Science For A Better Life

Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Title	New use of low-dose acetylsalicylic acid and risk of major bleeding: a cohort study with nested case–control analyses in the United Kingdom.
Keywords	low-dose acetylsalicylic acid; intracranial bleeds; upper gastrointestinal bleeds; lower gastrointestinal bleeds; nested case–control
Rationale and background	Use of low-dose acetylsalicylic acid (ASA) reduces the risk of ischaemic cardiovascular events and colorectal cancer (CRC) but may increase the risk of major bleeding events. Evaluations on the safety profile of low-dose ASA are warranted for incorporation into risk– benefit evaluations regarding long-term use in the general population.
Research question and objectives	To evaluate the risk of intracranial bleeding (ICB), upper gastrointestinal bleeding (UGIB) and lower gastrointestinal bleeding (LGIB) associated with new use of low-dose ASA in clinical practice. The primary objectives were to i) estimate the incidence of ICB, LGIB and LGIB in new users of low-dose ASA, and ii) estimate the risk of ICB, UGIB and LGIB associated with new use of low-dose ASA, including by sex and age, and to establish any duration or dose–response associations.
Study Design	Cohort study with nested case–control analyses.
Setting	UK general practice between 01 January 2000 and 31 December 2013.
Subjects and Study Size, including dropouts	199,079 individuals in the low-dose ASA cohort and 199,079 individuals in the comparison cohort followed for up to 13 years.
Variables and Data sources	The Health Improvement Network UK (THIN) primary care database of anonymized patient electronic medical records. Demographics, lifestyle factors, comorbidities and medication use were assessed for potential confounding effects and included in the analyses where required.
Results	There were 1611 incident cases of ICB, 1843 cases of UGIB and 2763 cases of LGIB (median follow-up of 5.4 years for each outcome). Among the low-dose ASA cohort and comparison cohort, respectively, incidence rates per 10,000 person-years were 3.52 vs. 3.12 for intracerebral haemorrhage (ICH), 2.45 vs. 1.86 for subdural haematoma (SDH) and 1.65 vs. 1.80 for subarachnoid haemorrhage (SAH). Comparable rates per 1000 person-years were 0.97 vs. 0.67 for UGIB and 1.68 vs .0.76 for LGIB. Rate ratios (RRs; 95% CIs) for ICB with current use of low-dose ASA vs. never use were 0.98 (0.84–1.13) for ICB, 0.88 (0.74–1.03) for non-traumatic ICB, 1.30 (1.00–1.68) for traumatic ICB, 0.63 (0.48–0.82) for fatal ICB, 1.14 (0.97–1.35) for non-fatal ICB, 0.98 (0.80– 1.20) for ICH, 1.23 (0.95–1.59) for SDH and 0.77 (0.58–1.01) for SAH. A significant 43% decreased risk of SAH was seen

	among women (RR 0.57, 95% CI: 0.39–0.82) but no corresponding association in men. Corresponding RRs (95% CIs) for gastrointestinal bleeding were 1.62 (1.40–1.87) for UGIB, 0.75 (0.49–1.15) for fatal UGIB, 1.73 (1.49–2.01) for non-fatal UGIB, 1.97 (1.75–2.22) for LGIB, 1.06 (0.40–2.81) for fatal LGIB and 1.98 (1.76–2.23) for non-fatal LGIB.
Discussion	Compared with never use, new use of low-dose ASA is not associated with a significant increase in the risk of ICB overall and may be associated with a significantly decreased risk of fatal ICB, and of SAH in women, or when used for a long duration. An approximate two-fold significant increased risk of non-fatal UGIB and LGIB was seen with new use of low-dose ASA but no association was seen with risk of fatal UGIB or LGIB, when compared with never use. These estimates should be weighed against the cardiovascular and CRC benefits of low-dose ASA to make an informed risk–benefit evaluation of low-dose ASA use in the general population.
Marketing Authorisation Holder(s)	Bayer AG
Names and affiliations of principal investigators	