Intravitreal Anti–Vascular Endothelial Growth Factor Use in France During the Coronavirus Disease 2019 Pandemic

The coronavirus disease 2019 (COVID-19) pandemic emerged in France in February 2020. On March 17, 2020, a national population lockdown restricted human contacts and travel to a strict minimum until May 11, 2020. Many patients experienced difficulties or fear of accessing health care during lockdown. We hypothesized that the COVID-19 pandemic may have modified the dispensing of intravitreal (IVT) anti–vascular endothelial growth factors (anti-VEGF), the main treatment for retinal vascular abnormalities. This study quantified changes in the use of IVT anti-VEGF since the pandemic began in France.

**Methods** | The study involved beneficiaries of the National Health Insurance scheme (covering about 77% of the French population, or 51.5 million people) using the Système National des Données de Santé (French National Health Data System) of individual anonymized pharmacy claims data. The research group has permanent regulatory access to the data from the French National Health Data System (French decree No. 2016-1871 of December 26, 2016, on the processing of personal data called National Health Data System and French law articles Art. R. 1461-13 and 14). No informed consent was required because data are anonymized.

The numbers of individuals using aflibercept or ranibizumab were determined by week for the first 23 weeks of 2018, 2019, and 2020. Individuals using bevacizumab were not included; this drug is rarely prescribed and used exclusively in hospitals in France. The study involved the 2 weeks preceding lockdown (March 2 to 15, 2020; weeks 10-11 of the year), 8 weeks of lockdown (March 16 to May 10, 2020; weeks 12-19 of the year), and the first 4 weeks of reopening (May 11 to June 7, 2020; weeks 20-23 of the year). Expected numbers of users per week during these periods of interest were extrapolated from the mean number of users recorded during corresponding weeks in 2018 and 2019. A ratio of 1.16, estimated over weeks 2 to 8 (the mean number of users per week in 2020 divided by the mean number of users per week in 2018 and 2019), was applied to account for the increase in prescriptions between 2018 and 2020. Differences between observed and expected numbers of patients using anti-VEGF were computed each week during periods of interest, overall, and after restrictions to only those using the drugs for the first time (ie, with no reimbursements for IVT anti-VEGF agents during the previous year). All analyses were performed using SAS software, version 9.4 (SAS Institute Inc).

| Week No. | Patients in 2020, No. | Difference of observed − expected, No. (%) |
|----------|----------------------|------------------------------------------|
| Period before lockdown | | |
| Week 10 (March 2-8) | 16 114 | 16 171 | −57 (−0.4) |
| Week 11 (March 9-15) | 17 178 | 17 386 | −208 (−1.2) |
| Total | 33 292 | 33 557 | −265 (−0.8) |
| Female, % | 20 146 (60.5) | 20 372 (60.7) | NA |
| Age, mean (SD), y | 77.3 (11.1) | 77.1 (11.1) | NA |
| New users, No.* | 2993 | 3128 | −135 (−4.3) |
| Lockdown period | | |
| Week 12 (March 16-22) | 14 978 | 17 318 | −2340 (−13.5) |
| Week 13 (March 23-29) | 10 118 | 16 751 | −6633 (−39.6) |
| Week 14 (March 30-April 5) | 8345 | 15 777 | −7432 (−47.1) |
| Week 15 (April 6-12) | 9099 | 17 294 | −8195 (−47.4) |
| Week 16 (April 13-19) | 9018 | 16 355 | −7337 (−44.9) |
| Week 17 (April 20-26) | 11 199 | 16 209 | −5010 (−30.9) |
| Week 18 (April 27-May 3) | 11 199 | 16 209 | −5010 (−30.9) |
| Week 19 (May 4-10) | 13 360 | 17 784 | −4424 (−24.9) |
| Total | 87 316 | 133 697 | −46 381 (−34.7) |
| Female, % | 52 461 (60.1) | 82 069 (61.4) | NA |
| Age, mean (SD), y | 76.8 (11.0) | 77.2 (11.1) | NA |
| New users, No.* | 4343 | 12 512 | −8169 (−65.3) |
| Reopening period | | |
| Week 20 (May 11-17) | 15 188 | 19 435 | −4247 (−21.9) |
| Week 21 (May 18-24) | 15 531 | 18 174 | −2643 (−14.5) |
| Week 22 (May 25-31) | 16 484 | 17 207 | −723 (−4.2) |
| Week 23 (June 1-7) | 15 817 | 16 398 | −581 (−3.5) |
| Total | 63 020 | 71 214 | −8194 (−11.5) |
| Female, % | 38 593 (61.2) | 43 820 (61.5) | NA |
| Age, mean (SD), y | 77.5 (11.0) | 77.3 (11.1) | NA |
| New users, No.* | 4463 | 4692 | −229 (−4.9) |

Abbreviations: NA, not applicable.

* New use of intravitreal anti–vascular endothelial growth factors was defined by the absence of any such reimbursement during the previous year.
Results | The study found that 33,292 individuals used IVT anti-VEGF drugs in 2020 before lockdown (20,146 women [60.5%]; mean [SD] age, 77.3 [11.1] years), 87,316 during lockdown (52,461 women [60.1%]; mean [SD] age, 76.8 [11.0] years), and 63,020 during reopening (38,593 women [61.2%]; mean [SD] age, 77.5 [11.0] years) (Table). Compared with expected numbers, observed numbers of individuals using IVT anti-VEGF markedly decreased by up to 47.1% (a decrease of 7,432 patients) during the first 3 weeks of lockdown (weeks 12-16, 2020) and remained at a low level until the last week of lockdown (~24.9% [4,424 fewer patients] during week 19). During the 8 weeks of lockdown, the shortfall represented a decrease of 46,381 injections. A gradual but incomplete recovery was observed in the first 4 weeks of reopening (difference of ~21.9% [4,247 fewer patients] in week 20 to ~4.2% [723 fewer patients] and ~3.5% [581 fewer patients] in weeks 22 and 23). Baseline sex and age characteristics of the patient cohort remained similar for each period (Table; Figure). The decrease was particularly marked (~63.5%) for treatment initiations during lockdown. This decrease corresponds to a total of 8,169 fewer treatment initiations during the lockdown period. A gradual recovery was observed during reopening (Table).

Discussion | This study shows a relatively marked decrease in IVT anti-VEGF dispensing during lockdown, which was not completely compensated during the first 4 weeks after unlocking. Extrapolation of these data to the entire French population leads to an estimated decrease of 60,000 injections, including 10,500 initiations of IVT anti-VEGF therapy during the 8 weeks of lockdown. These figures must be interpreted relative to the estimated 85,000 IVT anti-VEGF injections per month in France, including 8,000 treatment initiations. Limitations include the inability to determine whether these findings are associated with any permanent visual acuity loss.

The decrease in IVT anti-VEGF dispensing during the lockdown period could be explained by patients’ difficulty accessing an ophthalmology department or the ophthalmologist’s decision to postpone injections during the pandemic because of difficulties in disease monitoring, which usually include periodic visual acuity and retina examinations, imaging, or both. Most IVT anti-VEGF therapies, particularly with neovascular age-related macular degeneration, should not be delayed, because such delays can lead to permanent visual acuity loss. We believe this situation should continue to be monitored closely, to determine if persistent delays result in longer waiting times to obtain appointments for these treatments. Ideally, the health care system will work on approaches to try to ensure continuity of ophthalmological care in the event of future epidemics.

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Correction: This article was corrected in the February 2021 print issue to fix an incorrect surname. Author Sophie Billioti de Gage’s surname was listed as de Gage. Her full surname is Billioti de Gage. The error has been corrected.

Author Contributions: Mssrs Drouin and Desplas had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Dray-Spira, Zureik. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Billioti de Gage, Desplas, Zureik. Critical revision of the manuscript for important intellectual content: Billioti de Gage, Drouin, Cuenot, Dray-Spira, Weill, Zureik.
Ophthalmic Injuries by Less-Lethal Kinetic Weapons During the US George Floyd Protests in Spring 2020

Modern less-lethal weapons, or kinetic impact projectiles (KIPs), may cause ophthalmic morbidity and even mortality. Herein, we highlight devastating consequences of KIPs, investigate the experience of other United States–based academic ophthalmology residency programs, review current law enforcement KIP-use policies, and recommend policy changes that may prevent further injuries.

Method | Exemption from institutional review board review and waiver of consent and Health Insurance Portability and Accountability Act authorization under exempt category 4 (secondary data use for research under 45 CFR 164.501) was obtained from the Colorado Multiple Institutional Review Board; patient data are protected by hospital privacy safeguards.

A nonvalidated survey was distributed via email to 115 ophthalmology residency program directors using the database of the Association of University Professors of Ophthalmology from June to July 2020. Programs were queried about the total number and types of injuries seen without details of clinical course or outcomes. Consecutive individuals who sustained ophthalmic injuries during the George Floyd protests in Denver, Colorado, were identified, and clinical course and outcomes were collected.

Results | Surveys were emailed to 115 programs, and 82 (71%) responded. Twenty-two programs (27%; 95% CI, 22%-32%) noted caring for patients with ophthalmic injuries related to the protests; 16 (20%; 95% CI, 15%-24%) indicated at least 1 injury was KIP-related. A total of 41 KIP-related injuries were reported (range, 1-10 per program, with 9 reporting only 1 patient each). The most common injuries were hyphema (reported by 12 programs), orbital fractures (11 programs), and ruptured globe (10 programs) (Figure).

Projectiles retrieved from local protest sites (>1000 attendees) included rubber baton rounds, foam grenades, and pepper balls. In particular, our institution cared for 6 unique patients who sustained ophthalmic injuries from suspected KIPs. Four (patients 2-5) reported being struck by projectiles fired by law enforcement; 2 could not identify the source (Table). No patients with KIP injuries unassociated with the protests were identified.

Discussion | In addition to our own experience, survey results showed that 20% of other US academic programs also saw patients for ophthalmic injuries that occurred during the George Floyd protests and were suspected to be KIP-related.

Written policies typically forbid firing less-lethal weapons at close range and at vulnerable areas of the body. The Denver Police Department’s operational manual confirms: “an officer shall not intentionally deploy the less lethal shotgun projectile...to the head, eyes, throat, neck, breasts of a female, genitalia, or spinal column” or “from a range of less than ten (10) feet.” Furthermore, “when any person is struck by the projectile from a less lethal shotgun...immediate evaluation by medical personnel is required.” Similar regulations direct officers to aim at the head or neck area “only if deadly force becomes necessary.” The trauma seen in Denver, Colorado, and