**UDS-based outcomes used to establish effectiveness for trials in opioid use disorder**

* RELAPSE: these outcomes seem to ignore what happens after the relapse
* Every relapse outcome requires a period of abstinence 🡪 Relapse and Abstinence outcomes are always linked (sine qua non) 🡪 can any relapse outcome be re-conceptualized as an abstinence outcome (or vice versa)?
* Reduction/non-abstinence outcomes can be measured independently of abstinence; reduction outcomes should be considered to account for what happens after a relapse, or to have a measurement for those who never fully achieve abstinence (and can therefore not relapse)

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| **Variable** | **Definition/Assessment** | **Category** |
| Abstinence from heroin | Zero use (4 negative UDS, no missing) in the past 30 days | Abstinence (period) |
| Near Abstinence | <2 positive UDS | Abstinence (with “allowance” of pos. UDS) |
| Complete Abstinence | 0 positive UDS | Abstinence (complete) |
| % of participants continuously abstinent | Percentage of participants per treatment arm who maintained 12 consecutive negative UDS | Abstinence (continuous) |
| Slip/Occasional heroin use | <3 consecutive positive UDS (and no symptoms of withdrawal) | Abstinence (with “allowance” of pos. UDS) |
| Longest period of abstinence | Longest period of negative UDS between two positive UDS | Abstinence (period) |
| Relapse | 3 consecutive positive UDS | Relapse |
| Time to relapse (strict) | Number of days between baseline and occurrence of the first positive UDS | Relapse |
| Time to relapse (more lenient) | Days to 3 consecutive positive UDS | Relapse |
| Time to relapse or loss of persistent abstinence (CTN-51) | Participant has used non-protocol prescribed opioids starting at day 21 post-randomization as follows: 4 consecutive opioid use weeks OR 7 consecutive days of use by self-report  Use week: Any week during which a participant self-reports at least one day of non-prescribed opioid use, provides a urine sample positive for non-study opioids, or fails to provide a urine sample at the weekly assessment visit. | Relapse |
| % of participants in a drug free period | Time elapsed between the first day of naltrexone administration and the first evidence of use (positive UDS) | Relapse |
| Frequency of illicit opioid use | Mean number of negative UDS *OR* percentage of positive UDS (each per treatment arm) | Reduction/non-abstinent |
| Not-abstinent rate | Number of positive UDS divided by the number of weeks of study participation | Reduction/non-abstinent |
| Reduction of regular use | ≥50% negative UDS | Reduction/non-abstinent |
| Substantial Improvement (CTN-30) | Abstaining from opioids during the last week AND for at least 2 of the previous 3 weeks of the third month of BUP/NX treatment.  Abstinence is determined by self-reports of opioid abstinence (missing urines will be  considered positive for opioids). | Reduction/non-abstinent |

*Note.* Negative UDS: opioid-negative Urine Drug Screen