**Supplemental Figures**



**Supplemental Figure S1)** Number of indications mappable to each network year, split by approval year, with current indications mean those approved up-to and including the network year, and future those approved after the network year.



**Supplemental Figure S2)** Number of features selected in the models for each of the different network years.



**Supplemental Figures S3 & S4)** Edge substitution analysis results for edges AFFECTS\_PSafDO and ASSOCIATED\_WITH\_GawDO respectively.

**Supplemental Tables**

Supplemental Table S1: Number of training and testing examples in time-resolved analysis

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Network Year | Training Positives | Testing Positives | Total Positives | Training Negatives | Testing Negatives | Total Negatives |
| 1950 | 274 | 321 | 595 | 4760 | 1190 | 5950 |
| 1951 | 296 | 341 | 637 | 5096 | 1274 | 6370 |
| 1952 | 424 | 286 | 710 | 5680 | 1420 | 7100 |
| 1953 | 471 | 301 | 772 | 6176 | 1544 | 7720 |
| 1954 | 512 | 332 | 844 | 6752 | 1688 | 8440 |
| 1955 | 627 | 338 | 965 | 7720 | 1930 | 9650 |
| 1956 | 665 | 386 | 1051 | 8408 | 2102 | 10510 |
| 1957 | 703 | 371 | 1074 | 8592 | 2148 | 10740 |
| 1958 | 869 | 449 | 1318 | 10544 | 2636 | 13180 |
| 1959 | 948 | 429 | 1377 | 11016 | 2754 | 13770 |
| 1960 | 1099 | 435 | 1534 | 12272 | 3068 | 15340 |
| 1961 | 1132 | 465 | 1597 | 12776 | 3194 | 15970 |
| 1962 | 1220 | 529 | 1749 | 13992 | 3498 | 17490 |
| 1963 | 1289 | 535 | 1824 | 14592 | 3648 | 18240 |
| 1964 | 1398 | 496 | 1894 | 15152 | 3788 | 18940 |
| 1965 | 1470 | 482 | 1952 | 15616 | 3904 | 19520 |
| 1966 | 1498 | 520 | 2018 | 16144 | 4036 | 20180 |
| 1967 | 1579 | 504 | 2083 | 16664 | 4166 | 20830 |
| 1968 | 1644 | 537 | 2181 | 17448 | 4362 | 21810 |
| 1969 | 1665 | 590 | 2255 | 18040 | 4510 | 22550 |
| 1970 | 1726 | 590 | 2316 | 18528 | 4632 | 23160 |
| 1971 | 1822 | 590 | 2412 | 19296 | 4824 | 24120 |
| 1972 | 1884 | 624 | 2508 | 20064 | 5016 | 25080 |
| 1973 | 1956 | 652 | 2608 | 20864 | 5216 | 26080 |
| 1974 | 2106 | 603 | 2709 | 21672 | 5418 | 27090 |
| 1975 | 2189 | 642 | 2831 | 22648 | 5662 | 28310 |
| 1976 | 2289 | 692 | 2981 | 23848 | 5962 | 29810 |
| 1977 | 2363 | 724 | 3087 | 24696 | 6174 | 30870 |
| 1978 | 2455 | 698 | 3153 | 25224 | 6306 | 31530 |
| 1979 | 2532 | 693 | 3225 | 25800 | 6450 | 32250 |
| 1980 | 2604 | 783 | 3387 | 27096 | 6774 | 33870 |
| 1981 | 2742 | 695 | 3437 | 27496 | 6874 | 34370 |
| 1982 | 2848 | 730 | 3578 | 28624 | 7156 | 35780 |
| 1983 | 2939 | 725 | 3664 | 29312 | 7328 | 36640 |
| 1984 | 3018 | 766 | 3784 | 30272 | 7568 | 37840 |
| 1985 | 3140 | 708 | 3848 | 30784 | 7696 | 38480 |
| 1986 | 3272 | 651 | 3923 | 31384 | 7846 | 39230 |
| 1987 | 3387 | 616 | 4003 | 32024 | 8006 | 40030 |
| 1988 | 3440 | 656 | 4096 | 32768 | 8192 | 40960 |
| 1989 | 3497 | 659 | 4156 | 33248 | 8312 | 41560 |
| 1990 | 3602 | 658 | 4260 | 34080 | 8520 | 42600 |
| 1991 | 3707 | 590 | 4297 | 34376 | 8594 | 42970 |
| 1992 | 3788 | 561 | 4349 | 34792 | 8698 | 43490 |
| 1993 | 3864 | 549 | 4413 | 35304 | 8826 | 44130 |
| 1994 | 3925 | 537 | 4462 | 35696 | 8924 | 44620 |
| 1995 | 4005 | 539 | 4544 | 36352 | 9088 | 45440 |
| 1996 | 4141 | 450 | 4591 | 36728 | 9182 | 45910 |
| 1997 | 4215 | 410 | 4625 | 37000 | 9250 | 46250 |
| 1998 | 4280 | 425 | 4705 | 37640 | 9410 | 47050 |
| 1999 | 4343 | 404 | 4747 | 37976 | 9494 | 47470 |
| 2000 | 4413 | 374 | 4787 | 38296 | 9574 | 47870 |
| 2001 | 4475 | 351 | 4826 | 38608 | 9652 | 48260 |
| 2002 | 4532 | 314 | 4846 | 38768 | 9692 | 48460 |
| 2003 | 4580 | 295 | 4875 | 39000 | 9750 | 48750 |
| 2004 | 4643 | 242 | 4885 | 39080 | 9770 | 48850 |
| 2005 | 4674 | 229 | 4903 | 39224 | 9806 | 49030 |
| 2006 | 4715 | 194 | 4909 | 39272 | 9818 | 49090 |
| 2007 | 4745 | 167 | 4912 | 39296 | 9824 | 49120 |
| 2008 | 4772 | 140 | 4912 | 39296 | 9824 | 49120 |
| 2009 | 4814 | 104 | 4918 | 39344 | 9836 | 49180 |
| 2010 | 4826 | 96 | 4922 | 39376 | 9844 | 49220 |
| 2011 | 4855 | 71 | 4926 | 39408 | 9852 | 49260 |
| 2012 | 4879 | 58 | 4937 | 39496 | 9874 | 49370 |
| 2013 | 4896 | 42 | 4938 | 39504 | 9876 | 49380 |
| 2014 | 4916 | 23 | 4939 | 39512 | 9878 | 49390 |
| 2015 | 4928 | 15 | 4943 | 39544 | 9886 | 49430 |
| 2016 | 4930 | 13 | 4943 | 39544 | 9886 | 49430 |
| 2017 | 4943 | 0 | 4943 | 39544 | 9886 | 49430 |