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Risk of bleeding after dual antiplatelet therapy (DAPT) in patients treated with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)

Submission date
19/02/2016

Recruitment status
No longer recruiting

Registration date
19/02/2016

Overall study status
Completed

Last Edited
13/07/2023

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims

Blood clots happen when platelets (cells in the blood) clump together at the site of an injury to stop bleeding. Diseased arteries, such as those affected by fatty deposits (atherosclerosis), are particularly susceptible to blood clots. Antiplatelet drugs prevent heart disease and stroke by preventing the formation of blood clots in the arteries. In people who have had a heart attack or have diseased arteries, low-dose aspirin is recommended indefinitely to prevent another heart attack or a stroke. People who have had a coronary stent put in one or more of their arteries or have had coronary artery bypass grafting (CABG) surgery following a heart attack are prescribed low-dose aspirin and an additional antiplatelet drug for up to 12 months following the event. Combined treatment with aspirin and another antiplatelet drug is called dual antiplatelet therapy (DAPT). Some patients (e.g. those with atrial fibrillation) are also prescribed an anticoagulant in addition to DAPT. After this period of combined treatment, antiplatelet treatment is continued with low-dose aspirin alone. Antiplatelet drugs increase the risk of bleeding. About 1 in 100 people on aspirin and 2 in 100 people on DAPT have a major bleeding event that requires hospitalisation. However, many more people (about 9 in 100) experience minor bleeding, such as bleeding in the stomach or bowel, and nuisance bleeding, such as nosebleeds, bleeding from gums, and excessive bruising. These minor bleeding events cause discomfort and anxiety, take up consultations with GPs and may cause patients to stop taking their tablets as prescribed. Few studies have assessed how often bleeding events happen in people taking DAPT. Hospital doctors (cardiologists and surgeons) are increasingly prescribing more potent antiplatelet drugs to people who have had a stent or CABG surgery, without taking into account the risk of minor bleeding. They are doing this mainly because they do not know the extent of minor bleeding and the effect that it has on patients. This information is not known because most minor bleeding events are treated by GPs and patients do not go to hospital. Currently, decision-makers such as the National Institute for Clinical Excellent (NICE) are uncertain about the risk of minor and nuisance bleeding in people who take DAPT. Therefore, they cannot take it into account when making recommendations about which antiplatelet drugs should be used in people with heart disease and how long these drugs should taken for. In this

study we use a large GP database and a database of patients' attendance and admissions to hospital, to determine how many people experience bleeding after being prescribed DAPT or both DAPT and an anticoagulant.

Who can participate?
Patients over 18 years of age who have been treated with a stent, CABG surgery or medication only for acute coronary syndrome.

What does the study involve?
We compare the patients who take aspirin only with the patients taking different combinations of DAPT (with or without an anticoagulant) in the different patient groups (treated with stent, CABG surgery or medication only) in order to calculate the rate of bleeding events in these groups. We also review other research to determine how bleeding affects patients' quality of life.

What are the possible benefits and risks of participating?
Information from our study will help doctors to choose drugs that are more appropriate for individual patients' specific needs, which will reduce the risk of bleeding and increase adherence to treatment. There are no risks to participants as only their data is used.

Where is the study run from?
Bristol Royal Infirmary (UK)

When is the study starting and how long is it expected to run for?
April 2016 to May 2019

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
HTA 14/192/89

Study information

Scientific Title
Comprehensive ascertainment of bleeding in patients prescribed different combinations of dual antiplatelet therapy (DAPT) and triple therapy (TT, DAPT plus an anticoagulant) after coronary interventions in the UK: a population based cohort study (the ADAPTT study)

Acronym
ADAPTT

Study objectives
The study will quantify the incidence of all bleeding events (major and minor) in three cohorts of patients exposed to aspirin (Asp) and various dual antiplatelet therapy (DAPT) and triple therapy (TT, DAPT + an oral anticoagulant) regimens in three cohorts of patients:
1. Percutaneous coronary intervention (PCI)
2. Coronary artery bypass grafting (CABG)
3. Acute coronary syndrome (ACS) with no procedure

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1419289

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical approval is not required as the study is using the Clinical Practice Research Database (CPRD) which has obtained ethical approval from a National Research Ethics Service Committee (NRES) for all purely observational research using anonymised CPRD data.

Study design
Retrospective population-based cohort study.

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute coronary syndrome

Interventions

The health technologies that will be assessed are:
1. DAPT: aspirin (75mg) and clopidogrel (75mg) (AC); aspirin (75mg) and prasugrel (5mg or 10mg but not varying) (AP); aspirin (75mg) and ticagrelor (90mg). The DAPT regimen is prescribed according to guidelines and does not vary.
2. Aspirin monotherapy: aspirin (75-300mg). All cardiology patients will be prescribed low-dose aspirin (75mg) but there is variation in aspirin prescription for CABG patients, with some surgeons choosing to prescribe 150mg or 300mg.
3. Triple therapy (TT): DAPT + an anticoagulant (e.g. warfarin, dabigatran, rivaroxaban, apixaban).

We will compare:
1. AC (reference) vs. AP or AT for the PCI cohort
2. Asp (reference) vs. AC for the CABG and ACS but no procedure cohorts

We will attempt to compare risk of bleeding for groups receiving DAPT vs TT but we cannot guarantee that we will be able to do so for the different anticoagulants and any such analyses are likely to have low power.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Aspirin, clopidogrel, prasugrel, ticagrelor, warfarin, dabigatran, rivaroxaban, apixaban

Primary outcome(s)
Bleeding event (classified as minor or major by WHO bleeding scale)

These are all time to event outcomes, so duration of follow up will be time from index event (PCI, CABG or ACS event) to: date of first bleeding event (mortality, hospital admission for the secondary outcomes); 12 months after entry into the cohort (i.e. we will stop following people up if they had no event after 12 months); date of the end of period covered by the data extraction if this is less than 12 months after entry into the cohort; last date of continuous exposure to DAPT + 2 weeks to account for drug clearance (we will consider exposure to be continuous if < 2 weeks between repeat prescriptions); loss of follow up from CPRD.

We will also identify all bleeding events during follow-up (12 months)

Key secondary outcome(s))
1. All-cause mortality
2. Cardiovascular mortality
3. Mortality from bleeding
4. Hospital admission

These are all time to event outcomes, so duration of follow up will be time from index event (PCI, CABG or ACS event) to: date of first bleeding event (mortality, hospital admission for the secondary outcomes); 12 months after entry into the cohort (i.e. we will stop following people up if they had no event after 12 months); date of the end of period covered by the data

extraction if this is less than 12 months after entry into the cohort; last date of continuous exposure to DAPT + 2 weeks to account for drug clearance (we will consider exposure to be continuous if < 2 weeks between repeat prescriptions); loss of follow up from CPRD.

Completion date
31/05/2019

Eligibility

Key inclusion criteria
Patients will be included if they:
1. Are labelled as 'acceptable' for use in research by CPRD (a process that identifies and excludes patients with non-continuous follow up or patients with poor data recording that raises suspicion as to the validity of that patient's record)
2. Are over 18 years of age
3. Have one year of medical history in CPRD before cohort entry (time of index procedure or event)
4. Have a record of aspirin monotherapy (Asp) or dual antiplatelet therapy (DAPT: aspirin and clopidogrel, AC; aspirin and prasugrel, AP; aspirin and ticagrelor, AT) in the year following the index procedure or event
5. No record of DAPT in the 3 month prior to the index procedure or event

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Participants will excluded if they do not meet the above inclusion criteria

Date of first enrolment
01/04/2016

Date of final enrolment
30/09/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Clinical Trials and Evaluation Unit
School of Clinical Sciences
University of Bristol
Level 7, Bristol Royal Infirmary
Queen's Building
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Sponsor information

Organisation
University of Bristol (UK)

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI)	01/08/2022	15/08/2022	Yes	No
Results article		01/05/2023	13/07/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes