lymphoblastic\_leukemia | 16 | 6 | 37.50% | 19.53% |
| 106 | neoplasm\_metastasis | 16 | 6 | 37.50% | 0.94% |
| 107 | alzheimer\_disease | 17 | 6 | 35.29% | 2.80% |
| 108 | myocardial\_ischemia | 20 | 6 | 30.00% | 0.36% |
| 109 | pulmonary\_hypertension | 23 | 6 | 26.09% | 2.69% |
| 110 | benign\_prostatic\_hyperplasia | 24 | 6 | 25.00% | 1.45% |
| 111 | depression | 40 | 6 | 15.00% | 7.98% |
| 112 | head\_and\_neck\_cancer | 51 | 6 | 11.76% | 3.88% |
| 113 | psoriasis | 58 | 6 | 10.34% | 0.65% |
| 114 | influenza | 124 | 6 | 4.84% | 0.35% |
| 115 | anaplastic\_astrocytoma | 6 | 5 | 83.33% | 10.25% |
| 116 | venous\_thrombosis | 6 | 5 | 83.33% | 0.86% |
| 117 | recurrent\_uterine\_sarcoma | 7 | 5 | 71.43% | 13.92% |
| 118 | end\_stage\_renal\_disease | 7 | 5 | 71.43% | 4.51% |
| 119 | adult\_erythroleukemia\_(m6a) | 9 | 5 | 55.56% | 7.69% |
| 120 | adult\_pure\_erythroid\_leukemia\_(m6b) | 9 | 5 | 55.56% | 7.69% |
| 121 | non-small-cell\_lung\_cancer | 9 | 5 | 55.56% | 3.58% |
| 122 | adenocarcinoma | 9 | 5 | 55.56% | 1.07% |
| 123 | chronic\_myelomonocytic\_leukemia | 10 | 5 | 50.00% | 6.60% |
| 124 | squamous\_cell\_carcinoma | 10 | 5 | 50.00% | 5.69% |
| 125 | coronary\_disease | 11 | 5 | 45.45% | 3.97% |
| 126 | myelofibrosis | 12 | 5 | 41.67% | 17.98% |
| 127 | chronic\_myeloid\_leukemia | 12 | 5 | 41.67% | 1.46% |
| 128 | recurrent\_colon\_cancer | 13 | 5 | 38.46% | 20.21% |
| 129 | recurrent\_rectal\_cancer | 13 | 5 | 38.46% | 20.21% |
| 130 | unspecified\_adult\_solid\_tumor\_protocol\_specific | 16 | 5 | 31.25% | 5.25% |
| 131 | thromboembolism | 16 | 5 | 31.25% | 1.07% |
| 132 | colorectal\_neoplasms | 18 | 5 | 27.78% | 1.96% |
| 133 | kidney\_cancer | 19 | 5 | 26.32% | 10.31% |
| 134 | chronic\_lymphocytic\_leukemia | 21 | 5 | 23.81% | 8.88% |
| 135 | macular\_edema | 23 | 5 | 21.74% | 2.84% |
| 136 | kidney\_transplantation | 23 | 5 | 21.74% | 0.87% |
| 137 | neoplasms\_breast | 25 | 5 | 20.00% | 0.84% |
| 138 | crohn's\_disease | 41 | 5 | 12.20% | 0.21% |
| 139 | diphtheria | 43 | 5 | 11.63% | 0.26% |
| 140 | type\_2\_diabetes | 52 | 5 | 9.62% | 0.55% |
| 141 | hypercholesterolemia | 54 | 5 | 9.26% | 0.43% |
| 142 | asthma | 133 | 5 | 3.76% | 0.48% |

**Appendix – 3**

**Top 137 Frequent Diseases** (Note: Death- General disorders, 2591)

|  |  |  |  |
| --- | --- | --- | --- |
| **Index** | **Single adverse event** | **Category** | **Frequency (arms#)** |
| 1 | Pneumonia | Infections and infestations | 4765 |
| 2 | Dehydration | Metabolism and nutrition disorders | 2832 |
| 3 | Vomiting | Gastrointestinal disorders | 2645 |
| 4 | Pyrexia | General disorders | 2387 |
| 5 | Sepsis | Infections and infestations | 2099 |
| 6 | Nausea | Gastrointestinal disorders | 2096 |
| 7 | Anaemia | Blood and lymphatic system disorders | 2080 |
| 8 | Syncope | Nervous system disorders | 2036 |
| 9 | Cellulitis | Infections and infestations | 2012 |
| 10 | Abdominal\_pain | Gastrointestinal disorders | 1987 |
| 11 | Dyspnoea | Respiratory, thoracic and mediastinal disorders | 1976 |
| 12 | Atrial\_fibrillation | Cardiac disorders | 1901 |
| 13 | Gastroenteritis | Infections and infestations | 1891 |
| 14 | Urinary\_tract\_infection | Infections and infestations | 1863 |
| 15 | Myocardial\_infarction | Cardiac disorders | 1823 |
| 16 | Diarrhoea | Gastrointestinal disorders | 1754 |
| 17 | Pulmonary\_embolism | Respiratory, thoracic and mediastinal disorders | 1731 |
| 18 | Chest\_pain | General disorders | 1730 |
| 19 | Hypotension | Vascular disorders | 1643 |
| 20 | Hypertension | Vascular disorders | 1600 |
| 21 | Renal\_failure\_acute | Renal and urinary disorders | 1469 |
| 22 | Bronchitis | Infections and infestations | 1435 |
| 23 | Cerebrovascular\_accident | Renal and urinary disorders | 1419 |
| 24 | Fatigue | Infections and infestations | 1408 |
| 25 | Pleural\_effusion | Infections and infestations | 1333 |
| 26 | Deep\_vein\_thrombosis | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1317 |
| 27 | Back\_pain | Cardiac disorders | 1299 |
| 28 | Febrile\_neutropenia | Gastrointestinal disorders | 1269 |
| 29 | Angina\_pectoris | Respiratory, thoracic and mediastinal disorders | 1257 |
| 30 | Depression | General disorders | 1255 |
| 31 | Chronic\_obstructive\_pulmonary\_disease | Gastrointestinal disorders | 1244 |
| 32 | Renal\_failure | Renal and urinary disorders | 1228 |
| 33 | Respiratory\_failure | Metabolism and nutrition disorders | 1228 |
| 34 | Thrombocytopenia | Cardiac disorders | 1206 |
| 35 | Neutropenia | Gastrointestinal disorders | 1204 |
| 36 | Cholelithiasis | General disorders | 1201 |
| 37 | Appendicitis | General disorders | 1198 |
| 38 | Constipation | Gastrointestinal disorders | 1196 |
| 39 | Convulsion | Blood and lymphatic system disorders | 1176 |
| 40 | Acute\_myocardial\_infarction | Cardiac disorders | 1167 |
| 41 | Headache | Respiratory, thoracic and mediastinal disorders | 1164 |
| 42 | Cardiac\_failure\_congestive | Vascular disorders | 1137 |
| 43 | Dizziness | Nervous system disorders | 1120 |
| 44 | Fall | Nervous system disorders | 1114 |
| 45 | Cholecystitis | Musculoskeletal and connective tissue disorders | 1113 |
| 46 | Coronary\_artery\_disease | Blood and lymphatic system disorders | 1085 |
| 47 | Asthenia | Gastrointestinal disorders | 1080 |
| 48 | Osteoarthritis | Gastrointestinal disorders | 1063 |
| 49 | Gastrointestinal\_haemorrhage | Gastrointestinal disorders | 1005 |
| 50 | Cardiac\_failure | Cardiac disorders | 1004 |
| 51 | Hypoxia | Respiratory, thoracic and mediastinal disorders | 998 |
| 52 | Infection | Infections and infestations | 947 |
| 53 | Asthma | Blood and lymphatic system disorders | 940 |
| 54 | Pancreatitis | Cardiac disorders | 932 |
| 55 | Transient\_ischaemic\_attack | Vascular disorders | 924 |
| 56 | Cardiac\_arrest | Cardiac disorders | 913 |
| 57 | Non-cardiac\_chest\_pain | Nervous system disorders | 906 |
| 58 | Arthralgia | Infections and infestations | 902 |
| 59 | Gastritis | Psychiatric disorders | 864 |
| 60 | Pneumothorax | Respiratory, thoracic and mediastinal disorders | 862 |
| 61 | Diverticulitis | General disorders | 836 |
| 62 | Bronchopneumonia | Blood and lymphatic system disorders | 813 |
| 63 | Hypoglycaemia | Gastrointestinal disorders | 812 |
| 64 | Septic\_shock | Infections and infestations | 805 |
| 65 | Ileus | Injury, poisoning and procedural complications | 766 |
| 66 | Breast\_cancer | Metabolism and nutrition disorders | 764 |
| 67 | Pyelonephritis | Musculoskeletal and connective tissue disorders | 759 |
| 68 | Nephrolithiasis | Injury, poisoning and procedural complications | 753 |
| 69 | Hyponatraemia | Metabolism and nutrition disorders | 745 |
| 70 | Pain | General disorders | 732 |
| 71 | Small\_intestinal\_obstruction | Vascular disorders | 728 |
| 72 | Prostate\_cancer | Infections and infestations | 723 |
| 73 | Femur\_fracture | Gastrointestinal disorders | 710 |
| 74 | Colitis | Gastrointestinal disorders | 708 |
| 75 | Angina\_unstable | Injury, poisoning and procedural complications | 707 |
| 76 | Intestinal\_obstruction | Respiratory, thoracic and mediastinal disorders | 707 |
| 77 | Hyperglycaemia | Metabolism and nutrition disorders | 699 |
| 78 | Hypokalaemia | Metabolism and nutrition disorders | 687 |
| 79 | Confusional\_state | Psychiatric disorders | 687 |
| 80 | Dyspnea | Cardiac disorders | 687 |
| 81 | Intervertebral\_disc\_protrusion | Cardiac disorders | 681 |
| 82 | Diarrhea | Infections and infestations | 663 |
| 83 | Pneumonitis | Cardiac disorders | 659 |
| 84 | Vertigo | Ear and labyrinth disorders | 653 |
| 85 | Haematuria | Renal and urinary disorders | 651 |
| 86 | Upper\_respiratory\_tract\_infection | Nervous system disorders | 642 |
| 87 | Bradycardia | Cardiac disorders | 633 |
| 88 | Inguinal\_hernia | Gastrointestinal disorders | 625 |
| 89 | Hip\_fracture | Nervous system disorders | 623 |
| 90 | Pain\_in\_extremity | Musculoskeletal and connective tissue disorders | 622 |
| 91 | Dysphagia | Gastrointestinal disorders | 615 |
| 92 | Haemoptysis | Respiratory, thoracic and mediastinal disorders | 613 |
| 93 | Oedema\_peripheral | General disorders | 611 |
| 94 | Cholecystitis\_acute | Hepatobiliary disorders | 611 |
| 95 | Epistaxis | Respiratory, thoracic and mediastinal disorders | 610 |
| 96 | Urosepsis | Infections and infestations | 608 |
| 97 | Urinary\_retention | Renal and urinary disorders | 598 |
| 98 | Leukopenia | Gastrointestinal disorders | 589 |
| 99 | Herpes\_zoster | Gastrointestinal disorders | 585 |
| 100 | Lobar\_pneumonia | Infections and infestations | 583 |
| 101 | Cerebral\_infarction | Nervous system disorders | 581 |
| 102 | Colon\_cancer | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 580 |
| 103 | Road\_traffic\_accident | Hepatobiliary disorders | 579 |
| 104 | Abdominal\_pain\_upper | Gastrointestinal disorders | 578 |
| 105 | Lower\_respiratory\_tract\_infection | Infections and infestations | 576 |
| 106 | General\_physical\_health\_deterioration | General disorders | 574 |
| 107 | Cough | Respiratory, thoracic and mediastinal disorders | 568 |
| 108 | Myocardial\_ischaemia | Cardiac disorders | 564 |
| 109 | Ascites | Respiratory, thoracic and mediastinal disorders | 563 |
| 110 | Thrombosis | Infections and infestations | 557 |
| 111 | Acute\_respiratory\_failure | Respiratory, thoracic and mediastinal disorders | 546 |
| 112 | Multi-organ\_failure | General disorders | 545 |
| 113 | Anxiety | Respiratory, thoracic and mediastinal disorders | 541 |
| 114 | Respiratory\_tract\_infection | Infections and infestations | 540 |
| 115 | Pulmonary\_oedema | Respiratory, thoracic and mediastinal disorders | 533 |
| 116 | Lung\_infection | Infections and infestations | 532 |
| 117 | Cataract | Eye disorders | 528 |
| 118 | Acute\_coronary\_syndrome | Cardiac disorders | 526 |
| 119 | Osteomyelitis | Infections and infestations | 526 |
| 120 | Cardio-respiratory\_arrest | Cardiac disorders | 523 |
| 121 | Diabetes\_mellitus | Metabolism and nutrition disorders | 516 |
| 122 | Lung\_neoplasm\_malignant | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 515 |
| 123 | Pancreatitis\_acute | Gastrointestinal disorders | 511 |
| 124 | Supraventricular\_tachycardia | Cardiac disorders | 507 |
| 125 | Atrial\_flutter | Cardiac disorders | 506 |
| 126 | Hyperkalaemia | Metabolism and nutrition disorders | 506 |
| 127 | Arrhythmia | Cardiac disorders | 504 |
| 128 | Rectal\_haemorrhage | Gastrointestinal disorders | 497 |
| 129 | Pneumonia\_aspiration | Respiratory, thoracic and mediastinal disorders | 497 |
| 130 | Cerebral\_haemorrhage | Nervous system disorders | 490 |
| 131 | Tachycardia | Cardiac disorders | 490 |
| 132 | Ischaemic\_stroke | Nervous system disorders | 488 |
| 133 | Hypertensive\_crisis | Vascular disorders | 482 |
| 134 | Peritonitis | General disorders | 480 |
| 135 | Erysipelas | Infections and infestations | 457 |
| 136 | Subdural\_haematoma | Injury, poisoning and procedural complications | 456 |
| 137 | Femoral\_neck\_fracture | Injury, poisoning and procedural complications | 453 |

**Appendix – 4**

**Top 178 confidence sorted single serious adverse event** (with frequency and category)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Index** | **Degree** | **Source** | **Frequency** | **Category** | **Target** |
| 1 | 0.568181818 | Haematemesis | 352 | Gastrointestinal disorders | Death |
| 2 | 0.535168196 | Skin\_ulcer | 327 | Skin and subcutaneous tissue disorders | Death |
| 3 | 0.53313253 | Renal\_failure\_chronic | 332 | Renal and urinary disorders | Death |
| 4 | 0.531914894 | Orthostatic\_hypotension | 329 | Vascular disorders | Death |
| 5 | 0.525993884 | Bladder\_cancer | 327 | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | Death |
| 6 | 0.524390244 | Melaena | 328 | Gastrointestinal disorders | Death |
| 7 | 0.522077922 | Encephalopathy | 385 | Nervous system disorders | Death |
| 8 | 0.515513126 | Haematoma | 419 | Vascular disorders | Death |
| 9 | 0.507374631 | Malaise | 339 | General disorders | Death |
| 10 | 0.504780115 | Cardio-respiratory\_arrest | 523 | Cardiac disorders | Death |
| 11 | 0.504587156 | Multi-organ\_failure | 545 | General disorders | Death |
| 12 | 0.503875969 | Ventricular\_tachycardia | 387 | Cardiac disorders | Death |
| 13 | 0.501432665 | Musculoskeletal\_pain | 349 | Musculoskeletal and connective tissue disorders | Death |
| 14 | 0.5 | Cerebral\_haemorrhage | 490 | Nervous system disorders | Death |
| 15 | 0.49795082 | Ischaemic\_stroke | 488 | Nervous system disorders | Death |
| 16 | 0.497185741 | Pulmonary\_oedema | 533 | Respiratory, thoracic and mediastinal disorders | Death |
| 17 | 0.496031746 | Arrhythmia | 504 | Cardiac disorders | Death |
| 18 | 0.492341357 | Erysipelas | 457 | Infections and infestations | Death |
| 19 | 0.492094862 | Atrial\_flutter | 506 | Cardiac disorders | Death |
| 20 | 0.490066225 | Femoral\_neck\_fracture | 453 | Injury, poisoning and procedural complications | Death |
| 21 | 0.488721805 | Lung\_infection | 532 | Infections and infestations | Death |
| 22 | 0.488479263 | Haematuria | 651 | Renal and urinary disorders | Death |
| 23 | 0.487551867 | Hypertensive\_crisis | 482 | Vascular disorders | Death |
| 24 | 0.484771574 | Gastric\_ulcer | 394 | Gastrointestinal disorders | Death |
| 25 | 0.482871126 | Haemoptysis | 613 | Respiratory, thoracic and mediastinal disorders | Death |
| 26 | 0.481967213 | Epistaxis | 610 | Respiratory, thoracic and mediastinal disorders | Death |
| 27 | 0.480263158 | Subdural\_haematoma | 456 | Injury, poisoning and procedural complications | Death |
| 28 | 0.477922078 | Hydronephrosis | 385 | Renal and urinary disorders | Death |
| 29 | 0.477777778 | Respiratory\_tract\_infection | 540 | Infections and infestations | Death |
| 30 | 0.475378788 | Cataract | 528 | Eye disorders | Death |
| 31 | 0.474849095 | Rectal\_haemorrhage | 497 | Gastrointestinal disorders | Death |
| 32 | 0.4743083 | Hyperkalaemia | 506 | Metabolism and nutrition disorders | Death |
| 33 | 0.472837022 | Pneumonia\_aspiration | 497 | Respiratory, thoracic and mediastinal disorders | Death |
| 34 | 0.470588235 | Pericardial\_effusion | 442 | Cardiac disorders | Death |
| 35 | 0.470183486 | Rib\_fracture | 436 | Injury, poisoning and procedural complications | Death |
| 36 | 0.469248292 | Upper\_gastrointestinal\_haemorrhage | 439 | Gastrointestinal disorders | Death |
| 37 | 0.466898955 | General\_physical\_health\_deterioration | 574 | General disorders | Death |
| 38 | 0.466346154 | Presyncope | 416 | Nervous system disorders | Death |
| 39 | 0.465779468 | Acute\_coronary\_syndrome | 526 | Cardiac disorders | Death |
| 40 | 0.464467005 | Device\_related\_infection | 394 | Infections and infestations | Death |
| 41 | 0.463917526 | Benign\_prostatic\_hyperplasia | 388 | Reproductive system and breast disorders | Death |
| 42 | 0.463157895 | Renal\_impairment | 380 | Renal and urinary disorders | Death |
| 43 | 0.4625 | Peritonitis | 480 | Gastrointestinal disorders | Death |
| 44 | 0.462171053 | Urosepsis | 608 | Infections and infestations | Death |
| 45 | 0.459183673 | Tachycardia | 490 | Cardiac disorders | Death |
| 46 | 0.458385093 | Septic\_shock | 805 | Infections and infestations | Death |
| 47 | 0.457627119 | Contusion | 413 | Injury, poisoning and procedural complications | Death |
| 48 | 0.454991817 | Oedema\_peripheral | 611 | General disorders | Death |
| 49 | 0.453450164 | Cardiac\_arrest | 913 | Cardiac disorders | Death |
| 50 | 0.452488688 | Epilepsy | 442 | Nervous system disorders | Death |
| 51 | 0.451456311 | Arthritis | 412 | Musculoskeletal and connective tissue disorders | Death |
| 52 | 0.450549451 | Acute\_respiratory\_failure | 546 | Respiratory, thoracic and mediastinal disorders | Death |
| 53 | 0.450485437 | Lung\_neoplasm\_malignant | 515 | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | Death |
| 54 | 0.449612403 | Diabetes\_mellitus | 516 | Metabolism and nutrition disorders | Death |
| 55 | 0.449462366 | Humerus\_fracture | 465 | Injury, poisoning and procedural complications | Death |
| 56 | 0.446870451 | Hypokalaemia | 687 | Metabolism and nutrition disorders | Death |
| 57 | 0.446366782 | Abdominal\_pain\_upper | 578 | Gastrointestinal disorders | Death |
| 58 | 0.445422535 | Cough | 568 | Respiratory, thoracic and mediastinal disorders | Death |
| 59 | 0.444444444 | Lower\_respiratory\_tract\_infection | 576 | Infections and infestations | Death |
| 60 | 0.443349754 | Muscular\_weakness | 406 | Musculoskeletal and connective tissue disorders | Death |
| 61 | 0.443262411 | Myocardial\_ischaemia | 564 | Cardiac disorders | Death |
| 62 | 0.443155452 | Wound\_infection | 431 | Infections and infestations | Death |
| 63 | 0.44295302 | Hyponatraemia | 745 | Metabolism and nutrition disorders | Death |
| 64 | 0.442748092 | Head\_injury | 393 | Injury, poisoning and procedural complications | Death |
| 65 | 0.441041348 | Vertigo | 653 | Ear and labyrinth disorders | Death |
| 66 | 0.440835267 | Pneumothorax | 862 | Respiratory, thoracic and mediastinal disorders | Death |
| 67 | 0.439842209 | Supraventricular\_tachycardia | 507 | Cardiac disorders | Death |
| 68 | 0.439799331 | Urinary\_retention | 598 | Renal and urinary disorders | Death |
| 69 | 0.438625205 | Cholecystitis\_acute | 611 | Hepatobiliary disorders | Death |
| 70 | 0.436681223 | Confusional\_state | 687 | Psychiatric disorders | Death |
| 71 | 0.43490701 | Hyperglycaemia | 699 | Metabolism and nutrition disorders | Death |
| 72 | 0.434482759 | Colon\_cancer | 580 | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | Death |
| 73 | 0.433333333 | Decreased\_appetite | 450 | Metabolism and nutrition disorders | Death |
| 74 | 0.432520325 | Dysphagia | 615 | Gastrointestinal disorders | Death |
| 75 | 0.4312749 | Cardiac\_failure | 1004 | Cardiac disorders | Death |
| 76 | 0.430523918 | Respiratory\_distress | 439 | Respiratory, thoracic and mediastinal disorders | Death |
| 77 | 0.427756654 | Osteomyelitis | 526 | Infections and infestations | Death |
| 78 | 0.426614481 | Pancreatitis\_acute | 511 | Gastrointestinal disorders | Death |
| 79 | 0.426045016 | Pain\_in\_extremity | 622 | Musculoskeletal and connective tissue disorders | Death |
| 80 | 0.424875622 | Gastrointestinal\_haemorrhage | 1005 | Gastrointestinal disorders | Death |
| 81 | 0.422321429 | Dizziness | 1120 | Nervous system disorders | Death |
| 82 | 0.421955403 | Lobar\_pneumonia | 583 | Infections and infestations | Death |
| 83 | 0.42019544 | Renal\_failure | 1228 | Renal and urinary disorders | Death |
| 84 | 0.419218585 | Infection | 947 | Infections and infestations | Death |
| 85 | 0.41864139 | Bradycardia | 633 | Cardiac disorders | Death |
| 86 | 0.415781487 | Pneumonitis | 659 | Respiratory, thoracic and mediastinal disorders | Death |
| 87 | 0.415630551 | Ascites | 563 | Gastrointestinal disorders | Death |
| 88 | 0.414814815 | Asthenia | 1080 | General disorders | Death |
| 89 | 0.413092551 | Blood\_creatinine\_increased | 443 | Investigations | Death |
| 90 | 0.412568306 | Pain | 732 | General disorders | Death |
| 91 | 0.406196213 | Cerebral\_infarction | 581 | Nervous system disorders | Death |
| 92 | 0.406099518 | Hip\_fracture | 623 | Injury, poisoning and procedural complications | Death |
| 93 | 0.406005222 | Ileus | 766 | Gastrointestinal disorders | Death |
| 94 | 0.405518395 | Constipation | 1196 | Gastrointestinal disorders | Death |
| 95 | 0.4032 | Inguinal\_hernia | 625 | Gastrointestinal disorders | Death |
| 96 | 0.402542373 | Colitis | 708 | Gastrointestinal disorders | Death |
| 97 | 0.401408451 | Femur\_fracture | 710 | Injury, poisoning and procedural complications | Death |
| 98 | 0.400419287 | Mental\_status\_changes | 477 | Psychiatric disorders | Death |
| 99 | 0.400282885 | Angina\_unstable | 707 | Cardiac disorders | Death |
| 100 | 0.399141631 | Pancreatitis | 932 | Gastrointestinal disorders | Death |
| 101 | 0.399014778 | Hypoglycaemia | 812 | Metabolism and nutrition disorders | Death |
| 102 | 0.394136808 | Respiratory\_failure | 1228 | Respiratory, thoracic and mediastinal disorders | Death |
| 103 | 0.393787575 | Hypoxia | 998 | Respiratory, thoracic and mediastinal disorders | Death |
| 104 | 0.39321075 | Intestinal\_obstruction | 707 | Gastrointestinal disorders | Death |
| 105 | 0.393162393 | Herpes\_zoster | 585 | Infections and infestations | Death |
| 106 | 0.390847712 | Pleural\_effusion | 1333 | Respiratory, thoracic and mediastinal disorders | Death |
| 107 | 0.390018484 | Anxiety | 541 | Psychiatric disorders | Death |
| 108 | 0.388888889 | Gastritis | 864 | Gastrointestinal disorders | Death |
| 109 | 0.388794567 | Leukopenia | 589 | Blood and lymphatic system disorders | Death |
| 110 | 0.387453875 | Bronchopneumonia | 813 | Infections and infestations | Death |
| 111 | 0.387225549 | Ankle\_fracture | 501 | Injury, poisoning and procedural complications | Death |
| 112 | 0.385996409 | Thrombosis | 557 | Vascular disorders | Death |
| 113 | 0.383116883 | Transient\_ischaemic\_attack | 924 | Nervous system disorders | Death |
| 114 | 0.382413088 | Influenza | 489 | Infections and infestations | Death |
| 115 | 0.381619938 | Upper\_respiratory\_tract\_infection | 642 | Infections and infestations | Death |
| 116 | 0.37804878 | Arthralgia | 902 | Musculoskeletal and connective tissue disorders | Death |
| 117 | 0.376460018 | Cholecystitis | 1113 | Hepatobiliary disorders | Death |
| 118 | 0.375 | Sinusitis | 480 | Infections and infestations | Death |
| 119 | 0.374784111 | Road\_traffic\_accident | 579 | Injury, poisoning and procedural complications | Death |
| 120 | 0.373046875 | Bacteraemia | 512 | Infections and infestations | Death |
| 121 | 0.372745491 | Hypersensitivity | 499 | Immune system disorders | Death |
| 122 | 0.371880706 | Hypotension | 1643 | Vascular disorders | Death |
| 123 | 0.371152155 | Cardiac\_failure\_congestive | 1137 | Cardiac disorders | Death |
| 124 | 0.367975366 | Back\_pain | 1299 | Musculoskeletal and connective tissue disorders | Death |
| 125 | 0.365384615 | Pancytopenia | 520 | Blood and lymphatic system disorders | Death |
| 126 | 0.364953887 | Pyelonephritis | 759 | Infections and infestations | Death |
| 127 | 0.361505682 | Fatigue | 1408 | General disorders | Death |
| 128 | 0.361244019 | Diverticulitis | 836 | Infections and infestations | Death |
| 129 | 0.360995851 | Prostate\_cancer | 723 | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | Death |
| 130 | 0.358390281 | Deep\_vein\_thrombosis | 1317 | Vascular disorders | Death |
| 131 | 0.357414449 | Rash | 526 | Skin and subcutaneous tissue disorders | Death |
| 132 | 0.357009346 | Basal\_cell\_carcinoma | 535 | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | Death |
| 133 | 0.355769231 | Small\_intestinal\_obstruction | 728 | Gastrointestinal disorders | Death |
| 134 | 0.355343771 | Renal\_failure\_acute | 1469 | Renal and urinary disorders | Death |
| 135 | 0.354474982 | Cerebrovascular\_accident | 1419 | Nervous system disorders | Death |
| 136 | 0.353898886 | Acute\_myocardial\_infarction | 1167 | Cardiac disorders | Death |
| 137 | 0.352404643 | Thrombocytopenia | 1206 | Blood and lymphatic system disorders | Death |
| 138 | 0.351190476 | Convulsion | 1176 | Nervous system disorders | Death |
| 139 | 0.349192101 | Fall | 1114 | Injury, poisoning and procedural complications | Death |
| 140 | 0.347941567 | Nephrolithiasis | 753 | Renal and urinary disorders | Death |
| 141 | 0.34587899 | Sepsis | 2099 | Infections and infestations | Death |
| 142 | 0.345399698 | Diarrhea | 663 | Gastrointestinal disorders | Death |
| 143 | 0.345 | Hypertension | 1600 | Vascular disorders | Death |
| 144 | 0.340069686 | Bronchitis | 1435 | Infections and infestations | Death |
| 145 | 0.336106489 | Anorexia | 601 | Metabolism and nutrition disorders | Death |
| 146 | 0.33451417 | Dyspnoea | 1976 | Respiratory, thoracic and mediastinal disorders | Death |
| 147 | 0.333333333 | Angina\_pectoris | 1257 | Cardiac disorders | Death |
| 148 | 0.33295325 | Diarrhoea | 1754 | Gastrointestinal disorders | Death |
| 149 | 0.331993569 | Chronic\_obstructive\_pulmonary\_disease | 1244 | Respiratory, thoracic and mediastinal disorders | Death |
| 150 | 0.33102253 | Pulmonary\_embolism | 1731 | Respiratory, thoracic and mediastinal disorders | Death |
| 151 | 0.327403846 | Anaemia | 2080 | Blood and lymphatic system disorders | Death |
| 152 | 0.326267281 | Coronary\_artery\_disease | 1085 | Cardiac disorders | Death |
| 153 | 0.326144135 | Atrial\_fibrillation | 1901 | Cardiac disorders | Death |
| 154 | 0.326055313 | Dyspnea | 687 | Respiratory, thoracic and mediastinal disorders | Death |
| 155 | 0.325601375 | Headache | 1164 | Nervous system disorders | Death |
| 156 | 0.323399558 | Non-cardiac\_chest\_pain | 906 | General disorders | Death |
| 157 | 0.323064113 | Cholelithiasis | 1201 | Hepatobiliary disorders | Death |
| 158 | 0.320652174 | Alanine\_aminotransferase\_increased | 552 | Investigations | Death |
| 159 | 0.319253438 | Syncope | 2036 | Nervous system disorders | Death |
| 160 | 0.318303811 | Urinary\_tract\_infection | 1863 | Infections and infestations | Death |
| 161 | 0.316793893 | Nausea | 2096 | Gastrointestinal disorders | Death |
| 162 | 0.316086548 | Osteoarthritis | 1063 | Musculoskeletal and connective tissue disorders | Death |
| 163 | 0.31431706 | Myocardial\_infarction | 1823 | Cardiac disorders | Death |
| 164 | 0.314243759 | Intervertebral\_disc\_protrusion | 681 | Musculoskeletal and connective tissue disorders | Death |
| 165 | 0.311440678 | Dehydration | 2832 | Metabolism and nutrition disorders | Death |
| 166 | 0.310209424 | Breast\_cancer | 764 | Neoplasms benign, malignant and unspecified (incl cysts and polyps) | Death |
| 167 | 0.30982659 | Chest\_pain | 1730 | General disorders | Death |
| 168 | 0.308366534 | Depression | 1255 | Psychiatric disorders | Death |
| 169 | 0.305860113 | Vomiting | 2645 | Gastrointestinal disorders | Death |
| 170 | 0.295681063 | Neutropenia | 1204 | Blood and lymphatic system disorders | Death |
| 171 | 0.292903875 | Abdominal\_pain | 1987 | Gastrointestinal disorders | Death |
| 172 | 0.289264414 | Cellulitis | 2012 | Infections and infestations | Death |
| 173 | 0.283976732 | Gastroenteritis | 1891 | Infections and infestations | Death |
| 174 | 0.283687943 | Febrile\_neutropenia | 1269 | Blood and lymphatic system disorders | Death |
| 175 | 0.280851064 | Asthma | 940 | Respiratory, thoracic and mediastinal disorders | Death |
| 176 | 0.273565145 | Pyrexia | 2387 | General disorders | Death |
| 177 | 0.263772955 | Appendicitis | 1198 | Infections and infestations | Death |
| 178 | 0.225393494 | Pneumonia | 4765 | Infections and infestations | Death |

**Appendix – 5**

**Top 100 confidence sorted double serious adverse events**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Index** | **Confidence** | **Source** | **Frequency** | **Target** |
| 1 | 0.783783784 | Respiratory\_tract\_infection Septic\_shock | 222 | Death |
| 2 | 0.764705882 | Diverticulitis Renal\_failure | 238 | Death |
| 3 | 0.760869565 | Multi-organ\_failure Chest\_pain | 230 | Death |
| 4 | 0.759825328 | Multi-organ\_failure Bronchitis | 229 | Death |
| 5 | 0.756637168 | Appendicitis Renal\_failure | 226 | Death |
| 6 | 0.754237288 | Ischaemic\_stroke Respiratory\_failure | 236 | Death |
| 7 | 0.752988048 | Pneumothorax Dizziness | 251 | Death |
| 8 | 0.752173913 | Ischaemic\_stroke Gastrointestinal\_haemorrhage | 230 | Death |
| 9 | 0.751091703 | Hypokalaemia Cardiac\_failure | 229 | Death |
| 10 | 0.751072961 | Cerebral\_haemorrhage Cardiac\_failure | 233 | Death |
| 11 | 0.751054852 | Multi-organ\_failure Back\_pain | 237 | Death |
| 12 | 0.751004016 | Colon\_cancer Cardiac\_failure | 249 | Death |
| 13 | 0.75 | Haematuria Cardiac\_failure | 252 | Death |
| 14 | 0.75 | Cataract Bronchitis | 236 | Death |
| 15 | 0.747933884 | Septic\_shock Transient\_ischaemic\_attack | 242 | Death |
| 16 | 0.746268657 | Cardiac\_failure Convulsion | 268 | Death |
| 17 | 0.745901639 | Femur\_fracture Septic\_shock | 244 | Death |
| 18 | 0.745833333 | Cardiac\_arrest Depression | 240 | Death |
| 19 | 0.744855967 | Haematuria Cardiac\_arrest | 243 | Death |
| 20 | 0.743902439 | Haematuria Dizziness | 246 | Death |
| 21 | 0.743801653 | Cholecystitis\_acute Cardiac\_failure | 242 | Death |
| 22 | 0.74248927 | Epistaxis Respiratory\_failure | 233 | Death |
| 23 | 0.74137931 | Cholecystitis\_acute Pleural\_effusion | 232 | Death |
| 24 | 0.739495798 | Femoral\_neck\_fracture Dyspnoea | 238 | Death |
| 25 | 0.738461538 | Cataract Syncope | 260 | Death |
| 26 | 0.738396624 | Arrhythmia Bronchitis | 237 | Death |
| 27 | 0.737288136 | Cataract Cholelithiasis | 236 | Death |
| 28 | 0.736842105 | Vertigo Back\_pain | 247 | Death |
| 29 | 0.736625514 | Respiratory\_tract\_infection Back\_pain | 243 | Death |
| 30 | 0.736434109 | Multi-organ\_failure Myocardial\_infarction | 258 | Death |
| 31 | 0.736401674 | Acute\_coronary\_syndrome Cardiac\_failure | 239 | Death |
| 32 | 0.736220472 | Diverticulitis Pleural\_effusion | 254 | Death |
| 33 | 0.736170213 | Ischaemic\_stroke Dehydration | 235 | Death |
| 34 | 0.736 | Femur\_fracture Dizziness | 250 | Death |
| 35 | 0.735294118 | Haematuria Osteoarthritis | 238 | Death |
| 36 | 0.735294118 | Respiratory\_tract\_infection Cardiac\_failure | 238 | Death |
| 37 | 0.734126984 | Multi-organ\_failure Cerebrovascular\_accident | 252 | Death |
| 38 | 0.734082397 | Haemoptysis Urinary\_tract\_infection | 267 | Death |
| 39 | 0.733905579 | Vertigo Cardiac\_failure | 233 | Death |
| 40 | 0.733870968 | Haemoptysis Myocardial\_infarction | 248 | Death |
| 41 | 0.733050847 | Cholecystitis\_acute Renal\_failure | 236 | Death |
| 42 | 0.733050847 | Ischaemic\_stroke Cardiac\_failure | 236 | Death |
| 43 | 0.731914894 | Myocardial\_ischaemia Pleural\_effusion | 235 | Death |
| 44 | 0.731404959 | Angina\_unstable Renal\_failure | 242 | Death |
| 45 | 0.730290456 | Oedema\_peripheral Cardiac\_arrest | 241 | Death |
| 46 | 0.730290456 | Diverticulitis Cardiac\_failure | 241 | Death |
| 47 | 0.729957806 | Cardiac\_failure Constipation | 237 | Death |
| 48 | 0.72983871 | Myocardial\_ischaemia Back\_pain | 248 | Death |
| 49 | 0.729508197 | Haematuria Chronic\_obstructive\_pulmonary\_disease | 244 | Death |
| 50 | 0.728033473 | Cataract Dehydration | 239 | Death |
| 51 | 0.727272727 | Arrhythmia Gastroenteritis | 242 | Death |
| 52 | 0.727272727 | Epistaxis Renal\_failure | 242 | Death |
| 53 | 0.727272727 | Angina\_unstable Respiratory\_failure | 242 | Death |
| 54 | 0.726973684 | Cardiac\_failure Dizziness | 304 | Death |
| 55 | 0.726530612 | Dizziness Appendicitis | 245 | Death |
| 56 | 0.726277372 | Epistaxis Gastroenteritis | 274 | Death |
| 57 | 0.726235741 | Epistaxis Bronchitis | 263 | Death |
| 58 | 0.726190476 | Haemoptysis Gastroenteritis | 252 | Death |
| 59 | 0.725409836 | Respiratory\_tract\_infection Renal\_failure | 244 | Death |
| 60 | 0.725409836 | Septic\_shock Dizziness | 244 | Death |
| 61 | 0.725 | Urosepsis Gastrointestinal\_haemorrhage | 240 | Death |
| 62 | 0.724696356 | Haemoptysis Hypotension | 247 | Death |
| 63 | 0.724576271 | Angina\_unstable Hypotension | 236 | Death |
| 64 | 0.723849372 | Cholecystitis\_acute Bronchitis | 239 | Death |
| 65 | 0.723735409 | Angina\_unstable Cardiac\_arrest | 257 | Death |
| 66 | 0.723484848 | Haematuria Respiratory\_failure | 264 | Death |
| 67 | 0.723076923 | Multi-organ\_failure Syncope | 260 | Death |
| 68 | 0.722846442 | Cardiac\_arrest Dizziness | 267 | Death |
| 69 | 0.72243346 | Respiratory\_tract\_infection Respiratory\_failure | 263 | Death |
| 70 | 0.721518987 | Arrhythmia Diarrhoea | 237 | Death |
| 71 | 0.721311475 | Atrial\_flutter Gastroenteritis | 244 | Death |
| 72 | 0.720930233 | Multi-organ\_failure Gastrointestinal\_haemorrhage | 258 | Death |
| 73 | 0.720833333 | Ischaemic\_stroke Acute\_myocardial\_infarction | 240 | Death |
| 74 | 0.720164609 | Haematuria Acute\_myocardial\_infarction | 243 | Death |
| 75 | 0.720164609 | Urosepsis Renal\_failure | 243 | Death |
| 76 | 0.720164609 | Pneumothorax Cardiac\_failure | 243 | Death |
| 77 | 0.719665272 | Hyponatraemia Cardiac\_failure | 239 | Death |
| 78 | 0.71875 | Cardio-respiratory\_arrest Cardiac\_arrest | 256 | Death |
| 79 | 0.718518519 | Ischaemic\_stroke Dyspnoea | 270 | Death |
| 80 | 0.718487395 | Haemoptysis Convulsion | 238 | Death |
| 81 | 0.718487395 | Colon\_cancer Hypertension | 238 | Death |
| 82 | 0.718367347 | Femoral\_neck\_fracture Dehydration | 245 | Death |
| 83 | 0.717647059 | Respiratory\_tract\_infection Pleural\_effusion | 255 | Death |
| 84 | 0.717647059 | Vertigo Dizziness | 255 | Death |
| 85 | 0.717391304 | Femur\_fracture Renal\_failure | 276 | Death |
| 86 | 0.716981132 | Haematuria Gastrointestinal\_haemorrhage | 265 | Death |
| 87 | 0.716363636 | Confusional\_state Bronchitis | 275 | Death |
| 88 | 0.716312057 | Femur\_fracture Respiratory\_failure | 282 | Death |
| 89 | 0.716171617 | Septic\_shock Cardiac\_failure | 303 | Death |
| 90 | 0.716049383 | Lung\_neoplasm\_malignant Cardiac\_failure | 243 | Death |
| 91 | 0.716049383 | Femoral\_neck\_fracture Syncope | 243 | Death |
| 92 | 0.716049383 | Femur\_fracture Cholecystitis | 243 | Death |
| 93 | 0.716049383 | Urosepsis Cholecystitis | 243 | Death |
| 94 | 0.716 | Multi-organ\_failure Cardiac\_failure | 250 | Death |
| 95 | 0.716 | Ischaemic\_stroke Renal\_failure\_acute | 250 | Death |
| 96 | 0.715953307 | Cataract Anaemia | 257 | Death |
| 97 | 0.715867159 | Arrhythmia Anaemia | 271 | Death |
| 98 | 0.715481172 | Humerus\_fracture Sepsis | 239 | Death |
| 99 | 0.715447154 | Cerebral\_haemorrhage Myocardial\_infarction | 246 | Death |
| 100 | 0.715328467 | Femur\_fracture Cardiac\_failure | 274 | Death |

**Appendix -6**

**Cardiac failure death confidence influences to 40 Serious adverse events**, **sorted by confidence diff (Double confidence – Single confidence)** (Cardiac\_failure -> Death, Confidence 0.4312749)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Index** | **Single Confidence** | **Single Serious Adverse Event** | **Category** | **Double Confidence** | **Serious Adverse Event Pair** | **Confidence Diff (Double - Single)** | **Confidence diff (Double - Cardiac failure)** |
| 1 | 0.273565145 | Pyrexia | General disorders | 0.617647059 | Cardiac\_failure Pyrexia | 0.344081914 | 0.186372159 |
| 2 | 0.283976732 | Gastroenteritis | Infections and infestations | 0.6275 | Cardiac\_failure Gastroenteritis | 0.343523268 | 0.1962251 |
| 3 | 0.311440678 | Dehydration | Metabolism and nutrition disorders | 0.652068127 | Cardiac\_failure Dehydration | 0.340627449 | 0.220793227 |
| 4 | 0.30982659 | Chest\_pain | General disorders | 0.641723356 | Cardiac\_failure Chest\_pain | 0.331896766 | 0.210448456 |
| 5 | 0.33295325 | Diarrhoea | Gastrointestinal disorders | 0.664122137 | Cardiac\_failure Diarrhoea | 0.331168887 | 0.232847237 |
| 6 | 0.358390281 | Deep\_vein\_thrombosis | Vascular disorders | 0.688829787 | Cardiac\_failure Deep\_vein\_thrombosis | 0.330439506 | 0.257554887 |
| 7 | 0.292903875 | Abdominal\_pain | Gastrointestinal disorders | 0.6201373 | Cardiac\_failure Abdominal\_pain | 0.327233425 | 0.1888624 |
| 8 | 0.289264414 | Cellulitis | Infections and infestations | 0.616113744 | Cardiac\_failure Cellulitis | 0.32684933 | 0.184838844 |
| 9 | 0.326267281 | Coronary\_artery\_disease | Cardiac disorders | 0.650837989 | Cardiac\_failure Coronary\_artery\_disease | 0.324570708 | 0.219563089 |
| 10 | 0.331993569 | Chronic\_obstructive\_pulmonary\_disease | Respiratory, thoracic and mediastinal disorders | 0.656330749 | Cardiac\_failure Chronic\_obstructive\_pulmonary\_disease | 0.32433718 | 0.225055849 |
| 11 | 0.349192101 | Fall | Injury, poisoning and procedural complications | 0.668639053 | Cardiac\_failure Fall | 0.319446952 | 0.237364153 |
| 12 | 0.319253438 | Syncope | Nervous system disorders | 0.636761488 | Cardiac\_failure Syncope | 0.31750805 | 0.205486588 |
| 13 | 0.305860113 | Vomiting | Gastrointestinal disorders | 0.623036649 | Cardiac\_failure Vomiting | 0.317176536 | 0.191761749 |
| 14 | 0.340069686 | Bronchitis | Infections and infestations | 0.656641604 | Cardiac\_failure Bronchitis | 0.316571918 | 0.225366704 |
| 15 | 0.367975366 | Back\_pain | Musculoskeletal and connective tissue disorders | 0.683060109 | Cardiac\_failure Back\_pain | 0.315084743 | 0.251785209 |
| 16 | 0.316793893 | Nausea | Gastrointestinal disorders | 0.62797619 | Cardiac\_failure Nausea | 0.311182297 | 0.19670129 |
| 17 | 0.33102253 | Pulmonary\_embolism | Respiratory, thoracic and mediastinal disorders | 0.640167364 | Cardiac\_failure Pulmonary\_embolism | 0.309144834 | 0.208892464 |
| 18 | 0.422321429 | Dizziness | Nervous system disorders | 0.726973684 | Cardiac\_failure Dizziness | 0.304652255 | 0.295698784 |
| 19 | 0.383116883 | Transient\_ischaemic\_attack | Nervous system disorders | 0.685714286 | Transient\_ischaemic\_attack Cardiac\_failure | 0.302597403 | 0.254439386 |
| 20 | 0.318303811 | Urinary\_tract\_infection | Infections and infestations | 0.619450317 | Cardiac\_failure Urinary\_tract\_infection | 0.301146506 | 0.188175417 |
| 21 | 0.354474982 | Cerebrovascular\_accident | Nervous system disorders | 0.650655022 | Cardiac\_failure Cerebrovascular\_accident | 0.29618004 | 0.219380122 |
| 22 | 0.371880706 | Hypotension | Vascular disorders | 0.667655786 | Cardiac\_failure Hypotension | 0.29577508 | 0.236380886 |
| 23 | 0.345 | Hypertension | Vascular disorders | 0.64010989 | Cardiac\_failure Hypertension | 0.29510989 | 0.20883499 |
| 24 | 0.225393494 | Pneumonia | Infections and infestations | 0.518469657 | Cardiac\_failure Pneumonia | 0.293076163 | 0.087194757 |
| 25 | 0.353898886 | Acute\_myocardial\_infarction | Cardiac disorders | 0.63902439 | Cardiac\_failure Acute\_myocardial\_infarction | 0.285125504 | 0.20774949 |
| 26 | 0.414814815 | Asthenia | General disorders | 0.692063492 | Cardiac\_failure Asthenia | 0.277248677 | 0.260788592 |
| 27 | 0.31431706 | Myocardial\_infarction | Cardiac disorders | 0.588803089 | Cardiac\_failure Myocardial\_infarction | 0.274486029 | 0.157528189 |
| 28 | 0.355343771 | Renal\_failure\_acute | Renal and urinary disorders | 0.626582278 | Cardiac\_failure Renal\_failure\_acute | 0.271238507 | 0.195307378 |
| 29 | 0.326144135 | Atrial\_fibrillation | Cardiac disorders | 0.593806922 | Cardiac\_failure Atrial\_fibrillation | 0.267662787 | 0.162532022 |
| 30 | 0.34587899 | Sepsis | Infections and infestations | 0.612244898 | Cardiac\_failure Sepsis | 0.266365908 | 0.180969998 |
| 31 | 0.327403846 | Anaemia | Blood and lymphatic system disorders | 0.593283582 | Cardiac\_failure Anaemia | 0.265879736 | 0.162008682 |
| 32 | 0.33451417 | Dyspnoea | Respiratory, thoracic and mediastinal disorders | 0.598113208 | Cardiac\_failure Dyspnoea | 0.263599038 | 0.166838308 |
| 33 | 0.394136808 | Respiratory\_failure | Respiratory, thoracic and mediastinal disorders | 0.656934307 | Cardiac\_failure Respiratory\_failure | 0.262797499 | 0.225659407 |
| 34 | 0.333333333 | Angina\_pectoris | Cardiac disorders | 0.594235033 | Cardiac\_failure Angina\_pectoris | 0.2609017 | 0.162960133 |
| 35 | 0.390847712 | Pleural\_effusion | Respiratory, thoracic and mediastinal disorders | 0.650259067 | Cardiac\_failure Pleural\_effusion | 0.259411355 | 0.218984167 |
| 36 | 0.458385093 | Septic\_shock | Infections and infestations | 0.716171617 | Septic\_shock Cardiac\_failure | 0.257786524 | 0.284896717 |
| 37 | 0.371152155 | Cardiac\_failure\_congestive | Cardiac disorders | 0.628640777 | Cardiac\_failure Cardiac\_failure\_congestive | 0.257488622 | 0.197365877 |
| 38 | 0.424875622 | Gastrointestinal\_haemorrhage | Gastrointestinal disorders | 0.681940701 | Cardiac\_failure Gastrointestinal\_haemorrhage | 0.257065079 | 0.250665801 |
| 39 | 0.453450164 | Cardiac\_arrest | Cardiac disorders | 0.699115044 | Cardiac\_arrest Cardiac\_failure | 0.24566488 | 0.267840144 |
| 40 | 0.42019544 | Renal\_failure | Renal and urinary disorders | 0.658476658 | Cardiac\_failure Renal\_failure | 0.238281218 | 0.227201758 |