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- Methods/Design
 - Population: 19 studies including 3,931,532 people (child/adolescents, younger adults, & older adults)
 - Intervention: Meta-analysis of ADHD medication use and cardiovascular risk
 - Comparison: stimulants and non-stimulants; age groups; type of CV risk
 - Outcomes: CV event including HTN, IHD, cerebrovascular disease, HF, VTE, tachyarrhythmia, and cardiac arrest
 - Time frame: median follow up 1.5 years (range 0.25 to 9.5 years)
- Findings
 - No statistically elevated CV risk with ADHD med use in any age group
 - Child/adol RR 1.18 (95% CI 0.91 – 1.53)
 - Young adults RR 1.04 (0.43 – 2.48)
 - Older adults RR 1.59 (0.62 – 4.05)
 - No statistically elevated CV risk with stimulant or non-stimulant use
 - Stimulants RR 1.24 (0.84 – 1.83)
 - Non-stimulants RR 1.22 (0.25 – 5.97)
 - No statistically elevated risk of cardiac arrest or arrhythmias, cerebrovascular diseases, or MI with ADHD med use
 - **Cardiac arrest or arrhythmia RR 1.60 (0.94 – 2.72)**
 - While not statistically significant, this may be due to lack of power and may actually be a clinically significant finding given proximity of lower bound to 1 vs higher bound. Higher powered prospective studies are needed to determine this specific risk.
 - Cerebrovascular diseases RR 0.91 (0.72 - 1.15)
 - Myocardial infarction RR 1.06 (0.68 – 1.65)
 - No statistically elevated CV risk with ADHD med use in female patients RR 1.88 (0.43 – 8.24)
 - No statistically elevated CV risk with ADHD med use with pre-existing CV disease RR 1.31 (0.80 – 2.16)
- Summary
 - **Suggests no association with ADHD med use (stimulant or not; median duration 1.5 years) and increased CV risk in any population**, including those with pre-existing CV disease
 - A modest increase in risk, especially for cardiac arrest or arrhythmias, cannot be ruled out
 - Need to further study female patients, those with pre-existing CV disease, and longer-term use of ADHD meds

- Methods/Design
 - Population: people with ADHD age 6 – 64 years using ADHD meds for up to 14 years
 - 10,388 cases with CVD
 - 51,672 matched controls without CVD (match age, sex, calendar time)
 - Intervention: Case-controlled study with matching via incidence density sampling
 - Comparison: ADHD medication use with CVD vs ADHD medication use without CVD
 - Outcomes: CVD diagnosis including IHD, cerebrovascular disease, HTN, HF, arrhythmias, VTE, arterial disease, and other forms of CVD disease
 - Time frame: median follow up time 4.1 years (range 1.9 – 6.8)
- Findings
 - Longer ADHD med duration was associated with increased risk of CVD (vs no use)
 - 0 - <1 year RR 0.99 (95% CI 0.93 – 1.06)
 - **1- <2 years RR 1.09 (1.01 – 1.18)**
 - **2- <3 years RR 1.15 (1.05 – 1.25)**
 - **3- 5 years RR 1.27 (1.17 – 1.39)**
 - **>5 years RR 1.23 (1.12 – 1.36)**
 - Longer ADHD med duration was associated with increased risk of HTN (vs no use)
 - 0 - <1 year RR 1.06 (95% CI 0.96 – 1.18)
 - **1- <2 years RR 1.34 (1.18 – 1.52)**
 - **2- <3 years RR 1.30 (1.12 – 1.50)**
 - **3- 5 years RR 1.72 (1.51 – 1.97)**
 - **>5 years RR 1.80 (1.55 – 2.08)**
 - Longer ADHD med duration was associated with increased risk of arterial disease (vs no use)
 - **0 - <1 year RR 1.42 (95% CI 1.04 – 1.93)**
 - **1- <2 years RR 1.63 (1.15 – 2.32)**
 - **2- <3 years RR 1.72 (1.17 – 2.53)**
 - **3- 5 years RR 1.65 (1.11 – 2.45)**
 - **>5 years RR 1.49 (1.96 – 2.32)**
 - No statistically increased risk of arrhythmias, cerebrovascular disease, HF, IHD, or VTE
 - Risk increased with higher dose
 - For DDD 1.5 - 2 (e.g., MTH 45 - <60mg/day), each 1 year of ADHD medication increases CV risk 4% (range 2 – 5%)
 - For DDD > 2 (e.g., MTH 60mg or higher daily), increases risk 5% (range 3 – 6%)
 - Possible signals of increased CV risk with longer term methylphenidate (RR 1.19 for 3 years or longer) and lisdexamfetamine (RR ~1.20 for 2 years or longer)
 - Possible increased risk within the 1st year only for atomoxetine (RR 1.07)

- Summary
 - Longer duration of ADHD medications is associated with increased risk of CV disease, especially HTN and arterial disease