[Informatics gap – this is an opinion paper all on its own ]

Another potential limitation of INTOXICATE is the usage of APACHE IV diagnoses for classification of intoxicant, which was the only indication of intoxication type available to Brandenburg et. al. in their model development cohort. *Antidepressants*, for example, is the diagnosis given to an intoxication with *any* type of antidepressant, including SSRIs, tricyclics, lithium, and others, all of which have potentially different mechanisms of toxicity. A category is given for *analgesics*, presumably pharmaceuticals, however intoxication with opiates produced as drugs of abuse would be classified as a *street drug*, along with cocaine and amphetamines. A category is included for *CO, As, or CN*, but intoxications with other poisons, such as those found in household products or industrial settings, would presumably fall under *toxins not otherwise specified.* The category *combination of two subtypes of intoxication* serves as a catch-all for polysubstance intoxications, however this would fail to identify polysubstance intoxications in patients with two or more mechanistically different intoxicants within the same APACHE IV classification, and Brandenburg **(for reasons unknown and not explained in their paper)** did not include polysubstance intoxication as a covariate in their model or assign it a risk score. This is particularly important given the significant morbidity and mortality associated with polysubstance intoxications, being implicated in 48-58% of overdose deaths **(cited Peppin below, but will find more because that source is specific to unintentional drug overdose and there is definitely plenty more to cite and mention).** Accounting for polysubstance intoxication in clinical prediction models poses the additional challenge of frequently incomplete or inaccurate reporting of intoxicant by patients and collateral sources. **(I’ll try to find a source for how many patients present with unknown intoxication type later)**. We note that for 18/28 of intoxicated patients in our ED cohort, intoxication type was classified as *Intoxicant NOS* or *Combination*, with all but one of the remainder being classified as *Street drug.*