

University of Oxford
Nuffield Department of
Clinical Medicine

Monday, 14 March 2005

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852
USA
Docket 77N0-0094

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Ref: Primary Prevention Trials of aspirin vs control : Docket 77N0-0094

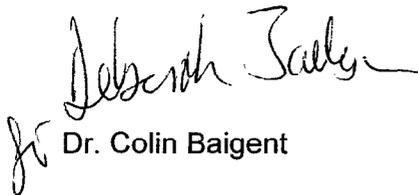
Dear Sir

I enclose 4 copies of the supporting documentation for the data from 3 trials of aspirin vs control: Primary Prevention Project; Thrombosis Prevention Trial; and US-Physicians.

The data for these trials have been sent under separate cover to Meg Pease-Fye Regulatory Health Project Manager, Division of Cardio-Renal Drug Products.

If you have any queries on this, then please contact Dr. Colin Baigent colin.baigent@ctsu.ox.ac.uk on +44 1865 404866

Yours sincerely,


Dr. Colin Baigent

77N-0094

SUP 54

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PPP dataformat key:

Variable Name	Parameter
Baseline information (recorded prior to treatment allocation)	
pat_id	Patient identifier
gender	Gender (1=male)
age	Age at randomisation
h_angina	History of angina (1=yes, 2=no)
h_mi	History of previous MI (1=yes, 2=no)
h_cvd	History of cerebrovascular disease (1=yes, 2=no, 3=major stroke, 4=minor stroke, 5=retinal infarct, 6=cerebral TIA, 7=ocular TIA)
h_pad	History of peripheral arterial disease (1=yes, 2=no)
h_dm	History of diabetes mellitus (1=yes, 2=no)
h_hypten	History of hypertension (1=yes, 2=no)
h_af	History of atrial fibrillation (1=yes, 2=no)
cur_smoke	Current smoker (1=yes, 2=no)
sbp	Systolic blood pressure (mmHg)
dbp	Diastolic blood pressure (mmHg)
tot_chol	Total cholesterol (mg/dL)
bmi	Body mass index (Kg/M ²)
hrt_fail	Heart failure at trial entry (1=yes, 2=no)
d_sched_end	Date of scheduled end of trial treatment
Randomisation data	
d_rand	Date of randomisation
asp	Randomised treatment allocation (1=Aspirin, 2=No Aspirin)
vite	Randomised treatment allocation (1=Vitamin E, 0=No Vitamin E)
Outcome data (record FIRST event of each type AFTER randomisation)	
cva	Stroke after randomisation (1=intracerebral haemorrhage, 2=subarachnoid haemorrhage, 3=subdural haematoma, 4=ischaemic [including embolic], 8=unknown type, 9=no stroke)
c_cva	Stroke confirmation (1=CT or MRI, 2=autopsy, 3=lumbar puncture, 8= other e.g. angiogram, 9= no confirmatory test)
d_cva	Date of first stroke
cva_outc	Outcome of first stroke (1=fatal, 2=non-fatal)
cva_nf_outc	Actual or predicted outcome after non-fatal stroke (1=disabled [i.e significant interference with daily life], 2=not disabled, 0=not known)
mi	Myocardial infarction (excluding sudden death and silent MI) (1=yes, 2=no)
d_mi	Date of first myocardial infarction
mi_outc	Outcome of first myocardial infarction(1=fatal, 2=non-fatal)
bleed	Major (i.e transfused or fatal) extracranial bleed (1=yes, 2=no)
d_bleed	Date of first major extracranial bleed
bleed_outc	Outcome of first major extracranial bleed (1=fatal, 2=non-fatal)
pe	Pulmonary embolism (1=yes, 2=no)
c_pe	Pulmonary embolism confirmation (1=Ventilation/perfusion scan, 2=autopsy, 3=pulmonary angiography, 4=perfusion scan alone, 8=other, 9=none)
d_pe	Date of first pulmonary embolism
pe_outc	Outcome of first pulmonary embolism (1=fatal, 2=non-fatal)
d_end_treat	Date patient actually ceased randomised treatment
Follow-up	
d_lfu	Date of last follow-up for vital status
lfu_state	Vital status on this date (1=dead, 2=alive)
cause_death	Cause of death (1=Definitely Cardiovascular, 2=Definitely NOT Cardiovascular, 3=Death caused by haemorrhage, 9=Unknown cause of death)

TPT dataformat key

Variable Name	Parameter
Baseline information (recorded prior to treatment allocation)	
pat_id	Patient identifier
gender	Gender (1=male)
d_birth	Date of birth
h_angina	History of angina (1=yes, 2=no)
h_mi	History of previous MI (1=yes, 2=no)
h_cvd	History of cerebrovascular disease (1=yes, 2=no, 3=major stroke, 4=minor stroke, 5=retinal infarct, 6=cerebral TIA, 7=ocular TIA)
h_pad	History of peripheral arterial disease (1=yes, 2=no)
h_dm	History of diabetes mellitus (1=yes, 2=no)
h_hypten	History of hypertension (1=yes, 2=no)
h_af	History of atrial fibrillation (1=yes, 2=no)
cur_smoke	Current smoker (1=yes, 2=no)
sbp	Systolic blood pressure (mmHg)
dbp	Diastolic blood pressure (mmHg)
tot_chol	Total cholesterol (mmol/L)
bmi	Body mass index (Kg/M ²)
hrt_fail	Heart failure at trial entry (1=yes, 2=no)
d_sched_end	Date of scheduled end of trial treatment
Randomisation data	
d_rand	
treat	Randomised treatment allocation (11=warfarin+aspirin, 12=warfarin+aspirin placebo, 21=warfarin placebo+aspirin, 22=warfarin placebo+aspirin placebo)
Outcome data (record FIRST event of each type AFTER randomisation)	
cva	Stroke after randomisation (1=intracerebral haemorrhage, 2=subarachnoid haemorrhage, 3=subdural haematoma, 4=ischaemic [including embolic], 8=unknown type, 9=no stroke)
c_cva	Stroke confirmation (1=CT or MRI, 2=autopsy, 3=lumbar puncture, 8= other e.g. angiogram, 9= no confirmatory test)
d_cva	Date of first stroke
cva_outc	Outcome of first stroke (1=fatal, 2=non-fatal)
cva_nf_outc	Actual or predicted outcome after non-fatal stroke (1=disabled [i.e significant interference with daily life], 2=not disabled)
mi	Myocardial infarction (excluding sudden death and silent MI) (1=yes, 2=no)
d_mi	Date of first myocardial infarction
mi_outc	Outcome of first myocardial infarction(1=fatal, 2=non-fatal)
bleed	Major (i.e transfused or fatal) extracranial bleed (1=yes, 2=no)
d_bleed	Date of first major extracranial bleed
bleed_outc	Outcome of first major extracranial bleed (1=fatal, 2=non-fatal)
pe	Pulmonary embolism (1=yes, 2=no)
c_pe	Pulmonary embolism confirmation (1=Ventilation/perfusion scan, 2=autopsy, 3=pulmonary angiography, 4=perfusion scan alone, 8=other, 9=none)
d_pe	Date of first pulmonary embolism
pe_outc	Outcome of first pulmonary embolism (1=fatal, 2=non-fatal)
d_end_treat	Date patient actually ceased randomised treatment
Follow-up	
d_lfu	Date of last follow-up for vital status
lfu_state	Vital status on this date (1=dead, 2=alive)
cause_death	Cause of death (1=stroke, 2=myocardial infarction, 3=coronary-sudden, 4=coronary-not sudden, 5=coronary-sudden/not sudden (unknown), 6=other cardiovascular, 7=cancer, 8=other/miscellaneous)

USP dataformat key

Variable Name	Parameter	Comment, see worksheet "USP-datakey comments "
Baseline information (recorded prior to treatment allocation)		
pat_id	Patient identifier	
gender	Gender (1=male)	1
age	Age at randomisation (years)	
h_angina	History of angina (1=yes, 2=no)	2
h_mi	History of previous MI (1=yes, 2=no)	3
h_cvd	History of cerebrovascular disease (1=yes, 2=no)	4
h_pad	History of peripheral arterial disease (1=yes, 2=no)	5
h_dm	History of diabetes mellitus (1=yes, 2=no)	6
h_hypten	History of hypertension (1=yes, 2=no)	7
h_af	History of atrial fibrillation (1=yes, 2=no)	8
cur_smoke	Current smoker (1=yes, 2=no)	9
sbp	Systolic blood pressure (mmHg)	
dbp	Diastolic blood pressure (mmHg)	
tot_chol	Total cholesterol (mg/dL)	
bmi	Body mass index (Kg/M ²)	
hrt_fail	Heart failure at trial entry (1=yes, 2=no)	10
d_sched_end	Date of scheduled end of trial treatment	
Randomisation data		
d_rand	Date of randomisation	
asa	Aspirin (1=Aspirin, 0=Aspirin Placebo)	
bc	Beta-Carotene (1=Beta-Carotene, 0=Beta-Carotene Placebo)	
Outcome data (record FIRST event of each type AFTER randomisation)		
cva	Stroke after randomisation (1=intracerebral haemorrhage, 2=subarachnoid haemorrhage, 3=subdural haematoma, 4=ischaemic [including embolic], 8=unknown type, 9=no stroke)	11
c_cva	Stroke confirmation (1=CT or MRI, 2=autopsy, 3=lumbar puncture, 8= other e.g. angiogram, 9= no confirmatory test)	12
d_cva	Date of first stroke	
cva_outc	Outcome of first stroke (1=fatal, 2=non-fatal)	13
cva_nf_outc	Actual or predicted outcome after non-fatal stroke (1=disabled [i.e significant interference with daily life], 2=not disabled)	14
mi	Myocardial infarction (excluding sudden death and silent MI) (1=yes, 2=no)	15
d_mi	Date of first myocardial infarction	
mi_outc	Outcome of first myocardial infarction(1=fatal, 2=non-fatal)	16
bleed	Major (i.e transfused or fatal) extracranial bleed (1=yes, 2=no)	17
d_bleed	Date of first major extracranial bleed	
bleed_outc	Outcome of first major extracranial bleed (1=fatal, 2=non-fatal)	18
pe	Pulmonary embolism (1=yes, 2=no)	19
c_pe	Pulmonary embolism confirmation (1=Ventilation/perfusion scan, 2=autopsy, 3=pulmonary angiography, 4=perfusion scan alone, 8=other, 9=none)	20
d_pe	Date of first pulmonary embolism	
pe_outc	Outcome of first pulmonary embolism (1=fatal, 2=non-fatal)	21
d_end_treat	Date patient actually ceased randomised treatment	22
Follow-up		
d_lfu	Date of last follow-up for vital status	23
lfu_state	Vital status on this date (1=dead, 2=alive)	
cause_death	Cause of death (ICD-9 codes)	24

USP comments page

Comment	Explanation	Trialists codes
1	These data weren't sent by trialists but as the trial consisted of male doctors, gender=1	
2	This was initially sent as 1=Yes, 0=No	
3	Email from trialists to say that no patients had a history of this illness, so set h_mi=2 (No)	
4	Email from trialists to say that no patients had a history of this illness, so set h_cvd=2 (No)	
5	These data weren't sent by trialists, so set to "." (missing)	
6	This was initially sent as 1=Yes, 0=No	
7	This was initially sent as 1=Yes, 0=No	
8	These data weren't sent by trialists, so set to "." (missing)	
9	This was initially sent as 1=Never/2=Past/3=Current, which we converted to "Never" or "Past"=No, and "Current"=Yes to current smoker	
10	These data weren't sent by trialists, so set to "." (missing)	
11	Originally sent as three separate variables (cnfrm_st, hemorrhha, ischemic), which we therefore converted to :-if cnfrm_st=1 & hemorrhha=1 then cva=1; else if cnfrm_st=1 & ischemic=1 then cva=4; else if cnfrm_st=1 & hemorrhha=. & ischemic=. then cva=8; else if cnfrm_st=. then cva=9;	
12	Originally sent with more groups than we asked for, which we therefore converted to :-if cnfrm_st=1 & stkevid in (1 8 12 16) then c_cva=8; else if cnfrm_st=1 & stkevid in (2 3 5 7 9 10 11 13 14 15) then c_cva=1; else if cnfrm_st=1 & stkevid= 4 then c_cva=2; else if cnfrm_st=1 & stkevid= 6 then c_cva=3; else if cnfrm_st=1 & stkevid in (19 20) then c_cva=9;	Value for stkevid (stroke evidence) 1='Sx/PE', 2='Sx & CT', 3='Sx & scan', 4='autopsy', 5='CT & scan', 6='Sx & LP', 7='PE & CT', 8='Surgery', 9='CT & LP', 10='CT, Angiogram, PE, surgery', 11='PE, CT, angiogram', 12='angiogram & Sx/PE', 13='Sx & MRI', 14='PE & MRI', 15='PE, CT, angiogram', 16='noted on DC', 19='self report of DX test w/out records or kin', 20='no records, no information'
13	Originally sent as two variables (fatalst and nfatlst) so recoded to :- if cnfrm_st=1 & fatalst=1 then cva_outc=1; else if cnfrm_st=1 & nfatlst=1 then cva_outc=2;	
14	Originally sent with more groups than we asked for, which we therefore converted to :- if cnfrm_st=1 & nfatlst=1 & stksev in (1 2 3) then cva_nf_outc=2; else if cnfrm_st=1 & nfatlst=1 & stksev in (4 5 9) then cva_nf_outc=1; else if cnfrm_st=1 & nfatlst=1 & stksev= 7 then cva_nf_outc=9;	Value for stksev (stroke severity) 1='no residual', 2='minor, nonfunctionally impairing deficit', 3='mild functional deficit', 4='moderate functional deficit', 5='severe requiring chronic care', 6='fatal', 7='no information/nonfatal', 8='no information/fatal', 9='fatal, statcat-nonfatal', 10='statcat-fatal-noncvd'
15	Initially sent as cnfrm_mi=1 for MI events so recoded to:- if cnfrm_mi=1 then mi=1;else mi=2;	
16	Originally sent as two variables (fatalMI and nfatmi) so recoded to :- if cnfrm_mi=1 & fatalmi=1 then mi_outc=1; else if cnfrm_mi=1 & nfatmi=1 then mi_outc=2;	
17	Only the bleed date was sent and from communications with the trialists we knew that they were all non fatal, so we converted this as :- if d_bleed>. Then do; bleed=1 (Yes) bleed_outc=2 (non fatal)	
18	Only the bleed date was sent and from communications with the trialists we knew that they were all non fatal, so we converted this as :- if d_bleed>. Then do; bleed=1 (Yes) bleed_outc=2 (non fatal)	
19	Initially sent as cnfrm_pe=1 for PE events so recoded to:- if cnfrm_pe=1 then pe=1;else pe=2;	
20	Originally sent with more groups than we asked for, which we therefore converted to :- if cnfrm_pe=1 & peevid=1 then c_pe=1; else if cnfrm_pe=1 & peevid=2 then c_pe=3; else if cnfrm_pe=1 & peevid=3 then c_pe=4; else if cnfrm_pe=1 & peevid=4 then c_pe=2; else if cnfrm_pe=1 & peevid in (5 6 7) then c_pe=8; else if cnfrm_pe=1 & peevid=20 then c_pe=9;	Value for peevid (PE evidence) 1= 'Angiogram and scan', 2= 'Angiogram', 3= 'Scan', 4= 'Autopsy', 5= 'Clinical only', 6= 'Noted on DC', 7= 'Path evidence', 20= 'No records, no information'
21	Initially sent as nfatpe=1 for non fatal PE event so recoded as :-if cnfrm_pe=1 & nfatpe=1 then pe_outc=2;	
22	These data weren't sent by trialists, so set to "." (missing)	
23	Only death dates sent by trialists, so for patients alive at end of study date of last follow up was set to 25/01/1988	
24	Sent as ICD-9 codes	