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Deaths from cardiovascular disease involving anticoagulants: a systematic synthesis of coroners' case reports

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Abstract

Background: The global burden of cardiovascular disease (CVD) is forecast to increase, and anticoagulants will remain important medicines for its management. Coroners' Prevention of Future Death reports (PFDs) provide valuable insights that may enable safer and more effective use of these agents.

Aim: To identify CVD-related PFDs involving anticoagulants.

Design and Setting: Retrospective observational study of coronial case reports in England and Wales between 2013 and 2019.

Method: We screened 3037 PFDs for eligibility and included PFDs where CVD and an anticoagulant caused or contributed to the death. We descriptively analysed included cases and used content analysis to assess concerns raised by coroners and who responded to them.

Results: We identified 113 cardiovascular disease-related PFDs involving anticoagulants. Warfarin (36%), enoxaparin (11%), and rivaroxaban (11%) were the most common anticoagulants reported. Concerns most frequently raised by coroners included poor systems (31%), poor communication (25%), and failures to keep accurate medical records (25%). These concerns were most often directed to NHS trusts (29%), hospitals (10%), and general practices (8%). Nearly two-thirds (60%) of PFDs had not received responses from such organisations, which are mandatory under regulation 28 of the Coroners' (Investigations) Regulations 2013. We created a publicly available tool, <https://preventabledeathstracker.net/>, which displays coroners' reports in England and Wales to streamline access and identify important lessons to prevent future deaths.

Conclusion: National organisations, healthcare professionals, and prescribers should take actions to address the concerns of coroners' in PFDs to improve the safe use of anticoagulants in patients with cardiovascular disease.

Keywords: cardiovascular diseases, anticoagulants, inappropriate prescribing, medication errors, premature mortality, coroners and medical examiners

Introduction

Cardiovascular disease (CVD) is the leading cause of mortality worldwide (1,2). In 2019, 18.6 million deaths (33% of all deaths) were due to CVD (3), with a projection of 24 million annual deaths by 2030 (4). In England and Wales, CVD was responsible for almost a quarter of all deaths in 2019 (5,6). Premature mortality from CVD in England has also been attributed to greater socioeconomic inequalities in people under 75 years of age (7).

In patients at high risk of strokes, heart attacks, deep vein thrombosis, or pulmonary embolism, anticoagulation is one possible prophylactic intervention (8). Anticoagulants target different points of the coagulation cascade, helping to prevent blood clot formation and the adverse effects of excessive clotting. In English primary care, the prescribing of anticoagulants increased from 15 million doses to 33 million between January 2014 and August 2019 (9). Three main types of anticoagulants are outlined in guidance published by The National Institute for Health and Care Excellence (NICE): low molecular weight heparin (e.g. enoxaparin), vitamin K antagonists (e.g. warfarin), and direct-acting oral anticoagulants (DOACs; e.g. rivaroxaban). The effectiveness of anticoagulants for cardiovascular disease is well established. For example, adjusted-dose warfarin reduced stroke by 62% (95% CI: 48% to 72%) in patients with atrial fibrillation (10). However, the narrow therapeutic index and frequent laboratory monitoring needed with warfarin administration have led to the development of DOACs (11). Bleeding associated with warfarin therapy is among the top three adverse drug reactions that cause hospital admissions in England (12).

Coroners' reports, previously named Rule 43 and now called Prevention of Future Death reports (PFDs), are written when the coroner believes that action is necessary to prevent a death (13). PFDs are sent to specific individuals or organisations, who, under regulation 28 and 29 of the Coroners (Investigations) Regulations 2013, have a duty to respond within 56 days of the date of report (14). Previous analysis of coroners' reports has shown that anticoagulants were the drugs most commonly reported to have been involved in fatal medication errors in England and Wales (15,16). This analysis also found that coroners' most commonly raised concerns regarding adverse drug reactions to prescribed medicines, followed by omissions of necessary treatment and monitoring failures. In this study, the authors examined only a proportion (n=500) of all published coroners' reports. Building on previous research (15,16), we aimed to assess all available PFDs between 2013 and 2019 for deaths that involved

individuals with CVD, in whom the use or lack of use of anticoagulants caused or contributed to the death. We sought to discover: 1) what concerns were highlighted by coroners; 2) to which individuals or organizations PFDs were addressed; 3) whether responses were made by the individuals or organizations to whom the PFDs were sent.

Methods

We designed a retrospective observational study and preregistered our study protocol on an open repository (17). We used the STROBE reporting guideline to write our manuscript.

Data collection

PFDs are openly available on the Courts and Tribunals Judiciary website (18). We used web scraping to automatically collect PFDs, and from the output created the Preventable Deaths Database and the Preventable Deaths Tracker: <https://preventabledeathstracker.net/> (19). The code to create the scraper is openly available on GitHub (20) and has been previously described (21). The Preventable Deaths Database contains: the case reference number; the date of the report; the name of the deceased; the coroner's name; the coroner's jurisdiction; the category of death (defined by the Chief Coroners' office); to whom the report was sent; and the URL to the Judiciary website. For population data on deaths from CVD, we used the most recent (2001-2019) dataset of deaths registered in England and Wales, released by the Office for National Statistics in 2020 (ONS) (5).

Eligibility of cases

We examined all cases (n=3037) in the Preventable Deaths Database from July 2013 (the first date on which they were uploaded to the Judiciary website) to December 2019. We screened the cases independently in duplicate (AA & GCR) to determine whether CVD caused or contributed to the death using a pre-defined algorithm (Supplementary Figure 1). We used Chapter IX (Diseases of the Circulatory System) of the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) to align with the ONS classifications of death. When the deceased suffered from a single condition listed under chapter IX that could not be unequivocally attributed to external causes, the case was included. We then screened for cases where one or more anticoagulant caused or contributed to the death or where the coroner suggested that had an anticoagulant been given, it would have prevented the death. We defined anticoagulants as agents targeting different points of the coagulation

pathway to prevent clot formation. Discrepancies were resolved by consensus discussion (AA, GCR, & JKA).

Data extraction

For included cases, one study author (AA) manually extracted the following variables into a predesigned Google Sheet, which was cross examined by another study author (GCR): the individuals or organizations to whom reports were sent, who responded, the due date of response and the date received; date of death; the dates on which the inquest started and ended; age; sex; setting or location of death; medical cause(s) of death; the coroner's conclusion(s) of the inquest; relevant medical, mental health, and social history; whether any substance(s) were implicated in the death and the type of substance(s); coroner's concern(s) and actions proposed by the coroner.

Data analysis

To determine the annual deaths from CVD in England and Wales, we filtered the ONS data (5) for deaths caused by conditions listed under chapter IX of ICD-10 (ICD-10 codes: I00-I99). We summed the number of reports written each year and compared the totals with ONS mortality data for CVD. We used descriptive statistics to report the quantitative findings and performed content analysis (22) to classify the concerns and actions raised by coroners with categories derived inductively. We calculated a response rate for each organisation as the proportion of reports to which a response was submitted over the total number received. Responses were further classified as either on-time (delivered within 56 days), late (submitted after 56 days), or overdue (when no response was found on the Judiciary website). A response rate of 100% means that individual or organisation adhered to regulation 28 of the Coroners' (Investigations) Regulations 2013 and responded to all PFDs issued by coroners.

Software and data sharing

We used Python v3.7 in Jupyter Notebooks with pandas, seaborn, and matplotlib libraries to analyse the data and create figures. The data, statistical code, and study materials are openly available via the Open Science Frame (23) and GitHub (24).

Results

In 659 cases (22% of all PFDs) CVD caused or contributed to the death (Figure 1). Of the CVD-related PFDs, 17% (n=113) involved or mentioned the use or lack of an anticoagulant. Over the seven-year study period, there was a median of 16 (IQR: 15-17) CVD-related anticoagulant PFDs each year (Supplementary Table 1).

In 99 cases, an anticoagulant caused or contributed to the death. Warfarin (36%) was the most common anticoagulant specified, followed by enoxaparin (11%) and rivaroxaban (11%) (Figure 2). In 14 cases, the coroner mentioned that the administration of an anticoagulant might have prevented the death (Figure 2). There were equal proportions of males (n=56) and females (n=57) in the 113 cases. The median age of the deceased were 76 years (IQR: 61-84 years; n=77).

Seventy-five coroners across 36 jurisdictions wrote 113 PFDs. Coroners in the North West (25%) and South East (19%) of England wrote the most, whereas those in the East (2%) and North East (3%) of England wrote very few (Table 1).

We identified 335 individual concerns raised by coroners in the 113 cases. Using content analysis, we categorised these concerns into 51 groups and five higher-order themes, including communication, failure to follow protocols, education and training, resources, and safety (Table 2). The most common concerns were poor systems (31%), poor communication (25%), failure to keep accurate medical records (25%), and failures or delays in having appropriate assessments done (17%). Concerns most frequently belonged to the theme of following protocols (36%), followed by communication (22%), and safety issues (21%).

In 82% of CVD-related PFDs involving anticoagulants, coroners stated that "action should be taken" (Supplementary Table 2). When coroners suggested further actions, we grouped their actions into 28 categories. Ensuring effective communication (3%), introducing new policies and protocols (2%), and reviewing the handling of prescriptions (2%) were the most common actions proposed (Supplementary Table 2).

For the 113 CVD-related PFDs involving anticoagulants, coroners sent 181 reports to 37 individuals and organisations (Table 3). Local services such as NHS Trusts (29%), hospitals

(10%), and general practices (8%), were addressed PFDs most frequently. By statute addressees must respond to the coroner within 56-days, but only 29% responded on time; 11% responded late and 60% were overdue. Medical societies (0%) and royal colleges (0%) had the lowest response rates, while NHS entities had the highest, albeit with half of their responses overdue. Ranking recipients by response rate and response time, NHS 111, NHS Wales, and CCGs performed best (Supplementary Table 3).

Discussion

Summary

We identified 113 premature deaths from cardiovascular disease involving anticoagulants. In 88% of cases, the use of one or more anticoagulant resulted in death. In 12% of cases, the administration of an anticoagulant may have prevented death. We found wide geographical variation in the issuing of PFDs and the type of information reported, with coroners in Greater Manchester writing the most. Coroners raised hundreds of concerns, some relating directly to the risks of anticoagulation and the caution with which patients on these drugs should be managed, though rarely were the concerns not already mentioned in guidance available to healthcare professionals. Most of these concerns were addressed locally and under regulation 28, 109 individuals or organisations were overdue in their response to coroners.

Strengths and limitations

We used a reproducible data-collection method to examine all available PFDs from inception to 2019, which provided an estimated 40-fold time saving (21), and reduced the potential for selection bias. However, the PFDs included in our study depend on the working practices of coroners and the Chief Coroner's Office in uploading PFDs and their responses to the website. The 113 PFDs cannot therefore represent all preventable deaths from CVD involving anticoagulants in England and Wales. There were also missing data; for example, 32% of PFDs did not report age and 16% did not specify the type of anticoagulant; this may be attributed to lack of PFD training provided to coroners. Our findings are also limited by the available data and information provided by coroners in PFDs, thus it is not possible to examine the relationship between cardiovascular disease and anticoagulants in causing death, or to differentiate between the appropriate use, misuse, and underuse of anticoagulants.

Comparison with existing literature

Our study builds on prior research that evaluated smaller samples of coroners' reports (15,16,25–27). Compared with previous studies (26,28), we did not identify a sex imbalance. However, we found that new hazards were rarely identified and that most PFDs were addressed locally, as shown by Ferner et al. (15), which means that valuable lessons were not widely disseminated and may be why we found that coroners repeatedly expressed similar concerns, in line with former research (25). This questions whether PFDs are fulfilling their purpose. Similar to Fox and Jacobson (26), we found pronounced geographical variation in the issuing of PFDs and poor response rates. A review of the coronial system in England and Wales highlighted a lack of accountability, leadership, and quality assurance (29). Since there is no system in place for enforcing or auditing compliance with regulation 28 or assessing the quality of PFDs and the adequacy of responses and actions taken to prevent deaths, our findings show that the system has scope for improvement.

General practices were sent the third highest number of CVD-related PFDs involving anticoagulants, but collectively only 36% responded. This may be because of a lack of awareness of the statutory requirements and medico-legal training of GPs, as identified by previous research (30). During the COVID-19 pandemic, GPs called for deaths of colleagues to be reported to the coroner and PFDs to be issued (31). Fortunately, the value of PFDs as a tool for improving clinical practice is being recognised, and efforts are underway to widely disseminate their lessons to healthcare professionals, policymakers, and the public (32–37).

Implications for research and/or practice

Concerns raised by coroners provide lessons for prescribers and policymakers on the safety and proper use of therapies. During the COVID-19 pandemic, patients were switched from warfarin to other oral anticoagulants, given the need for less frequent blood testing (38). Drugs such as andexanet alfa could prove critical in the outcome of patients with severe bleeding during treatment with apixaban or rivaroxaban. Since the coroner expressed concerns (Case: 2018-0032), NICE has drafted an appraisal for andexanet alfa (39), and its publication is expected on 12 May 2021 (40). There has also been a phased launch of andexanet alfa in UK hospitals (41). However, it is unclear whether this was a direct result of the PFD, since no response from the MHRA was published on the Judiciary website.

When PFDs are addressed to the appropriate recipients at the national level, their actions can help prevent deaths. For example, a PFD was sent to NICE when the deceased suffered a fall

while taking an anticoagulant without having the appropriate neuroimaging performed (Case: 2019-0106). The coroner's concerns were acknowledged in a NICE surveillance report (42) and resulted in updating of the NICE guideline on head injury, to emphasise that people taking DOACs should be investigated with the same care as those taking warfarin (43). However, we also identified unaddressed concerns about national guideline; three-quarters of PFDs sent to NICE have no responses listed on the Judiciary website. Restarting warfarin after a head injury is particularly important, as delays could leave the patient at risk of a stroke, but resuming too soon may lead to haemorrhage. A retrospective review of the medical charts of 256 patients admitted to a trauma centre in West Texas between 2009 and 2012 showed that patients who resumed anticoagulant therapy at 7-10 days after the injury had the best prognosis (44). PFDs can therefore be used to update guidance and inform future prospective cohort studies.

Our study provides a database and resource (<https://preventabledeathstracker.net/>) for future evaluations of PFDs. Further content analysis should be used to assess the 181 responses to the 113 PFDs, to assess the adequacy of actions proposed to prevent deaths and their implementation. Future research could use our open data to examine coroners' concerns in the 546 CVD-related PFDs not involving anticoagulants and their responses. In building the web scraper to collect PFDs, we found various inconsistencies and omissions on the Judiciary website, which should be addressed to improve the quality of data. The missing data from PFDs we have highlighted reveal target areas for coronial training in the writing of PFDs.

Conclusions

This study used sophisticated, reproducible, and internationally recognised data-collection methods (21) to demonstrate that PFDs provide valuable lessons when prescribing anticoagulants and managing patients with CVD. However, it is unclear whether actions are being taken to incorporate such lessons. To improve patient safety, lessons should be widely disseminated and used in practice.

Funding: No funding was obtained to undertake this study.

Ethical approval: As the case reports are publicly available on the Judiciary website, approval from an ethics committee was not required.

Competing interests: AA has no competing interest to disclose. CH is a National Institute for Health Research (NIHR) Senior Investigator and has received expenses and fees for his media work, received expenses from the World Health Organisation (WHO), Food and Drug Administration (FDA), and holds grant funding from the NIHR School for Primary Care Research (SPCR), and the NIHR SPCR Evidence Synthesis Working Group [Project 380], the NIHR BRC Oxford and the WHO. On occasion, CH receives expenses for teaching EBM and is also paid for his GP work in NHS out of hours (contract with Oxford Health NHS Foundation Trust). CH is the Director of the CEBM. JKA has published articles and edited textbooks on adverse drug reactions and interactions and has often given medicolegal advice, including appearances as an expert witness in coroners' courts, dealing with the adverse effects of drugs. NJD has no conflicts related to the submitted work. Outside the submitted work, he declares a doctoral studentship from the Naji Foundation, grant funding from the Fetzer Franklin Memorial Fund, and employment on grants from the Laura and John Arnold Foundation, The Good Thinking Society, and the German Federal Ministry of Education and Research (BMBF). GCR was financially supported by the NIHR SPCR, the Naji Foundation, and the Rotary Foundation to study for a Doctor of Philosophy (2017-2020) but no longer has any financial COIs. GCR is an Associate Editor of BMJ Evidence Based Medicine. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care.

Acknowledgements and contributions: AA proposed the topic for research, contributed to the protocol and devised the algorithm for the eligibility of cases, screened the database for eligible case reports, extracted and analysed the data, and wrote the first draft of the manuscript. GCR designed the study, wrote the protocol, sourced the data, contributed to the web scraper, provided data management, dual screened the database for eligible cases, analysed the data, provided primary supervisory support and substantiality contributed to subsequent manuscript drafts. JKA and CH reviewed the protocol and preliminary findings and provided supervisory support. NJD wrote the code and advised on the web scraper. All authors have full access to

all the data in the study, read and approved the final manuscript, and accept responsibility to submit for publication.

Data availability: Study materials, protocol, data, and statistical code are openly available on the OSF (<https://osf.io/qkfjp/>) and GitHub (https://github.com/georgiarichards/CVD_anticoags).

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References

1. Cardiovascular diseases (CVDs). who.int. 2017. Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))
2. CVD risk assessment and management. NICE. 2019. Available from: <https://cks.nice.org.uk/topics/cvd-risk-assessment-management/>
3. GBD Results Tool. Global Health Data Exchange. 2020. Available from: <http://ghdx.healthdata.org/gbd-results-tool>
4. The Future of CVD. who.int. Available from: https://www.who.int/cardiovascular_diseases/en/cvd_atlas_25_future.pdf?ua=1
5. Deaths registered in England and Wales – 21st century mortality. Office for National Statistics. 2020. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/the21stcenturymortalityfilesdeathsdataset>
6. ICD-10 Version:2019. who.int. 2019. Available from: <https://icd.who.int/browse10/2019/en#/IX>
7. Lewer D, Jayatunga W, Aldridge RW, et al. Articles Premature mortality attributable to socioeconomic inequality in England between 2003 and 2018: an observational study. *Lancet Public Health*. 2020;5:e33–41.
8. Anticoagulants, including direct-acting oral anticoagulants (DOACs). NICE. 2016. Available from: <https://www.nice.org.uk/advice/ktt16/resources/anticoagulants-including-directacting-oral-anticoagulants-doacs-pdf-58757956094149>
9. Ho KH, Van Hove M, Leng G. Trends in anticoagulant prescribing: A review of local policies in English primary care. Vol. 20, *BMC Health Serv Res*. BioMed Central Ltd.; 2020.
10. Hart RG, Benavente O, McBride R, et al. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: A meta-analysis. *Ann Intern Med*. 1999 Oct 5;131(7):492–501.
11. Harter K, Levine M, Henderson SO. Anticoagulation drug therapy: A review. *West J Emerg Med*. 2015;16(1):11–7.
12. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: Prospective analysis of 18 820 patients. *BMJ*. 2004 Jul 3;329(7456):15–9.

13. Coroners and Justice Act 2009. legislation.gov.uk. 2009. Available from: https://www.legislation.gov.uk/ukpga/2009/25/pdfs/ukpga_20090025_en.pdf
14. The Coroners (Investigations) Regulations 2013. legislation.gov.uk. 2013. Available from: https://www.legislation.gov.uk/uksi/2013/1629/pdfs/uksi_20131629_en.pdf
15. Ferner RE, Easton C, Cox AR. Deaths from Medicines: A Systematic Analysis of Coroners' Reports to Prevent Future Deaths. *Drug Saf.* 2018;41(1):103–10.
16. Ferner RE, Ahmad T, Babatunde Z, et al. Preventing Future Deaths from Medicines: Responses to Coroners' Concerns in England and Wales. *Drug Saf.* 2019 Mar 7;42(3):445–51.
17. Deaths from cardiovascular disease: A systematic analysis of coroners' reports to prevent future deaths in England and Wales. OSF Registries. Available from: <https://osf.io/rvw43>
18. Prevention of Future Deaths. Courts and Tribunals Judiciary. Available from: <https://www.judiciary.uk/subject/prevention-of-future-deaths/>
19. Preventable Deaths Tracker. Available from: <https://preventabledeathstracker.net/>
20. GitHub - georgiarichards/georgiarichards.github.io. Available from: <https://github.com/georgiarichards/georgiarichards.github.io>
21. DeVito NJ, Richards GC, Inglesby P. How we learnt to stop worrying and love web scraping. *Nature.* 2020 Sep 1;585(7826):621–2.
22. Kleinheksel AJ, Rockich-Winston N, Tawfik H, et al. Demystifying content analysis. *Am J Pharm Educ.* 2020 Jan 1;84(1):127–37.
23. Deaths from cardiovascular disease: A systematic analysis of coroners' reports to prevent future deaths in England and Wales. OSF. Available from: <https://osf.io/qkfjp/>
24. GitHub - georgiarichards/CVD_anticoags. Available from: https://github.com/georgiarichards/CVD_anticoags
25. Leary A, Bushe D, Oldman C, et al. A thematic analysis of the prevention of future deaths reports in healthcare from HM coroners in England and Wales 2016–2019. *J Patient Saf Risk Manag.* 2021 Feb 3;26(1):14–21.
26. Fox AW, Jacobson J. How well do Regulation 28 reports serve future public health and safety? *Med Sci Law.* 2021;

27. Holden J, O'Donnell S, Brindley J, et al. Analysis of 1263 deaths in four general practices. *Br J Gen Pract.* 1998;48(432).
28. Mclean M, Roach J, Armitage R. Local variations in reporting deaths to the coroner in England and Wales: A postcode lottery? *J Clin Pathol.* 2013 Nov;66(11):933–6.
29. Berry C, Heaton-Armstrong A. A review of the coroner system in England and Wales: A commentary. Vol. 5, *Clin Med (London)*. Royal College of Physicians; 2005. p. 455–9.
30. Start RD, Usherwood TP, Carter N, et al. General practitioner's knowledge of when to refer deaths to a coroner. *Br J Gen Pract.* 1995;45(393).
31. Kendrick D, Agius R, McKee M, et al. Covid-19: Learning lessons from the deaths of our colleagues. *BJGP Life.* 2020. Available from: <https://bjgplife.com/2020/05/18/gp-deaths/>
32. Richards GC, Aronson JK, Heneghan C. Coroners' concerns to prevent harms: A series of coroners' case reports to serve patient safety and educate the public, clinicians and policy-makers. *BMJ Evid Based Med.* BMJ Publishing Group; 2020.
33. Richards GC. Alcohol-based hand sanitisers: A warning to mitigate future poisonings and deaths. *BMJ Evid Based Med.* 2020 Apr 1;26(2):65–8.
34. Bilip MK, Richards GC. Emollients and smoking: a fire hazard that could be prevented to reduce future deaths. *BMJ Evid Based Med.* 2021 Apr 9;0:bmjebm-2020-111648.
35. Thomas ET, Richards GC. Diclofenac in adolescents: Diagnosing and treating gastrointestinal adverse drug reactions can prevent future deaths. *BMJ Evid Based Med.* 2020 Feb 10;
36. Cox AR, Ferner R. Tramadol: Repeated prescriptions and repeated warnings. *BMJ Evid Based Medicine.* BMJ Publishing Group; 2021.
37. Swift B, Heneghan C, Aronson JK, et al. Preventable deaths from SARS-CoV-2 in England and Wales: a systematic analysis of coroners' case reports from the COVID-19 pandemic. *medRxiv.* 2021 Jul 23;2021.07.15.21260589.
38. Curtis HJ, MacKenna B, Walker AJ, et al. OpenSAFELY: impact of national guidance on switching from warfarin to direct oral anticoagulants (DOACs) in early phase of COVID-19 pandemic in England. *medRxiv.* 2020 Dec 4;2020.12.03.20243535.
39. Single Technology Appraisal (STA): Andexanet alfa for reversing anticoagulation

- [ID1101]. NICE. 2019. Available from: <https://www.nice.org.uk/guidance/gid-ta10440/documents/scope-consultation-comments-and-responses>
40. Andexanet alfa for reversing anticoagulation [ID1101]. NICE. 2020. Available from: <https://www.nice.org.uk/guidance/indevelopment/gid-ta10440>
41. Andexanet alfa. Specialist Pharmacy Service. 2020. Available from: <https://www.sps.nhs.uk/medicines/andexanet-alfa/>
42. 2019 surveillance of head injury: assessment and early management (NICE guideline CG176). NICE. 2019. Available from: <https://www.nice.org.uk/guidance/cg176/resources/2019-surveillance-of-head-injury-assessment-and-early-management-nice-guideline-cg176-pdf-8944653877477>
43. Head injury: assessment and early management. NICE. 2019. Available from: <https://www.nice.org.uk/guidance/cg176/chapter/1-Recommendations#investigating-clinically-important-brain-injuries>
44. Puckett Y, Zhang K, Blasingame J, et al. Safest Time to Resume Oral Anticoagulation in Patients with Traumatic Brain Injury. *Cureus*. 2018 Jul 3;10(7).

Table 1: Jurisdictions of coroners who issued the 113 Prevent Future Death reports involving an anticoagulant and cardiovascular disease

Region	No. of cases (%)
North West England	28 (25)
Greater Manchester	20 (18)
Blackpool & Fylde	4 (4)
Blackburn, Hyndburn & Ribble Valley	3 (3)
Cumbria	1 (1)
South East England	21 (19)
Surrey	4 (4)
Kent	3 (3)
Milton Keynes	3 (3)
Portsmouth & South East Hampshire	3 (3)
West Sussex	3 (3)
Buckinghamshire	2 (2)
Berkshire	1 (1)
Isle of Wight	1 (1)
Oxfordshire	1 (1)
Wales	15 (13)
Powys, Bridgend & Glamorgan Valleys	6 (5)
North Wales	2 (2)
South Wales	2 (2)
Swansea	2 (2)
Cardiff & Vale of Glamorgan	1 (1)
Carmarthenshire & Pembrokeshire	1 (1)
Gwent	1 (1)
London	10 (9)
West Midlands	13 (12)
Black Country	5 (4)
Birmingham & Solihull	4 (4)
Coventry	1 (1)
Shropshire, Telford & Wrekin	1 (1)
South Staffordshire	1 (1)
Worcestershire	1 (1)
Yorkshire and The Humber	8 (7)
South Yorkshire	5 (4)

West Yorkshire	3 (3)
East Midlands	7 (6)
Leicestershire	4 (4)
Nottinghamshire	3 (3)
South West England	6 (5)
Plymouth, Torbay & South Devon	4 (4)
Avon	1 (1)
Gloucestershire	1 (1)
North East England	3 (3)
Sunderland	3 (3)
East of England	2 (2)
Cambridgeshire	1 (1)
Norfolk	1 (1)

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Table 2: Concerns raised by coroners, grouped by five higher-order themes, and how often they were reported

Theme (% of concerns)	Concern	No. of cases (%)
Failure to follow protocols (36%)	Failure/delay in appropriate assessments	19 (17)
	Failure to monitor treatment	15 (13)
	Omission of necessary treatment	13 (12)
	Delayed treatment	12 (11)
	Failure to review medicines	11 (10)
	Failure to take a history or see the patient	10 (9)
	Failure/delay in performing necessary scans	8 (7)
	Failure to triage patients appropriately	7 (6)
	Failure to follow recommended practices	6 (5)
	Failure to follow a protocol	6 (5)
	Failure to review medical records	4 (4)
	Failure to implement national guidelines	3 (3)
	Administration of drug in error	1 (1)
	Failure to arrange supervision	1 (1)
	Inability to care for both a patient's physical and mental health	1 (1)
Management of medication for care home residents	1 (1)	
Medication administered despite known allergy	1 (1)	
Communication (22%)	Poor communication	28 (25)
	Failure to keep accurate medical records	28 (25)
	Failure to escalate deterioration in patient to the relevant medical professionals	5 (4)
	Failure to seek specialist advice when indicated	4 (4)
	Failure to follow the advice of a senior clinician	2 (2)
	Failure to warn of the consequences of not taking medication	2 (2)
	Failure to inform the patient about a medical procedure and aftercare	2 (2)
	Failure to warn of adverse drug reactions	1 (1)
	Failure to obtain informed consent	1 (1)
Safety (21%)	Poor systems	35 (31)
	Discharge process	16 (14)
	Non-robust investigation following the death	15 (13)
	Safety of facilities	2 (2)
	Nature of inspections of care homes	1 (1)
	Failure to address measures identified in risk assessment	1 (1)
	Failure to make a reasonable effort to ensure patient adherence	1 (1)
Education and training (14%)	Inadequate training	12 (11)
	Inappropriate dosage for the patient	9 (8)
	Failure to appreciate the risk (of giving/not giving a drug)	6 (5)
	Lack of clinical knowledge	5 (4)
	Poor clinical decision-making	5 (4)
	Poor awareness of symptoms	4 (4)

	Poor awareness of rare ADRs	2 (2)
	Poor awareness of rare complications of medical procedures	1 (1)
	Failure of training	1 (1)
	Drug awareness	1 (1)
	Poor awareness of drug-drug interactions	1 (1)
	Wrong method of administration	1 (1)
Resources (7%)	Absence of national guidelines	10 (9)
	Under staffing	7 (6)
	Shortage/lack of availability of appropriate medical equipment	3 (3)
	Hospital opening times/availability	2 (2)
	Unavailable drug	1 (1)
	Inability to deliver care	1 (1)

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Table 3: Recipients of coroners Prevent Future Death reports (PFDs) and their response rates to reports

Addressee	No. of reports received	No. of responses	Response rate (%)	Classification of responses		
				% On time	% Late	% Overdue
NHS entities	118	60	51	38	13	49
CCGs	3	3	100	67	33	0
NHS 111	1	1	100	100	0	0
NHS Wales	1	1	100	100	0	0
Ambulance services	7	5	71	57	14	29
NHS Trusts	53	32	60	45	15	40
NHS England hospitals	4	2	50	50	0	50
General practices	19	7	37	26	11	63
Local Health Boards	14	5	36	29	7	64
University Health Boards	3	1	33	0	33	67
Mental Health Trusts	10	3	30	20	10	70
NHS Pathways	2	0	0	0	0	100
Government	17	5	29	18	12	71
DHSC	7	3	43	14	29	57
Local authorities	3	1	33	33	0	67
Welsh Government	7	1	14	14	0	86
Professional bodies	21	4	19	10	10	81
CQC	6	2	33	17	17	67
NICE	8	2	25	13	13	75
GMC	2	0	0	0	0	100
BMA	1	0	0	0	0	100
GDC	1	0	0	0	0	100
MHRA	1	0	0	0	0	100
AACE	1	0	0	0	0	100
The Renal Association	1	0	0	0	0	100
Others	18	3	17	11	6	83
Police	1	1	100	0	100	0
Private companies	4	1	25	25	0	75
Care homes	9	1	11	11	0	89

Carewatch	1	0	0	0	0	100
Highway maintenance	1	0	0	0	0	100
Housing Associations	1	0	0	0	0	100
Local Charities	1	0	0	0	0	100
Medical societies	4	0	0	0	0	100
BCS	1	0	0	0	0	100
BRS	1	0	0	0	0	100
ICS	1	0	0	0	0	100
RPS	1	0	0	0	0	100
Medical royal colleges	3	0	0	0	0	100
RCGP	1	0	0	0	0	100
RCOG	1	0	0	0	0	100
RCP	1	0	0	0	0	100
Total	181	72	40	29	11	60

AACE: Association of Ambulance Chief Executives; BCS: British Cardiovascular Society; BMA: British Medical Association; BRS: British Renal Society; CQC: Care Quality Commission; DHSC: Department of Health and Social Care; GDC: General Dental Council; GMC: General Medical Council; ICS: Intensive Care Society; MHRA: Medicines and Healthcare products Regulatory Agency; NICE: The National Institute for Health and Care Excellence; NHS: National Health Service; RCGP: Royal College of General Practitioners; RCOG: Royal College of Obstetricians and Gynaecologists; RCP: Royal College of Physicians; RPS: Royal Pharmaceutical Society

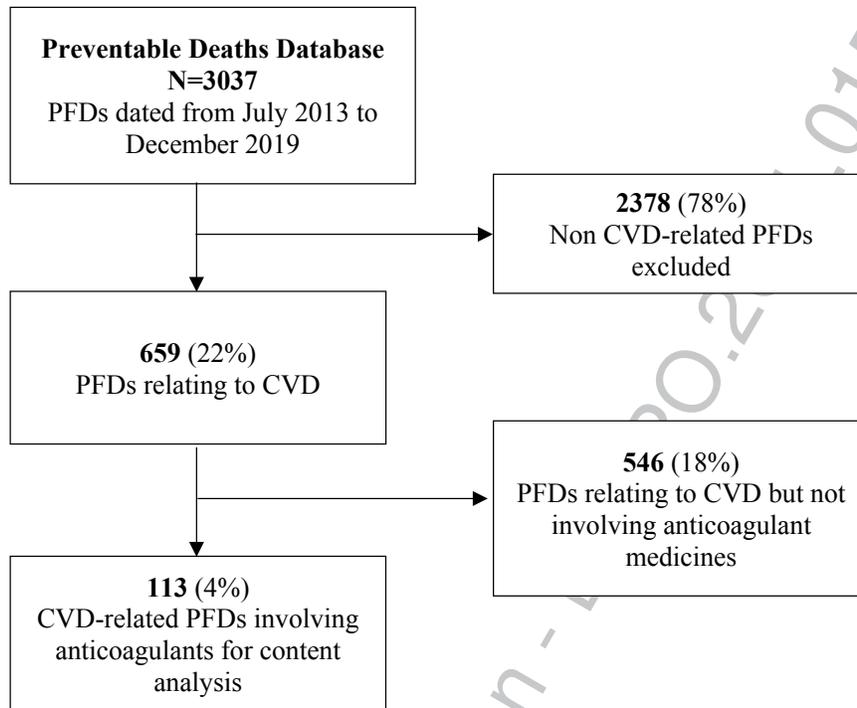


Figure 1: Flow diagram showing the numbers of Prevent Future Death reports (PFDs) included and excluded from the Preventable Deaths Database using the eligibility criteria for this study

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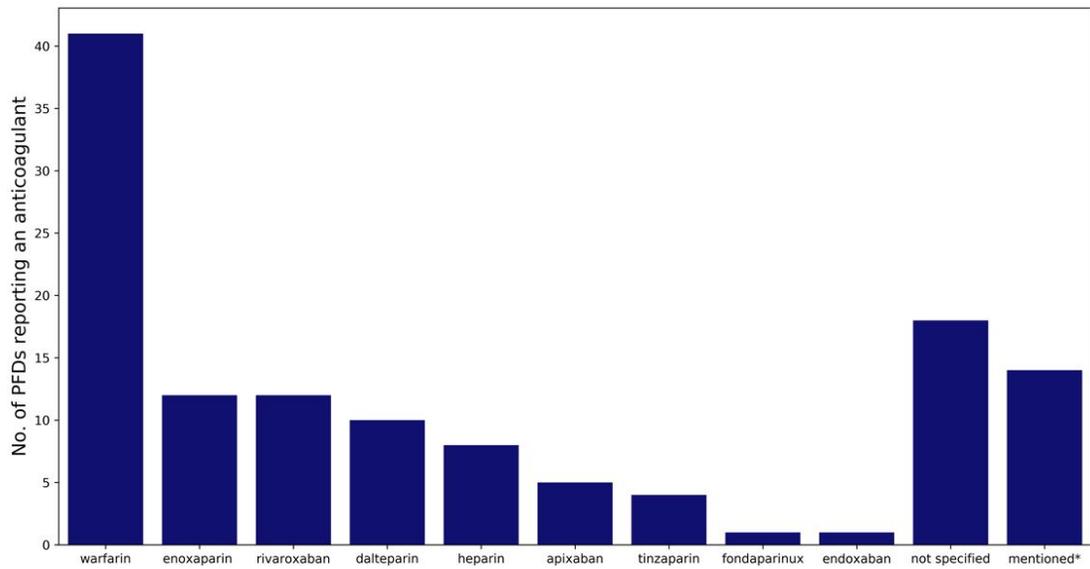


Figure 2: Anticoagulants reported in cardiovascular disease-related Prevent Future Death reports (PFDs). *in these PFDs, the coroner suggested that if an anticoagulant had been used the death might have been prevented

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