representative of the current US population, based on various demographic criteria obtained from the US census. For this study, baseline and Year 2 functional MRI imaging data and parent and youth reports of depression, non-suicidal self-injury (NSSI), and suicidal thoughts and behaviors (STB) from the ABCD Study, were used for this analysis. Clinical and imaging data were added into a statistical model (linear mixed-effects model) to describe how the relationship between suicide risk and brain development changes over time. RESULTS/ANTICIPATED RESULTS: A total of 9653 subjects (51% Female), between the ages of 8.9 – 13.8 years, across two timepoints: Baseline (N=6493) and Year 2 (N=3,160), were included in the analysis. Of this sample, 861 (8.9%) endorsed depression, 1428 (14.8%) NSSI, 2146 (22.2%) STB, and 3012 (31.2%) any of the three suicide risk factors at any timepoint. Results showed a significant interaction between the association of network connectivity and STB group status with age in the approach (B = -15.0, 95%CI [-26.4, -3.8]), avoidance (B = -8.5, 95%CI [-16.3, -0.9]), regulation (B = -14.4, 95%CI [-26.2, -3.1]), approach-avoidance (B = -14.4, 95%CI [-28.3, -0.5]), and approach-regulation (B = -15.6, 95%CI [-28.8, -2.7]) network. DISCUSSION/SIGNIFICANCE OF IMPACT: Findings suggest, in early adolescence, presence of STBs is associated with changes in communication in regions involved in reward-(approach), emotion/threat-processing (avoidance), and their cognitive regulation (regulation). The causal relationship is unclear, but it's an important step to understanding the neural mechanisms of suicide.

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Predictors of glaucoma development in children with ocular hypertension

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OBJECTIVES/GOALS: Pediatric ocular hypertension (OHTN) carries a variable risk of glaucoma progression, yet its progression to true glaucoma is not well-defined. This study characterizes the clinical course of a cohort of pediatric eyes with OHTN and identifies predictors to glaucoma conversion. METHODS/STUDY POPULATION: A retrospective review of 119 eyes from 81 pediatric glaucoma suspects (IOP >21 mmHg on ≥2 visits) between 2005–2016. Conversion to glaucoma was defined by the Childhood Glaucoma Research Network criteria (progressive optic nerve cupping, visual field loss, or other structural changes associated with elevated IOP). Demographics, comorbidities, and tonometry methods were analyzed. Logistic regression identified independent risk factors for glaucoma conversion. Thus far, analyses include data from the 2005–2016 cohort, with additional data from the 2017–2023 patient cohort under collection and expected to be ready by the conference date. RESULTS/ANTICIPATED RESULTS: Of 119eyes (age 9.4±4.7years; baseline IOP27.7±5.7mmHg), 47(39.5%) converted to glaucoma over average 1.9years.Among 72 non-converters, 23(31.9%) normalized without treatment, 17(23.6%) with treatment, 17(23.6%)remained elevated untreated, and 15(20.8%) with treatment. Conversion was most frequent with baseline IOP 24–28mmHg(16.0%)and less with <24mmHg(8.3%). Absence of ocular (11.8%vs50.6%) and systemic risk factors (36.0%vs48.5%) reduced conversion, lowering treatment need and improving normalization. On multivariable analysis, younger age (OR0.84/year, p=0.002), ocular risk factors (OR4.95,p=0.01), and time to therapy initiation (OR0.74/year, p<0.001) predicted conversion. DISCUSSION/SIGNIFICANCE OF IMPACT: This study establishes baseline age and ocular risk factors as strong predictors of glaucoma conversion in pediatric ocular hypertensives. These findings are critical for clinicians, directly guiding an evidence-based approach to patient risk stratification, surveillance frequency, and treatment initiation.

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Hazard ratio ≠ risk ratio: Quantifying exaggeration of benefit in cancer randomized clinical trials

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OBJECTIVES/GOALS: Misinterpreting hazard ratio (HR) as absolute risk reduction is common in randomized trials (RCTs) with time-to-event endpoints, inflating benefit. We quantify this by describing risk ratio (RR) estimators for survival data and compare HRs with milestone and time-averaged RRs across a large collection of cancer RCTs. METHODS/STUDY POPULATION: We conducted a meta-epidemiological study in a convenience sample of more than 650 cancer RCTs (2002–2024), excluding trials without reported benefit, those stopped early, or non-inferiority designs. Pseudo-individual patient data were reconstructed from survival curves for overall survival and other event-free endpoints (such as progression-free survival). From these, we calculated Cox HRs and milestone-based RRs on common time supports. We also calculated time-constant RRs and weighted-averages of time-varying RRs. Primary contrasts were inverse-variance pooled HR/RR ratios for each RR definition. HR/RR < 1 indicates larger effects with HR as compared to RR. RESULTS/ANTICIPATED RESULTS: In a preliminary subset (n=120 trials), the pooled HR/RR ratio was 0.80 (95% confidence interval, 0.76 to 0.82): interpreting the HR as a RR would overstate benefit by 20%. Although all included trials reported statistically significant HR < 1, only 73% had RR < 1 and statistically significant: over one quarter failed to show benefit on the absolute risk scale. Results were consistent when using time-constant and weighted-average RRs. We anticipate comparable findings in the full sample. DISCUSSION/SIGNIFICANCE OF IMPACT: This study quantifies the inflation that arises when HRs are read as RRs. Reporting RR estimators for time-to-endpoints alongside HRs would improve communication of trial effects. Our findings also have design implications: to detect absolute risk reductions, RCTs would often need larger N or longer follow-up.

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