Increased problems, and also increased resilience as a result of COVID-19

Adolescents claim they have more behavioral problems, less social emotional skills, and are less prosocial because of COVID-19. A study found reductions in social emotional skills, prosocial behavior, and resilience scores. Still, the study found that the changes are not significant, and that changes in adolescents’ social emotional skills are negatively and significantly related to changes in internalized and externalized problems and positively and significantly related to changes in prosocial behavior and resilience. The implication is that adolescents who experienced larger development in social emotional learning also experienced more increase in resilience and prosocial behavior and a decrease in difficulties. [Martinsone B, et al. Adolescent social emotional skills, resilience and behavioral problems during the COVID-19 pandemic: A longitudinal study in three European countries. *Front Psychiatry* 2022 Aug 1; 13:942692. doi: 10.3389/fpsyt.2022.942692.]

Smartphone deprivation beneficial for hospitalized teens

Youth in psychiatric hospitals are not allowed to have smartphones for the duration of treatment, but little is known about the response to this deprivation. So, researchers in this small-scale study looked at 181 adolescents, with a mean age of 15 years, to find out more about the experience. They found that the youths were not unduly upset by the loss of their phones, but they were less ready to engage in treatment than youth who did not have their phones taken away. Analyses additionally evaluated whether reactions to smartphone deprivation were associated with clinical symptom severity (e.g., suicidal ideation, internalizing and externalizing symptoms) and readiness for psychotherapy. Negative reactions to smartphone deprivation were significantly positively correlated with daily smartphone hours, addictive patterns of use, and both negative and positive emotional responses to social media use. [Burke TA, et al. Reactions to naturalistic smartphone deprivation among psychiatrically hospitalized adolescents. *J Psychiatr Res* 2022 Aug 1; 155:17–23. doi: 10.1016/j.jpsychires.2022.07.061. Online ahead of print.]

### From the FDA

**FDA at work on applying the non-inferiority paradigm to assess exposure-response and dosing comparisons between pediatric and adult patients**

Pediatric drug development often encounters challenges that don’t typify adult drug development. The pediatric patient populations available for conducting clinical studies, for example, tend to be smaller, and the ethical considerations surrounding pediatric trials may impose particular restrictions and concerns. As a result, investigators have in many instances opted to extrapolate evidence for drug approvals in adults and older pediatric patients to inform aspects of drug review relevant to younger pediatric patients. The use of extrapolation of efficacy into pediatric drug development programs has been found useful when disease progression and treatment response are similar in adult and pediatric populations.

Several methods have proven useful in extrapolating adult data into matters of pediatric drug assessments, one of which draws from analyses of exposure-response similarity between adults and children. In this method, a measure of exposure, such as the maximum concentration (Cmax), is plotted against a measure of treatment response for all the patients in both populations. The relationship between the exposure and response in each population can be presented as an exposure-response curve, and comparison of the two exposure-response curves may then provide a basis for determining the suitability of extrapolating data from adults into pediatric patients.

Historically, exposure-response curves have been inspected visually to assess comparability. Visual inspections, however, are somewhat subjective, potentially undermining the interpretation of clinical trial data and leading to irreproducible or unwarranted conclusions. The development of a quantitative framework to assess exposure-response similarity in pediatric and adult patients, based on accumulated experience in pediatric drug development programs, is thus an important goal. A quantitative framework can provide more objective criteria for assessments of exposure-response similarity, strengthening the scientific evidence available for determining whether drugs approved in adult populations can be assessed as safe and effective for pediatric use.

The main basis for the quantitative approach is based on a concept often used in clinical trials called non-inferiority. In drug development, there may be circumstances where it is appropriate to test a new drug against a control drug that is expected to provide a similar level of benefit. Statistically, however, showing a test drug has the same level of benefit as

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