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An Algorithm for 510(k) Clearance Times 1996-2020

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Medical devices and manufacturers of these devices are regulated by the Center for Devices and Radiological Health (CDRH) at the U.S. Food and Drug Administration (FDA). These devices receive one of three classifications: Class I, II, or III. Class I devices "generally pose the lowest risk to the patient and/or user [while] Class III devices pose the highest risk."[1] The vast majority of devices are approved under Premarket Approval (PMA) or cleared under Premarket Notification 510(k),[2] often referred to simply as 510(k).[3] However, the FDA does exempt certain Class I and II devices from 510(k) requirements.[4]

PMAs are required for "high risk devices that pose a significant risk of illness or injury, or devices found not substantially equivalent to Class I and II [legally marketed device] through the 510(k) process."[5] By contrast, a 510(k) application must "demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent,[6] to a legally marketed device (section 513(i)(1)(A) FD&C Act)."[7] Since Class III are most commonly approved under PMA, we will focus our discussion of 510(k) clearance times on Class I and II devices.[8]

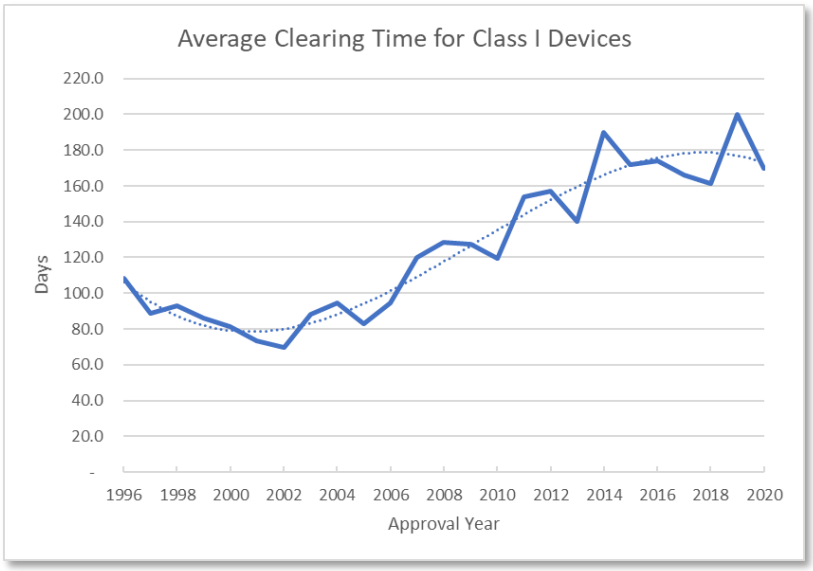
On average, the clearance time for a 510(k) device was approximately 128 days based on devices cleared between 1996 and 2020.[9] However, clearance times for this period range widely and take up to multiple years. Why such a large variation in clearance times?

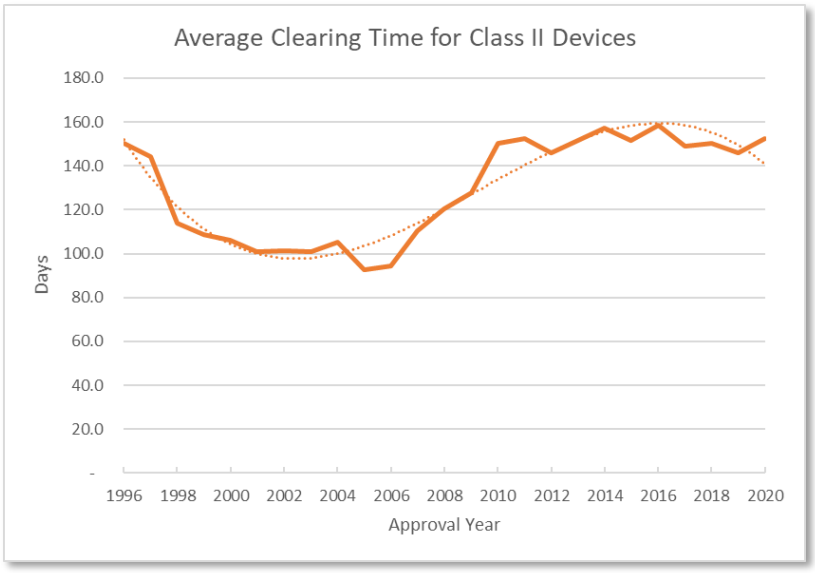
We explore the relationship between clearance times and many observable factors (such as the device's Class, 510(k) Submission Type, and Medical Specialty) using medical device data made publicly available by the FDA.[10] This dataset contains information on all devices cleared under the 510(k) pathway from 1996 to 2020. We will begin by using a heuristic approach that calculates average clearance times by specific factors and follow that with a more exacting analysis based on a linear regression model.

Device Class

On average, Class I and II devices were cleared through the 510(k) pathway in 109 and 130 days, respectively. However, this calculation does not include the Class I and II devices that are exempt from 510(k) requirements.[11] For example, the FDA exempts specifically defined Class I and II devices and other devices meeting certain criteria such as "preamendments"[12] (devices legally marketed in the U.S. before the Medical Device Amendments of 1976 and meeting certain additional criteria).[13]

The chart below shows the average clearance times for Class I and II devices cleared between 1996 and 2020. In both cases, the clearance times appear to go through three distinct periods of shifting trends: an initial downward trend through the early-to-mid 2000s; an upward trend through the early-to-mid 2010s; and a flatter trend thereafter.[14]





Another interesting result from these charts is that average clearance times in the recent past are at, or near, peak levels for the period examined. In the case of Class I devices, average clearance times increased from 108 days in 1996 to 170 days in 2020. For Class II devices, the average clearance time was 150 days in 1996 and ranged from 146 to 159 days between 2015 and 2020.

Third Party Review Program

The FDA allows accredited Third-Party Review Organizations (referred to as 3P510k Review Organizations) to review certain "low-to-moderate risk" medical devices through the 510(k) Third Party Review Program, formally known as the Accredited Persons Program (APP). The FDA states that use of APP is voluntary and intended to yield more rapid 510(k) decisions while simultaneously allowing the FDA to focus its resources on higher risk devices.[15] The FDA makes the final determination on the 510(k) submission based on the review and recommendation received from the 3P510k Review Organization.[16] By law, FDA must issue a final determination within 30 days after receiving a recommendation from an Accredited Person.[17] However, based on 510(k) devices cleared through the APP between 1996 and 2020, the average time the FDA took to clear devices was 47 days.[18] In fact, the FDA clearance time exceeded 30 days for approximately 40% of devices that were reviewed through the APP.

Approximately 4% of devices cleared through 510(k) were reviewed through the APP. A closer look at the data reveals that only 2% of Class I devices and 4% of Class II devices were reviewed through the APP. By contrast, the FDA has stated that approximately half of 510(k)s received by the FDA are eligible for the APP program.[19] Indeed, the data reveals that 53% of devices cleared under 510(k) were deemed eligible for the APP by the FDA, however our analysis indicates that 96% of Class I and II devices cleared under 510(k) were cleared directly by the FDA. Given the FDA's intention for the APP, it does not appear that the program has lived up to its full potential.

Type of 510(k) Submission

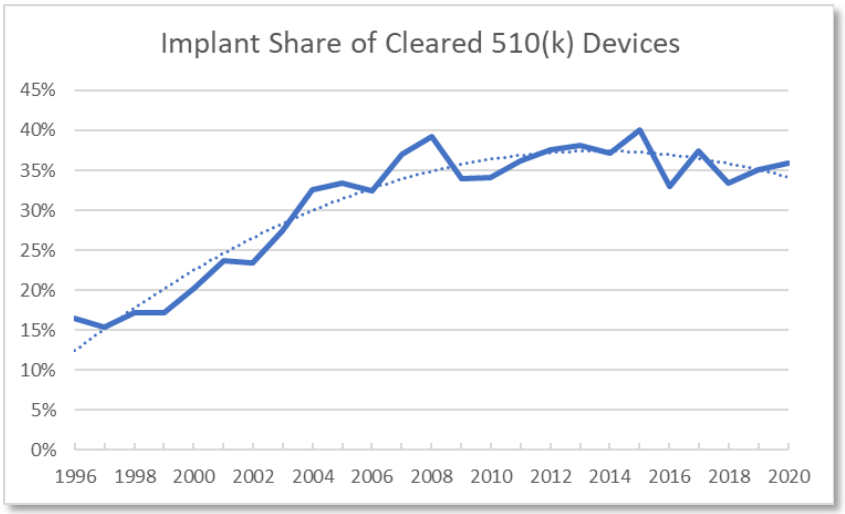
There are three 510(k) submission programs: (1) Traditional; (2) Special; and (3) Abbreviated.[20] The Special and Abbreviated 510(k) submissions can be used when a submission meets certain criteria outlined by the FDA.[21] For example, the Abbreviated program "uses guidance documents, special controls, and/or voluntary consensus standards" to facilitate the review process.[22] Approximately 80% of devices cleared under 510(k) used a Traditional submission, 17% used a Special submission, and 3% used an Abbreviated submission.

The average clearance time for a Traditional submission was 143 days. Surprisingly, the average clearance time for an Abbreviated submission was very similar at 142 days. By contrast, the average clearance time for a Special submission was 53 days. Given the surprising similarity in average clearance times for Traditional and Abbreviated submissions, we examine these results further by device Class to determine if differences in the underlying composition of device Class may be affecting these numbers. The table below shows that the average clearance time for Class I and II devices was relatively similar across both the Abbreviated and Traditional submission types. These results indicate that the Abbreviated program may not be facilitating the review process as intended by the FDA.

	Abbreviated	**Traditional**
Class I	122 days	111 days
Class II	144 days	147 days

Medical Implants

The average clearance time for a medical implant was 121 days whereas the average clearance time for all other devices was 130 days. Medical implants, defined as "devices or tissues that are placed inside or on the surface of the body,"[23] have become increasingly more common. These medical implants can consist of prosthetics as well as other devices that "deliver medication, monitor body functions, or provide support to organs and tissues."[24] The chart shows the relative share of medical implant devices has approximately doubled between 1996 and 2020. However, while the share generally grew between 1996 and the mid-to-late 2000s, the share of medical implants was generally flat thereafter.



Life-Saving and Life-Sustaining

Approximately 3% of devices were identified as either life-saving or life-sustaining, hereafter jointly referred to as life-critical. Unsurprisingly, these devices were all classified as Class II devices. Approximately 97% of these devices fell into one of three medical specialties: (1) Gastroenterology & Urology; (2) Anesthesiology; and (3) Cardiovascular. The average clearance time for devices deemed as life-critical was 157 days whereas the average time for all other devices was 127 days.

Medical Specialty

The FDA categorizes devices in one of 20 medical specialties ranging from Anesthesiology to Radiology based on descriptions found in Title 21 of the Code of Federal Regulations (CFR), Parts 862-892.[25] The Medical Devices Advisory Committee, which advises the FDA on matters concerning development, safety and effectiveness and regulation, consists of 18 panels that cover these medical specialties.[26] The five specialties with the most cleared 510(k) devices between 1996 and 2020 constitute more than half of all 510(k) cleared devices:

Medical Specialty	**Cleared Devices (% Share)**
Orthopedic	15%
Cardiovascular	12%
Radiology	9%
General & Plastic Surgery	9%
General Hospital	9%
Total	**54%**

The average clearance time varies greatly by medical specialty as shown in the table below. The average clearance time ranged between 104 days to 178 days.

Medical Specialty	Average Clearance Time		Medical Specialty	Average Clearance Time
Anesthesiology	178 days		Immunology	142 days
Cardiovascular	132 days		Molecular Genetics	175 days
Clinical Chemistry	113 days		Microbiology	119 days
Clinical Toxicology	115 days		Neurology	148 days
Dental	133 days		Obstetrics/Gynecology	158 days
Ear, Nose & Throat	104 days		Ophthalmic	125 days
Gastroenterology & Urology	135 days		Orthopedic	114 days
General Hospital	130 days		Pathology	153 days
General & Plastic Surgery	123 days		Physical Medicine	143 days
Hematology	144 days		Radiology	104 days

Regression Analysis

Thus far, the analysis has indicated that several factors (medical specialty, device Class, etc) may have impacted the average clearance time for 510(k) devices. However, while averages may be useful as a heuristic, more exacting analysis can identify the potential impact of any one factor when two or more factors are correlated. For example, we discussed earlier that the average clearance time for life-critical devices was approximately 30 days longer than the average clearance time for devices that were not life-critical. However, we also discussed how all life-critical devices were Class II devices and that Class II devices also had a higher average clearance time than Class I devices. Due to the positive correlation between these two factors, simple heuristics cannot separately identify the potential impact of having the classification of a life-critical device and a Class II device. Economists refer to this issue as Omitted Variable Bias. One common approach to overcome this issue, if done correctly, is to use a multiple variable linear regression which isolates the potential impact of any one factor (e.g., life-critical device classification) while holding constant all of the other factors (e.g., device Class). In this case we can run a multiple variable regression that includes the factors we have discussed to examine the potential impact of each factor separately.

We highlight the results of our regression analysis factor-by-factor rather than show one large table with all of the statistics.[27] Since the factors we analyze are all categorical (i.e., defined by categorical status like Class I or Class II), the regression will tell us the average clearance time for a baseline device and also how each factor further increased or decreased the average clearance time. We chose a baseline device that matches a 510(k) device with the most common characteristics between 1996 and 2020.

Baseline Device: 125 days was the average clearance time for an orthopedic, Class II device, that was not reviewed by APP, used a Traditional submission, was not an implanted device and was not classified as life-critical.

If a device that was cleared between 1996 and 2020 differed from the Baseline Device regarding any of the factors that we have explored, then one can calculate the average clearance time using the algorithm below. For example, suppose we wanted to calculate the average clearance time for a device

that was similar to the Baseline device apart from being both a medical implant and life-critical device. We would start with a baseline of 125 days, add 8 days because the device-in-question was an implant and add another 15 days because the device was also classified as life-critical. Consequently, the average clearance time for the device-in-question is estimated as 148 days.

Class I? Subtract 24 days if a Class I device instead of a Class II device.

Abbreviated submission? Subtract 4 days if the device instead had an Abbreviated submission.

Special submission? Subtract 93 days if the device instead had a Special submission**.**

Implant? Add 8 days if the device was instead recognized as a medical implant.

Life-critical? Add 15 days if a device was instead classified as life-critical.

Medical Specialty: Add or subtract days if the device instead had one the following medical specialties.[28]

Anesthesiology	Add 65 days		Immunology	Add 34 days
Cardiovascular	Add 32 days		Molecular Genetics	No change
Clinical Chemistry	Add 13 days		Microbiology	Add 8 days
Clinical Toxicology	Add 11 days		Neurology	Add 39 days
Dental	Add 16 days		Obstetrics/Gynecology	Add 44 days
Ear, Nose & Throat	Subtract 6 days		Ophthalmic	Add 14 days
Gastroenterology & Urology	Add 24 days		Pathology	No change
General Hospital	Add 26 days		Physical Medicine	Add 34 days
General & Plastic Surgery	Add 13 days		Radiology	Subtract 7 days
Hematology	Add 39 days			

1 "Overview of Medical Device Classification and Reclassification," U.S. Food and Drug Administration, available at https://www.fda.gov/about-fda/cdrh-transparency/overview-medical-device-classification-and-reclassification, accessed on January 13, 2021.

2 Some devices are approved under the De Novo or Humanitarian Device Exemption pathway. "Step 3: Pathway to Approval," U.S. Food and Drug Administration, https://www.fda.gov/patients/device-development-process/step-3-pathway-approval, accessed on January 13, 2021.

3 "Overview of Device Regulation," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation, accessed on January 13, 2021.

4 "Class I/II Exemptions," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/classify-your-medical-device/class-i-ii-exemptions, accessed on January 13, 2021.

5 "Overview of Device Regulation," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation, accessed on January 13, 2021.

6 For more information on what constitutes "substantial equivalence," please refer to the source on this footnote. "Premarket Notification 510(k)," U.S. Food and Drug Administration, available at

https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k, accessed on January 13, 2021.

[7] For more information on what constitutes a "legally marketed device," please refer to the source in this footnote. "Premarket Notification 510(k)," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k, accessed on January 13, 2021.

[8] "Overview of Device Regulation," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation, accessed on January 13, 2021.

[9] Clearance time is calculated as the difference between the "decision date" and "date received" published in the FDA file PMN96CUR.ZIP. The calculations in this article are limited to devices classified as Class I or II, devices that were not reviewed by third parties as part of the Accredited Persons Program, and devices that had Traditional, Abbreviated or Special submission types. Some of the analyses in this article also used information from the FDA file FOICLASS.ZIP. The file PMN96CUR.ZIP is available at "Downloadable 510(k) Files," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/510k-clearances/downloadable-510k-files, accessed on January 13, 2021. The file FOICLASS.ZIP is available at "Download Product Code Classification Files," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/classify-your-medical-device/download-product-code-classification-files, accessed on January 13, 2021.

[10] "Downloadable 510(k) Files," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/510k-clearances/downloadable-510k-files, accessed on January 13, 2021.

[11] "Class I/II Exemptions," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/classify-your-medical-device/class-i-ii-exemptions, accessed on January 13, 2021.

[12] For a list of medical devices that are exempt from 510(k) requirements see the following: "Medical Device Exemptions 510(k) and GMP Requirements," U.S. Food and Drug Administration, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/315.cfm, accessed on January 13, 2021.

[13] "Class I/II Exemptions," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/classify-your-medical-device/class-i-ii-exemptions, accessed on January 13, 2021.

[14] The two charts shown include third degree polynomial trends.

[15] "510(k) Third Party Review Program," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/premarket-submissions/510k-third-party-review-program, accessed on January 13, 2021.

[16] "510(k) Third Party Review Program," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/premarket-submissions/510k-third-party-review-program, accessed on January 13, 2021.

[17] "Overview of Device Regulation," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation, accessed on January 13, 2021.

[18] Although the Accredited Persons Program was created by the FDA Modernization Act of 1997, there were two 510(k) devices reviewed through the APP in 1996. "Third Party Performance Metrics," U.S. Food and Drug Administration, available at https://www.fda.gov/about-fda/cdrh-transparency/third-party-performance-metrics, accessed January 13, 2021.

[19] "510(k) Third Party Review Program," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/premarket-submissions/510k-third-party-review-program, accessed on January 13, 2021.

[20] "510(k) Submission Programs," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/premarket-notification-510k/510k-submission-programs, accessed on January 13, 2021.

[21] "How to Prepare an Abbreviated 510(k)," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/premarket-notification-510k/how-prepare-abbreviated-510k, accessed on January 13, 2021.

[22] "The Abbreviated 510(k) Program," U.S. Food and Drug Administration, available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/abbreviated-510k-program, accessed on January 13, 2021.

[23] "Implants and Prosthetics," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/products-and-medical-procedures/implants-and-prosthetics, accessed on January 13, 2021.

[24] "Implants and Prosthetics," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/products-and-medical-procedures/implants-and-prosthetics, accessed on January 13, 2021.

[25] There are 19 medical specialties listed on the source in this footnote. However, the data used in this article includes an additional medical specialty denoted as "MG" for Molecular Genetics. "Device Classification Panels," U.S. Food and Drug Administration, available at https://www.fda.gov/medical-devices/classify-your-medical-device/device-classification-panels, accessed on January 13, 2021.

[26] "Medical Devices," U.S. Food and Drug Administration, available at https://www.fda.gov/advisory-committees/committees-and-meeting-materials/medical-devices, accessed on January 13, 2021.

[27] The regression includes year fixed-effects based on the decision year and robust standard errors. For additional information about the regression, please contact orobles@emerginghealthllc.com.

[28] "No change" is stated when the p-value for a coefficient exceeds 10%.