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An observed rise in γ -hydroxybutyrate-associated deaths in London: evidence to suggest a possible link with concomitant rise in chemsex

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Highlights

- Reported data shows an increase in γ -hydroxybutyrate-associated deaths in London.
- Data suggests deaths are disproportionally high compared to use.
- Evidence is reported to suggest a possible link with concomitant rise in chemsex.
- Gamma-hydroxybutyrate-associated deaths are likely to be under-reported.

ABSTRACT

Background

Gamma-hydroxybutyrate (GHB) is the drug most linked to acute harm out of those used in chemsex, the incidence of which is reported to be increasing. However, there have been few systematic studies of the harms associated with GHB use. We investigated GHB-associated deaths from London Coroners' jurisdictions between 2011 and 2015.

Methods

Blood and urine samples were collected by pathologists and submitted for toxicological analysis at the request of coroners. Data from the Toxicology Unit, Imperial College London was retrospectively analysed. This comprised of 6633 cases from six out of seven Coroners' jurisdictions in London that underwent toxicological analysis between January 2011 and December 2015.

Results

A total of 61 GHB-associated deaths (0.92% of total cases), 184 cocaine-associated deaths (2.8% of total cases) and 83 MDMA-associated deaths (1.3% of total cases) were identified. There was a 119% increase in the proportion of GHB-associated deaths detected in 2015 compared to 2014. Over the same time period there was a 25% increase in cocaine-associated deaths and a 10% decrease in MDMA-associated deaths.

Conclusions

Our data suggest that GHB-associated deaths are increasing in London, and that this is likely at least in part due to increasing use of GHB for chemsex. Further studies on the use of GHB are urgently required to understand the extent of its use, whether this is as prevalent in other major urban areas in the UK, and the full extent of the harms it causes.

Keywords: Drug deaths, γ -hydroxybutyrate, Chemsex

1. Introduction

Gamma-hydroxybutyrate (GHB) is a central nervous system depressant produced naturally in the body in small quantities and is also an illegal drug used recreationally for its aphrodisiac, euphoric and relaxant effects.[1] Regular use of GHB is thought to be relatively higher in the lesbian, gay, bisexual, and transgender community, though other populations also use it. [1] Anecdotal evidence suggests that GHB use is increasing, and this may be driven in part by an increase in the incidence of chemsex.

Chemsex is a specific form of recreational drug use involving specific drugs - GHB/ γ -butyrolactone (GBL), methylamphetamine and mephedrone alone or in combination to enhance or prolong sexual sessions. Such sessions can last for several days, involve multiple partners and include high risk behaviour. Chemsex mainly occurs amongst men who have sex with men (MSM). [2] It is recognised that MSM are more likely to take drugs than the general population. [3] In the United States and Australia the practice is known as ‘party and play’ (PNP) and is more common in urban areas with a large gay population. [4,5]

Whilst chemsex is not a new phenomenon, healthcare professionals are worried that increased availability and accessibility of drugs and sex through websites and mobile applications has increased the acceptability, fashionableness and incidence of chemsex. [6,7] The mainstream media are becoming increasingly aware of the issue and drug treatment centres report being overwhelmed by the number of men seeking help. [8] However, it is difficult to know how harmful chemsex is. The Chemsex Study (2014) reported that whilst chemsex has received significant media attention, evidence on the extent of the issue and potential harms was limited. [7] There is a lack of reliable statistics about the number of men involved, though it is believed that the proportion of MSM participating in chemsex is relatively small. [9]

GHB is the drug most linked to acute harm out of those used in chemsex. However, though recent publications have highlighted chemsex-associated harms to health including addiction and sexually transmitted diseases, [2,7,10] the risks and rates of overdose have been relatively little explored.

Data collected over a 12 month period (2013-2014) from the European Drug Emergencies Network found that GHB/GBL was the fourth most common acute drug toxicity presentation (after heroin, cocaine and cannabis), based on self-reported use. For the two centres located in London, GHB/GBL was the most common drug reported, with a combined total of 380 presentations over the 12 month period. [11]

The onset of GHB effects usually occurs within 15 minutes of ingestion. Effects last for 3 hours on average with a typical dose but can be indefinitely prolonged through repeated dosing. [12] Previous studies have shown that GHB is rapidly eliminated from the body with reported half-lives ranging from 20-53 minutes and being completely eliminated, and therefore undetectable in blood, within 4-8 hours following ingestion. [13]

Recreational doses are reportedly between 1-3 grams of GHB but some users with tolerance can take up to 4-5 grams. GHB is commonly available as a liquid of variable concentration and is often measured in doses such as a capful or teaspoon. [14] Online advice states that an initial safe recreational dose of GBL is 0.5-1 millilitres with no redosing within a 3 hour period. [14] At low doses the effects of GHB are similar to alcohol. However, higher doses have anaesthetic effects, rapidly causing unconsciousness and can lead to coma, respiratory depression and apnoea. [1] Coma is relatively common with many men reporting becoming unconscious after taking GHB. [7] In the majority of cases these individuals awake spontaneously within approximately 1.5 to 3 hours, but the coma can lead to death. GHB has a steep dose-response curve and there is large variability in effects of a particular dose

between and within individuals. [1] This means that a euphoric dose for one person could be a sedative dose for another, and it is relatively easy to accidentally overdose. [15] In addition, GHB and GBL are used and described interchangeably with each other, GBL converts rapidly to GHB in vivo and the perceived effects are indistinguishable. Therefore, it is often difficult to know both for the user and healthcare professionals whether GHB or GBL has been consumed. However, GBL is absorbed much faster and eliminated more slowly than GHB, resulting in faster and more prolonged effects. Pure GBL is approximately three times more potent than GHB preparations. [16] In addition, alcohol or other psychoactive substances, both depressants and stimulants, may intensify the toxic effects of GHB. [1,17]

The main risks of overdosing are thus from taking too much GHB/GBL, redosing too soon or taking the drug in combination with alcohol or other psychoactive substances.

GHB-associated deaths have been reported from the USA, Canada, Europe and Australia. [18,19] However, there has been little systematic investigation of the incidence of GHB-associated deaths. Zyosec *et al* analysed 226 GHB-associated deaths that occurred between 1995 and 2005 in the USA, Canada, and the UK, but suggested that this was likely a significantly under-representation because, amongst other reasons, many routine toxicology tests do not include or request GHB analysis, and there is no central database recording such deaths. [18] Corkery *et al* described 159 deaths associated with GHB and derivatives between 1995 and 2013 in the UK's National Programme on Substance Abuse Deaths database, providing comprehensive and detailed data, but acknowledged that their study likely underestimates the number of deaths due to the fact that GHB analysis is not routinely performed in post-mortem investigations in the UK. [19]

As reports suggest that the use of GHB and the incidence of chemsex are increasing, and GHB is the drug most linked to acute harm out of those used in Chemsex, we systematically

investigated the numbers of GHB-associated deaths from London Coroners' jurisdictions to see whether there was evidence of increased deaths associated with GHB which suggest increased and/or more dangerous use of the drug.

2. Material and Methods

2.1. Study Design

The Human Tissue Act 2004 gives coroners consent only to conduct analysis relevant to the investigation into the cause of death. The analyses carried out were therefore determined on a case-by-case basis and were limited by the case history provided and analyses requested by the pathologist. Routine analyses included gas chromatographic measurement of ethanol in blood, urine, and/or vitreous humor; a general Gas Chromatography-Mass Spectrometry (GC-MS) screen of blood (or liver, gastric contents, vitreous humor if blood unavailable) for drugs including unknown, licit, and illicit drugs; [20] and a GC-MS screen of urine for illicit drugs. [21] Quantification and/or confirmation of any drugs was carried out according to the UK and Ireland Association of Forensic Toxicologists' guidelines. [22] Approval for the use of data generated from this analysis was granted by South West London Research Ethics Committee 1 (reference 11/LO/0033).

GHB is not detected in blood during routine analysis; specific analysis is required. GHB analysis was historically performed when requested or when ingestion was indicated from the history provided with the case. As we observed an increase in requests for GHB analysis, the drug was incorporated into the GC-MS urine illicit drugs screen in May 2012. This screen is performed on approximately half of all cases received (A total of 709 cases received in 2011, 974 cases in 2012, 1534 cases in 2013, 1624 cases in 2014 and 1792 cases in 2015).

Femoral blood samples from individuals with detectable GHB in their urine were subsequently analysed for GHB. If no urine was received, blood analysis was determined based on the history received with the case.

GHB concentrations in post-mortem blood can vary widely, and there appears to be no definable fatal concentration. It is generally accepted that post-mortem femoral blood concentrations greater than 50 mg/L are indicative of GHB/GBL ingestion rather than endogenous production. [19] A case was therefore considered to be a GHB-associated death if GHB was detected in the post-mortem femoral blood at a concentration greater than 50 mg/L.

2.2 Study Population

The Toxicology Unit, Imperial College London routinely analysed samples from all of the Coroners jurisdictions in London, with the exception of West London. This study took place between 2011 and 2015. The total number of cases analysed during this time was 6633.

Cases in which recreational use of either cocaine or methylenedioxymethylamphetamine (MDMA) was identified were also investigated for comparison. This included all cases where MDMA or cocaine was detected during the general screen (limit of detection 0.05 mg/L) but excluded 'body packers' and people with a history of heroin use who tend to take 'crack' cocaine rather than cocaine recreationally. While cocaine or MDMA may not have been the direct cause of death, they were present in the body at the time of death and were thus defined as associated deaths.

3. Results

3.1. Prevalence

We identified 61 GHB-associated deaths (0.92% of total cases), between 2011 and 2015, with post-mortem femoral blood concentrations ranging from 108 – 2444 mg/L (see figure 1).

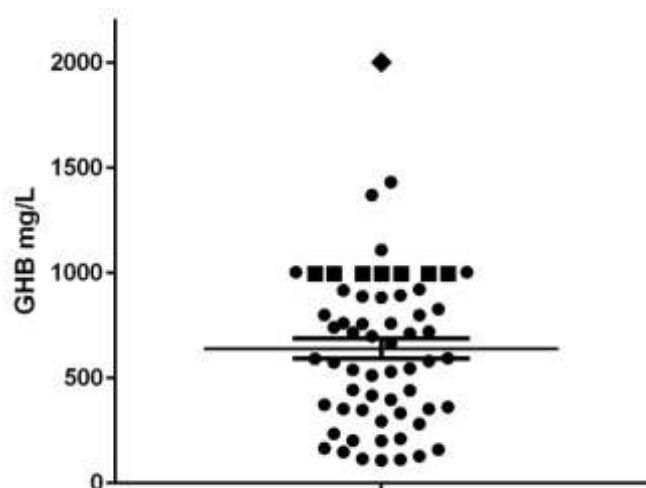


Figure 1. Concentrations of γ -hydroxybutyrate (GHB) in post-mortem femoral blood samples in which it was detected 2011- 2015. Scatterplot of concentrations (mg/L) with mean \pm standard error of the mean shown (n=57). Squares, concentration recorded as >1000 mg/L, and diamond, concentration recorded as >2000 mg/L.

A total of 184 cocaine-associated deaths (2.8% of total cases) and 83 MDMA-associated deaths (1.3% of total cases) were also identified in this time period.

There was a notable increase in the number of GHB-associated deaths, with 29 of these occurring in 2015, representing 1.62% of the total 2015 cases analysed; a 119% increase in the proportion of GHB-associated deaths detected compared to in 2014 (0.74% of total 2014 cases). Over the same time period there was 25% increase in the proportion of cocaine-

associated deaths and a 10% decrease in the proportion of MDMA-associated deaths (see figure 2).

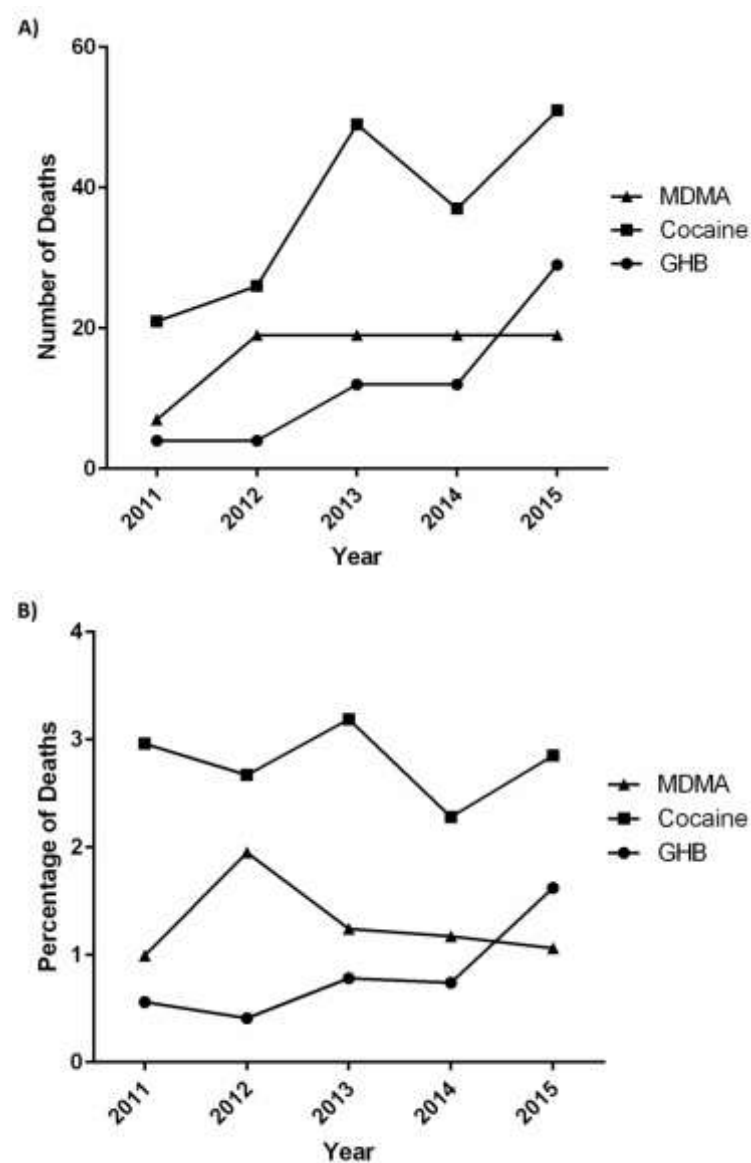


Figure 2. Gamma-hydroxybutyrate (GHB), cocaine and 3,4-methylenedioxymethylamphetamine (MDMA) associated deaths from six of the seven Coroners' jurisdictions in London 2011- 2015. Deaths are shown as (A) number detected by year and (B) percentage of the total cases analysed.

3.2 Demographics

All of the GHB-associated deaths except one were male (98%), with a median age of 37 years (range 22-67 years) and 84% over the age of 30 years. In comparison, recreational cocaine-associated deaths were mostly male (91%), with a median age of 35 years (range 17-79 years), and 73% over the age of 30 years. MDMA-associated deaths were mainly male (88%), with a median age of 31 years (range 16-65 years), and 59% over the age of 30 years.

In 57% of the GHB-associated deaths there was a known history of previous drug use.

Alcohol was detected in 26% of the GHB-associated deaths compared to 29% of MDMA-associated deaths and 48% of cocaine-associated deaths. Other stimulants (cocaine, cathinones, amphetamines, methiopropamine) were detected in 72% of the GHB-associated deaths compared to 58% of MDMA-associated deaths and 14% of cocaine-associated deaths. Notably, mephedrone and/or methylamphetamine, drugs associated with chemsex, were detected in 65% of GHB-associated cases compared to 11% of MDMA-associated deaths and 4% of cocaine-associated deaths.

GHB-associated deaths were identified across all London jurisdictions analysed with the exception of City of London. Over a third of all deaths occurred in Inner North London, 23% in Inner South London, 21% in Inner West London, 10% in East London, 8% in North London and 3% in South London. Figure 3 shows the distribution of GHB-associated deaths per year across the coroners' jurisdictions.

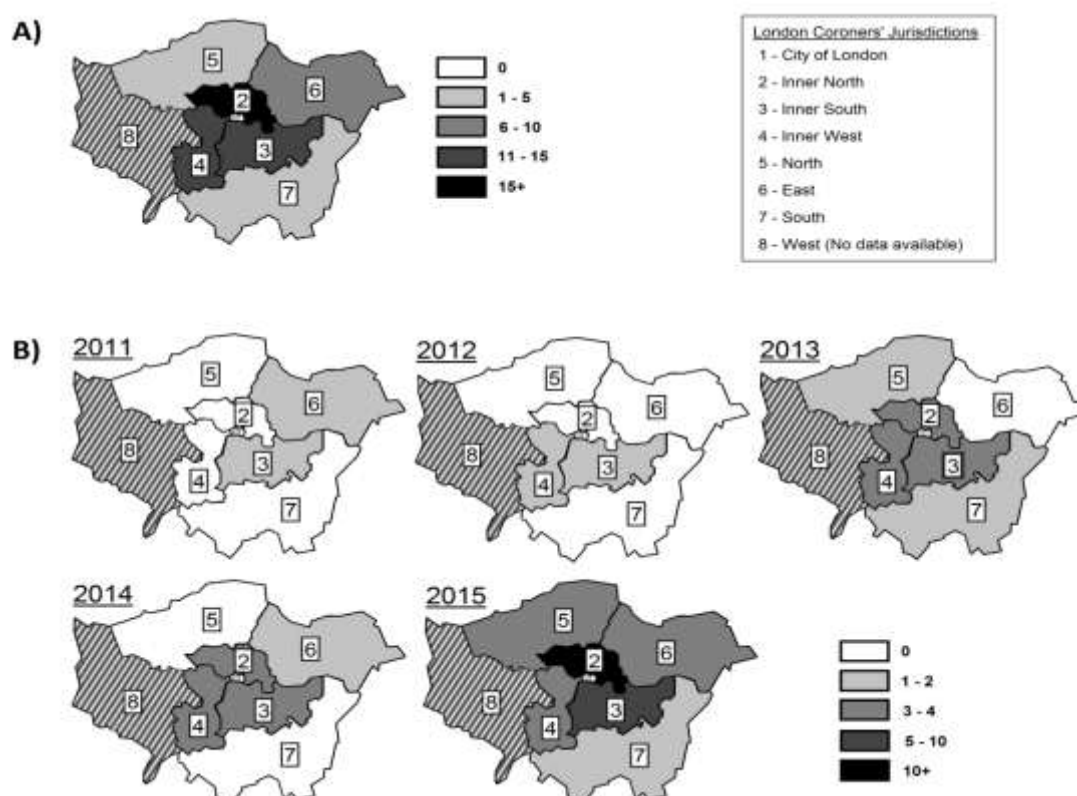


Figure 3. Location of γ -hydroxybutyrate (GHB) associated deaths by Coroners' jurisdiction. GHB-associated deaths are shown as (A) Total number of deaths detected from 2011-2015 and (B) Number of deaths detected per year.

Of the GHB-associated deaths, 49% occurred at the deceased's home or a friend's address, 20% died in hospital, 13% occurred in a hotel room, 11% occurred outside and 5% occurred in a sauna. Chemsex was specifically mentioned in the case history in 25% of the deaths. Of the GHB-associated deaths, 77% occurred after consuming drugs in a private location, compared to 53% of MDMA-associated deaths and 64% of cocaine-associated deaths. However, it should be noted that over half of cocaine-associated deaths involved self-suspension, self-inflicted trauma or road traffic accidents.

The deceased was diagnosed with the human immunodeficiency virus (HIV) in 33% of the GHB related deaths compared to 8% of MDMA-associated deaths and 3% of cocaine-associated deaths.

The demographics of GHB-, MDMA- and cocaine-associated deaths are summarised in Table 1.

Table 1. Comparison of demographics between γ -hydroxybutyrate (GHB)-associated deaths, cocaine-associated deaths and 3,4-methylenedioxymethamphetamine (MDMA)-associated deaths from six of the seven Coroners' jurisdictions in London 2011-2015.

Drug	Male (%)	Median age (Range)	Alcohol (%)	Stimulants (%)	Mephedrone/methylamphetamine (crystal meth) (%)	Diagnosed HIV+ (%)	Drugs taken in private location (%)	History of previous Drug Use (%)
GHB (n=61)	98	37 (22-67)	26	72	67	33	77	57
Cocaine (n=184)	91	35 (17-79)	48	14	4	3	64	41
MDMA (n=83)	88	31 (16-65)	29	58	11	8	53	35

4. Discussion

Our data suggests there has been a substantial rise in the number of GHB-associated deaths in London in 2015.

The trend for increased numbers of GHB-associated deaths is evident whether analysed in absolute numbers or percentage of associated deaths, unlike, for example, the cocaine-associated deaths identified over the same period, for which the spike in absolute associated deaths in 2013 is much attenuated when looking at these figures as a percentage of those tested.

There is little hard data available on the prevalence of GHB use as it is not included in many drugs surveys, but evidence suggests GHB is taken by a small proportion of people compared to other recreational drugs. The UK crime study (2014/15) estimated that 2.3% of adults (aged 16 to 59) have used powder cocaine in the last year and that 1.7% of adults have used ecstasy but did not record GHB use. [23] A survey by the Independent Drug Monitoring Unit in 2000 found that fewer than 3% of interviewees at pop festivals and comparable events had

ever used GHB. [24] The self-reported Global Drug survey found that amongst a selection of regular club goers in the EU last year, 37% had used ecstasy and 22% cocaine, but only 2% had used GHB. [25] These data imply the percentage of users of GHB is likely to be considerably lower than those of the other drugs, which would suggest that GHB-associated deaths are disproportionately high compared to the relative use of the drug.

This observed rise coincides with an increased media awareness of chemsex and echoes findings of increased presentations at drug treatment centres. [26] Recent reports suggest that an increasing number of men are taking part in chemsex, which often involves the use of GHB, highlight the potential harms to health and suggest it should be a public health priority. The use of GHB in MSM is reported to be much higher than for the general population; over 30% of gay males interviewed in the south London boroughs of Lambeth, Southwark and Lewisham in 2013/2014 had used GHB/GBL in their lifetime. [7]

Overall the GHB-associated deaths were concentrated in inner London boroughs. A previous study of UK GHB-associated deaths from 1995-2013 found that nearly half of all GHB-associated deaths in Greater London occurred in one coroners' jurisdiction, Inner London South. [19] This area includes Vauxhall which is well-known for its gay bars and nightclubs, venues traditionally associated with drug use and specifically GHB/GBL use. Whilst this area was the only jurisdiction in which at least one death per year was identified, it was not the most common area where deaths occurred. A third of all deaths occurred in Inner North London; strikingly 12 deaths occurred in this jurisdiction in 2015.

Although only 25% of GHB-associated deaths occurred at what was described as a Chemsex party, the majority of these deaths occurred in private locations rather than in a social environment such as a nightclub. This supports anecdotal evidence that GHB/GBL is more commonly used in private rather than public nightlife settings, [27] and is in accord with the

use of these drugs in Chemsex. Users in private settings are potentially isolated from advice services and more vulnerable to harm.

The relatively high number of GHB-associated deaths who also tested positive for crystal meth and/or mephedrone is also suggestive of involvement in Chemsex. The high percentage of people mixing the drugs with alcohol and stimulants is a major concern. Together with the high levels of GHB detected in some cases, this suggests that users are unaware of some of the basic steps that can be taken to minimise the risks of GHB/GBL overdose, i.e. the importance of measuring and timing GHB doses and not taking it in combination with other substances. [28] More public health awareness is needed to make the participants of chemsex aware of the dangers of the drugs they are taking.

Nearly a third of the deceased were known to have HIV and it is possible others were undiagnosed; 12% of people living with HIV in London are estimated to be undiagnosed. Data for London from 2014 estimates that 9% of MSM (aged 15-44 years) were living with HIV. There is also a long term rise in new diagnoses amongst MSM which account for 63% of all diagnoses, with 1586 men being diagnosed in London in 2014. [29] It has been suggested the rise in HIV could be linked to a rise in risky behaviour associated with chemsex. [27,30,31]

Our findings show that the lower age limit for GHB-associated deaths was higher than for cocaine- or MDMA-associated deaths, and the majority had a history of previous drug use. This corroborates anecdotal reports that GHB is not commonly taken by naïve users. Users have generally experimented with other substances and start taking GHB/GBL at a later age than they do other recreational drugs. [7]

GHB-associated deaths are likely to be under-reported; GHB is often not included in routine analysis, and the short half-life of GHB means that it may not always be detected in post-

mortem samples even if analysis is carried out. Until May 2012 GHB analysis was only carried out in our unit on cases where requested by the pathologist or ingestion was indicated by the case history. Since then, GHB blood analysis has additionally been performed in cases where it was detected in the urine GC-MS drugs of abuse screen. The similar numbers of samples analysed in 2014 and 2015 strongly suggests that the detected doubling of GHB-associated deaths in 2015 reflects a rise in actual deaths. However, since the urine drugs of abuse screen is only performed in approximately half of cases received it is possible that some cases involving GHB/GBL ingestion may not have been identified.

Our data suggests that GHB-associated deaths are increasing in London, and that this is likely at least in part due to increasing use of GHB for chemsex. They also suggest that GHB is associated with a disproportionate number of deaths compared to its incidence of use, and that better education of GHB users regarding the risks of over-dosing, particularly when using GHB in combination with other substances, might reduce these fatalities. GHB should be included in drug use surveys to obtain an indication of the prevalence of GHB use. It would also be helpful to routinely test for GHB in all cases of unexplained sudden death. Further studies are thus urgently required to better understand the extent of GHB use, the prevalence in other major urban areas worldwide, and the full extent of its harmful consequences.

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