

# Lothian drug trends relative to Scotland drug-related deaths

Scottish Drug Forum Conference  
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Scotland leads Europe in Drug-Related deaths.

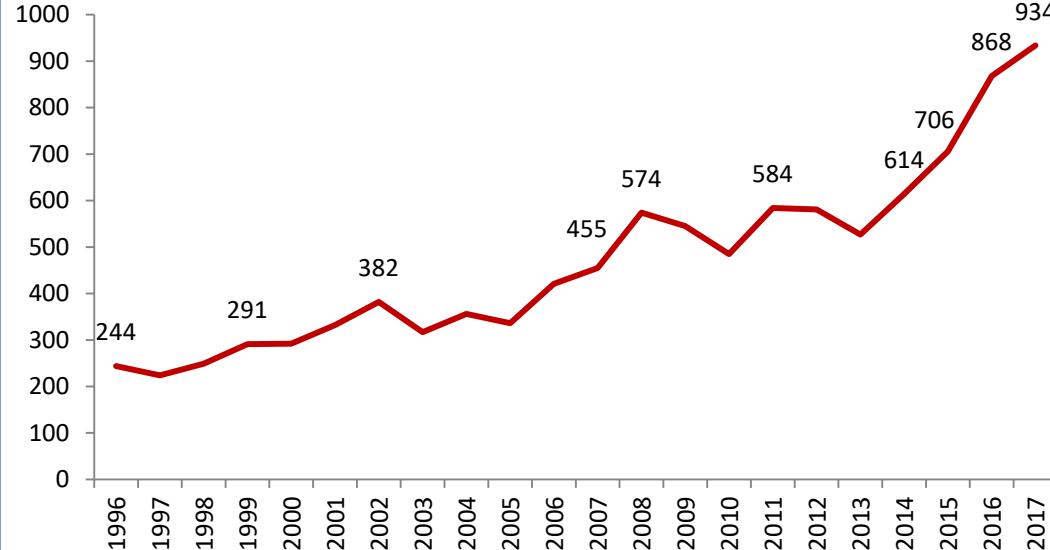
2016 had a 23% increase over 2015.  
2017 had an 8% increase over 2016

There were regional differences in 2016 with:

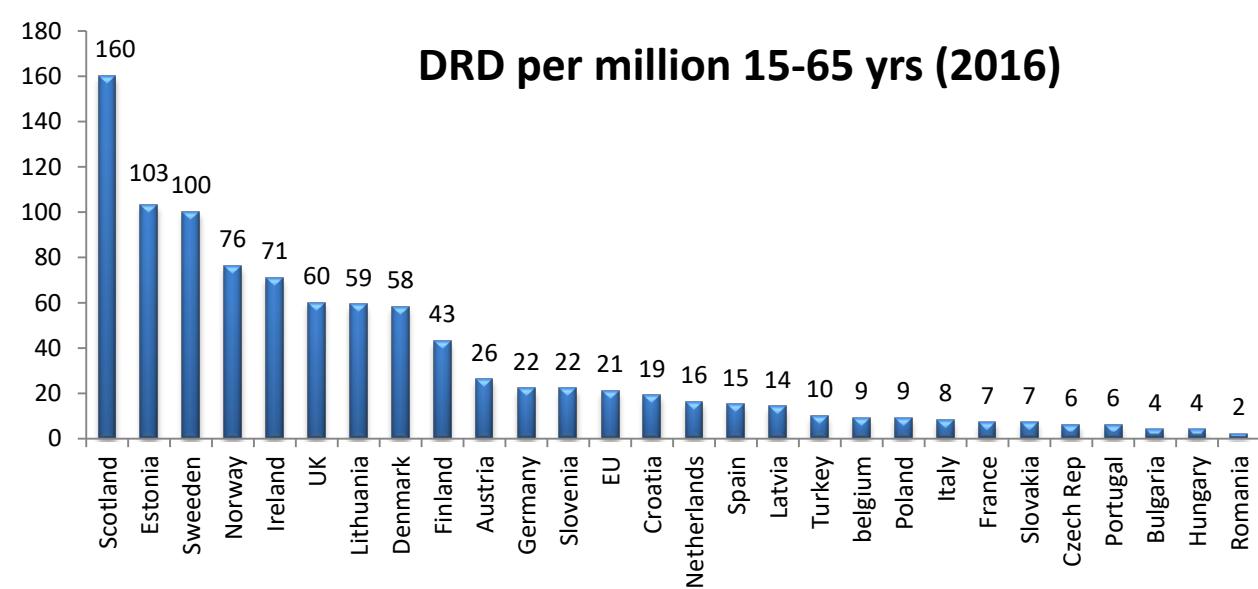
Ayrshire +99%  
Forth Valley +61%  
Lanarkshire +55%  
Lothian +28%  
Glasgow/Clyde +16%

2017:  
Tayside +52%  
Fife +47%  
Grampian +25%  
Glasgow/Clyde +9%  
Lothian +8%

## Drug-related deaths Scotland trend



## DRD per million 15-65 yrs (2016)



Gabapentinoids (opioid boosters) were implicated in 26% of DRDs in 2016.

Gabapentin increased by 51% in 2016 but decreased in 2017.

Pregabalin increased by 69% in 2016 and a further 70% in 2017.

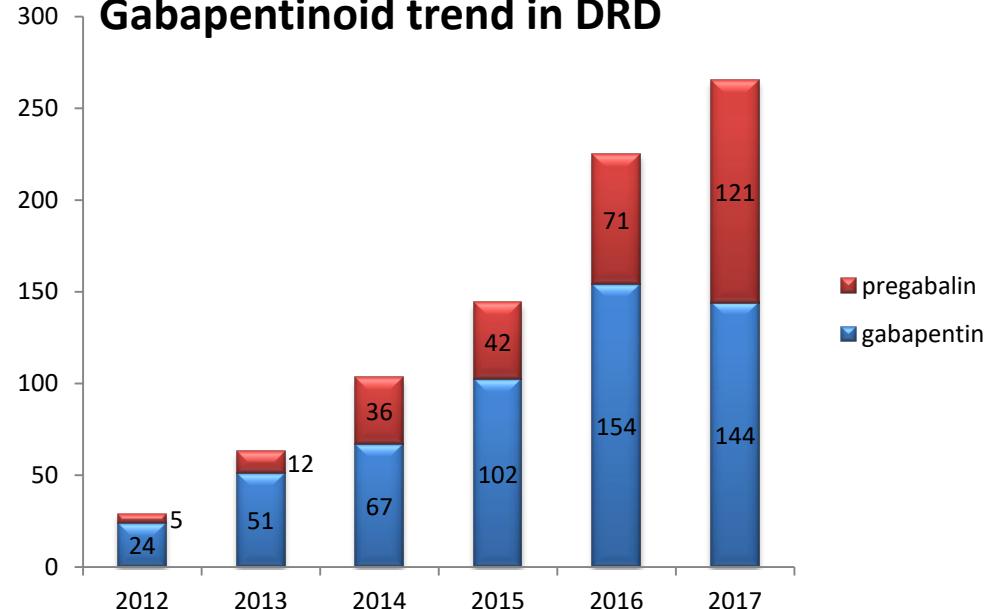
Street benzodiazepines increased from 63 cases in 2015 to 294 in 2016 and 446 in 2017.

Etizolam and Diclazepam were the main findings in 2016.

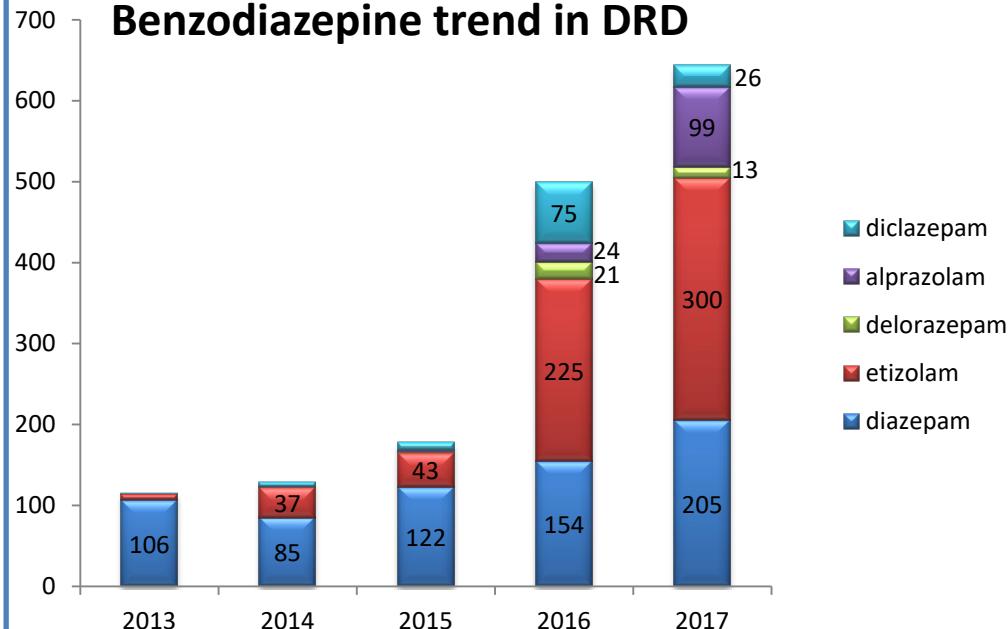
Etizolam and Alprazolam were the main findings in 2017

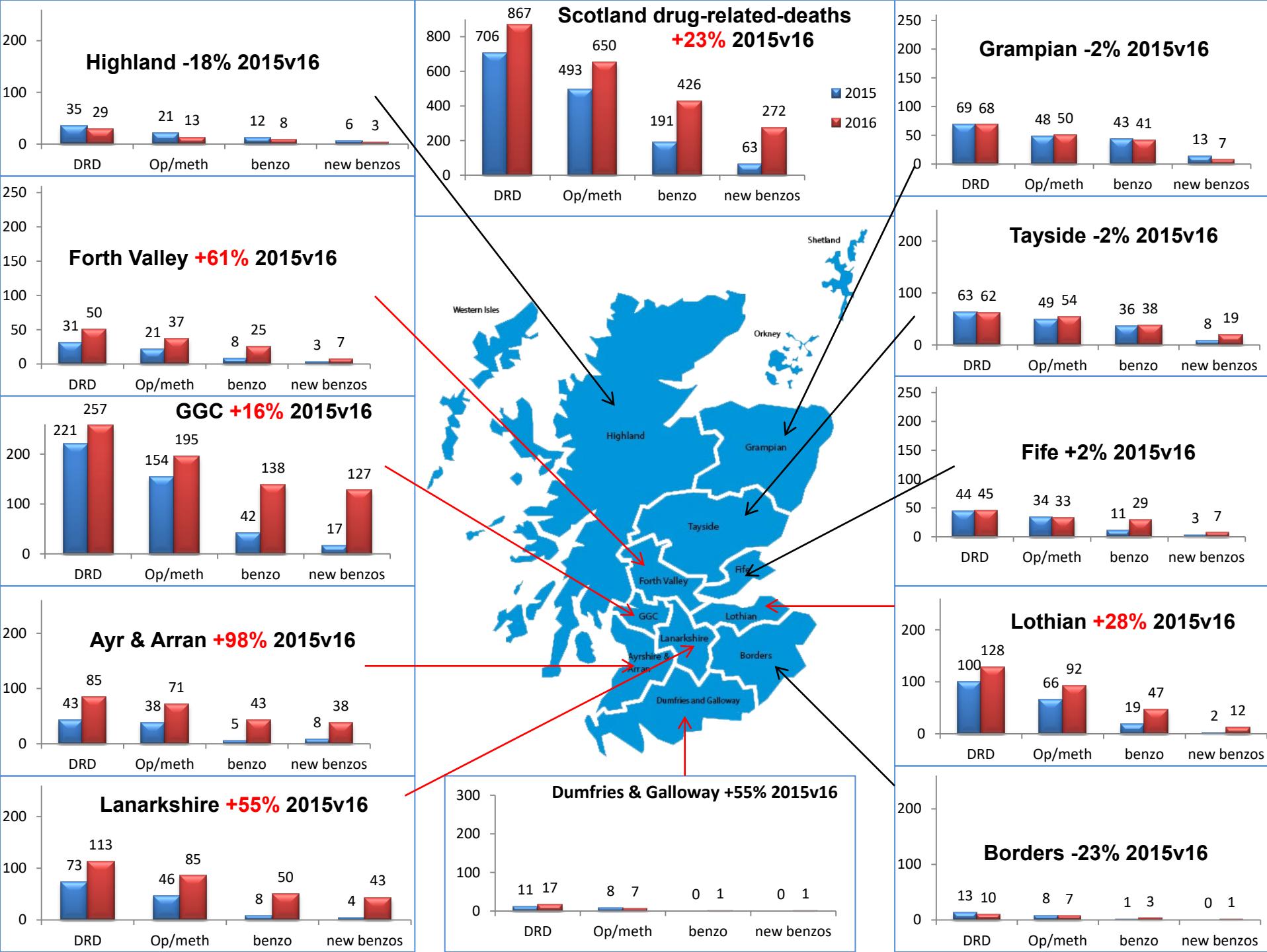
Correlates with increased DRD in Ayrshire, Lanarkshire and Glasgow / Clyde in 2016, and the East of Scotland in 2017.

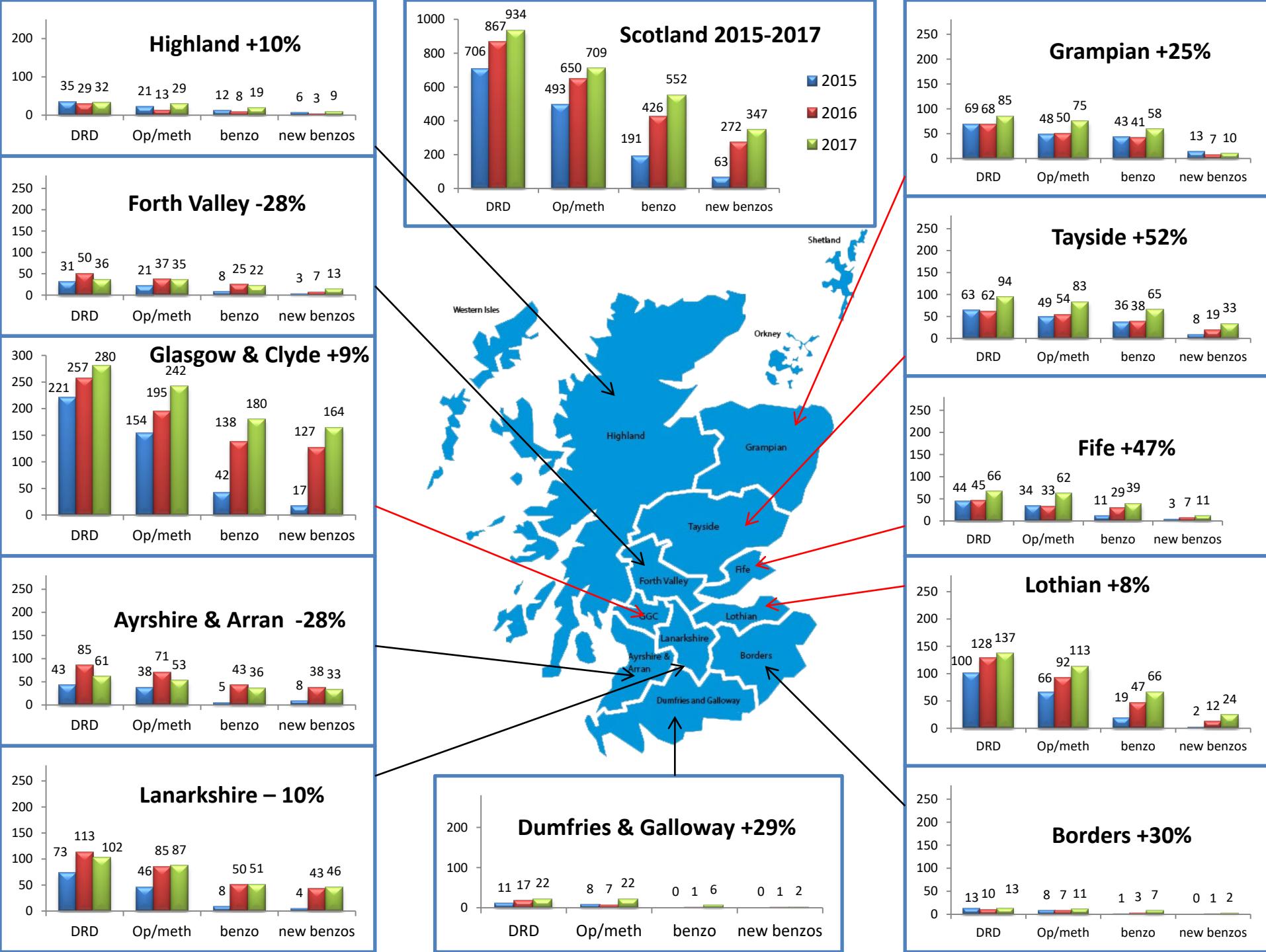
### Gabapentinoid trend in DRD



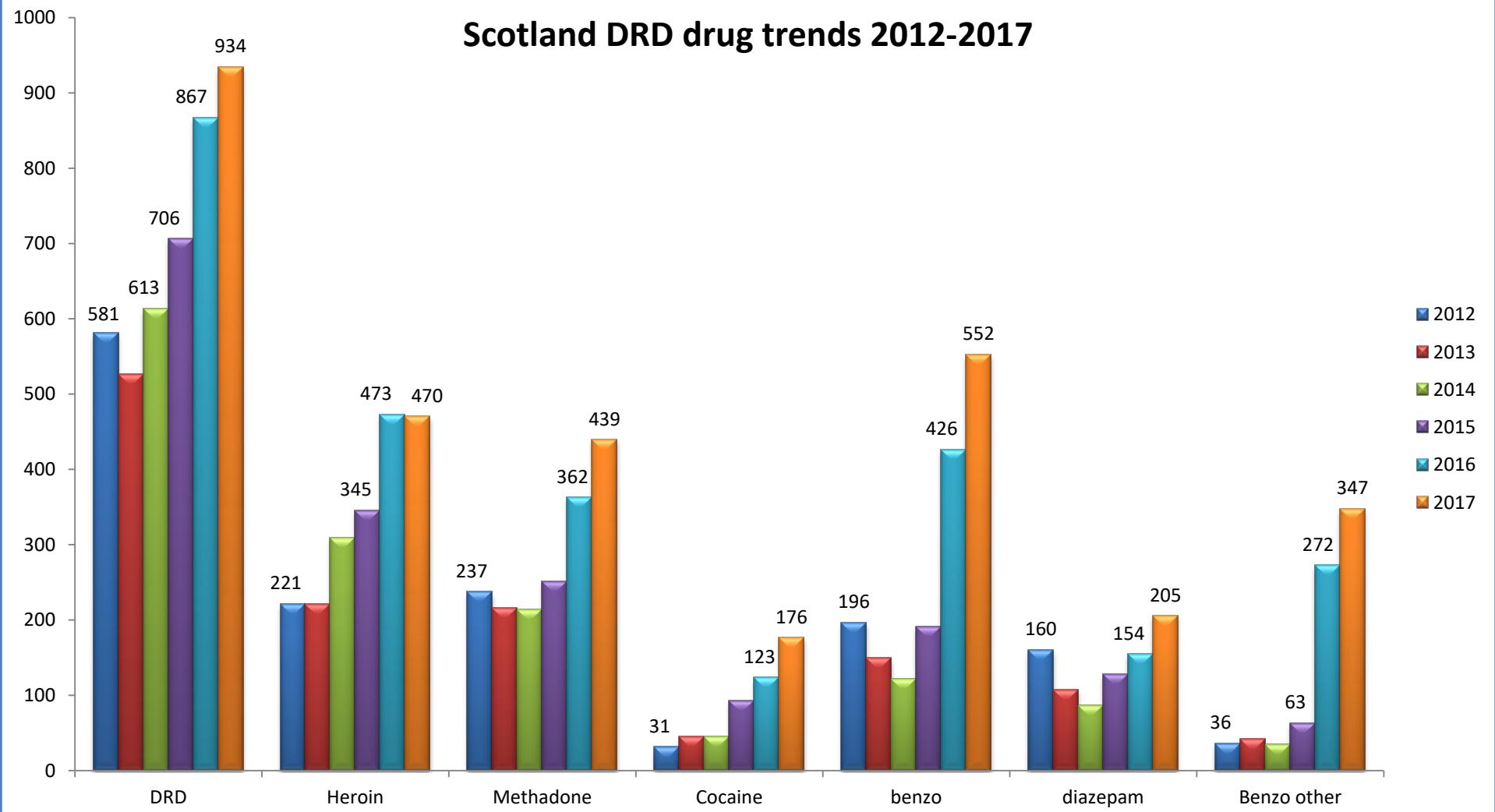
### Benzodiazepine trend in DRD







## Scotland DRD drug trends 2012-2017



# What is killing drug users in Scotland?

- Opiates/methadone are implicated in most DRD, but poly drug use is likely to be a major contributing factor.
- Heroin implicated in 55% of DRD in 2016 falling to 50% in 2017.
- Methadone implicated in 42% of DRD in 2016 increasing to 47% in 2017.
- Gabapentinoids implicated in 26% of DRD in 2016 increasing to 28% in 2017. Switch from gabapentin to more potent pregabalin in 2017.
- Benzodiazepines implicated in 59% of DRD in 2017 with large increase in more potent street benzodiazepines but with regional variations.
- Etizolam and Xanax implicated in 43% of DRD in 2017.
- Trend of increase in cocaine: implicated in 14.2% DRD in 2016 and 18.9% in 2017.

# **Benefits of specific drug analysis by tandem MS v immunoassay**

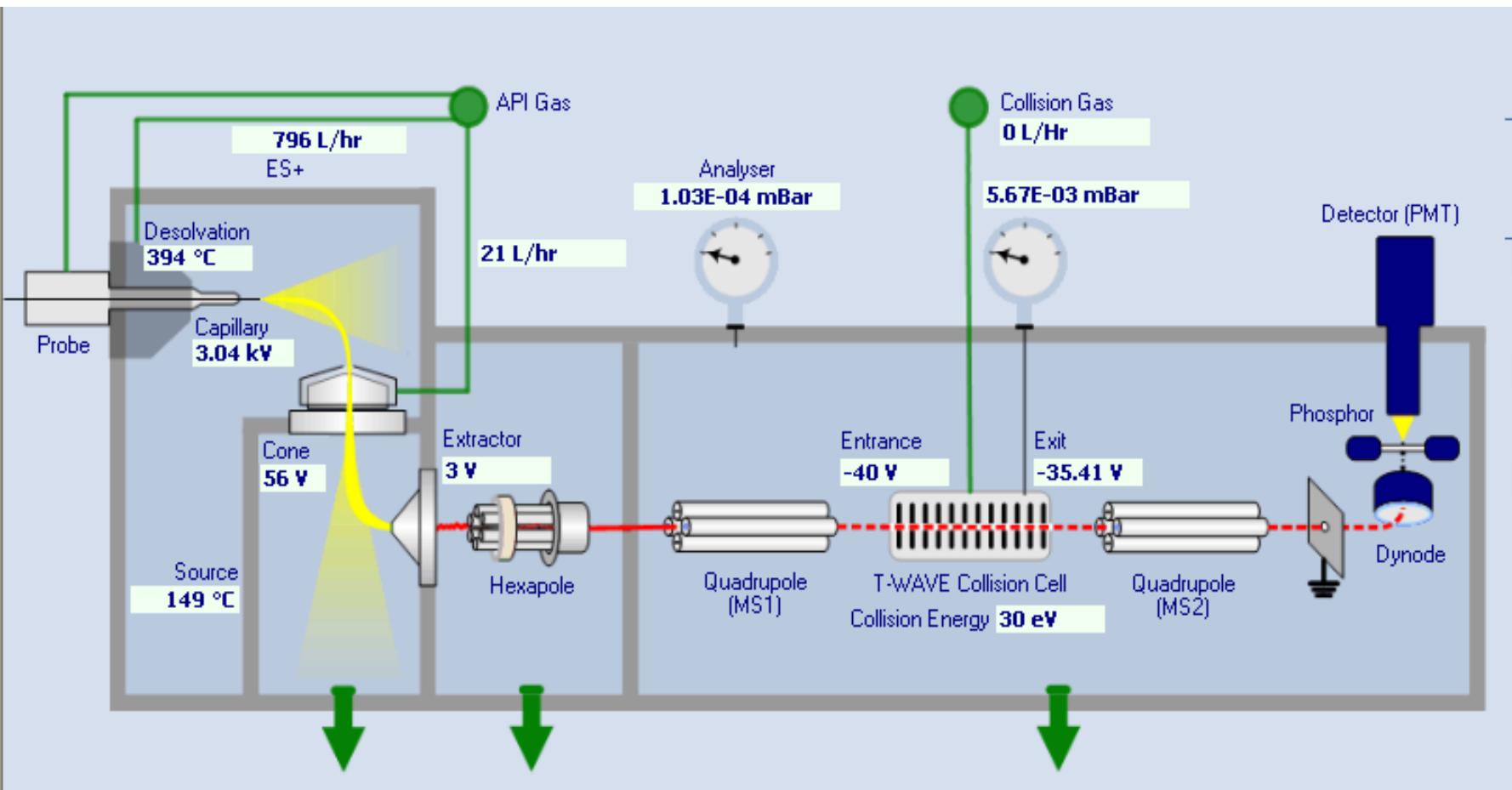
- Cost effective: £12 per sample

**24 drugs analysed to confirmation standards on every sample:**

- Opiates: morphine, codeine, 6MAM, DHC, Oxycodone
- Methadone, buprenorphine, tramadol
- Amphetamine, MDMA, Methamphetamine
- Cocaine + benzoyl ecgonine
- Gabapentin + Pregabalin
- Benzos: Diazepam Nordiazepam temazepam oxazepam nitrazepam
- Street benzo: etizolam, diclazepam, delorazepam, alprazolam.
- No false positive and more sensitive than immunoassay.

# Liquid Chromatography - Tandem Mass Spectrometer Detector





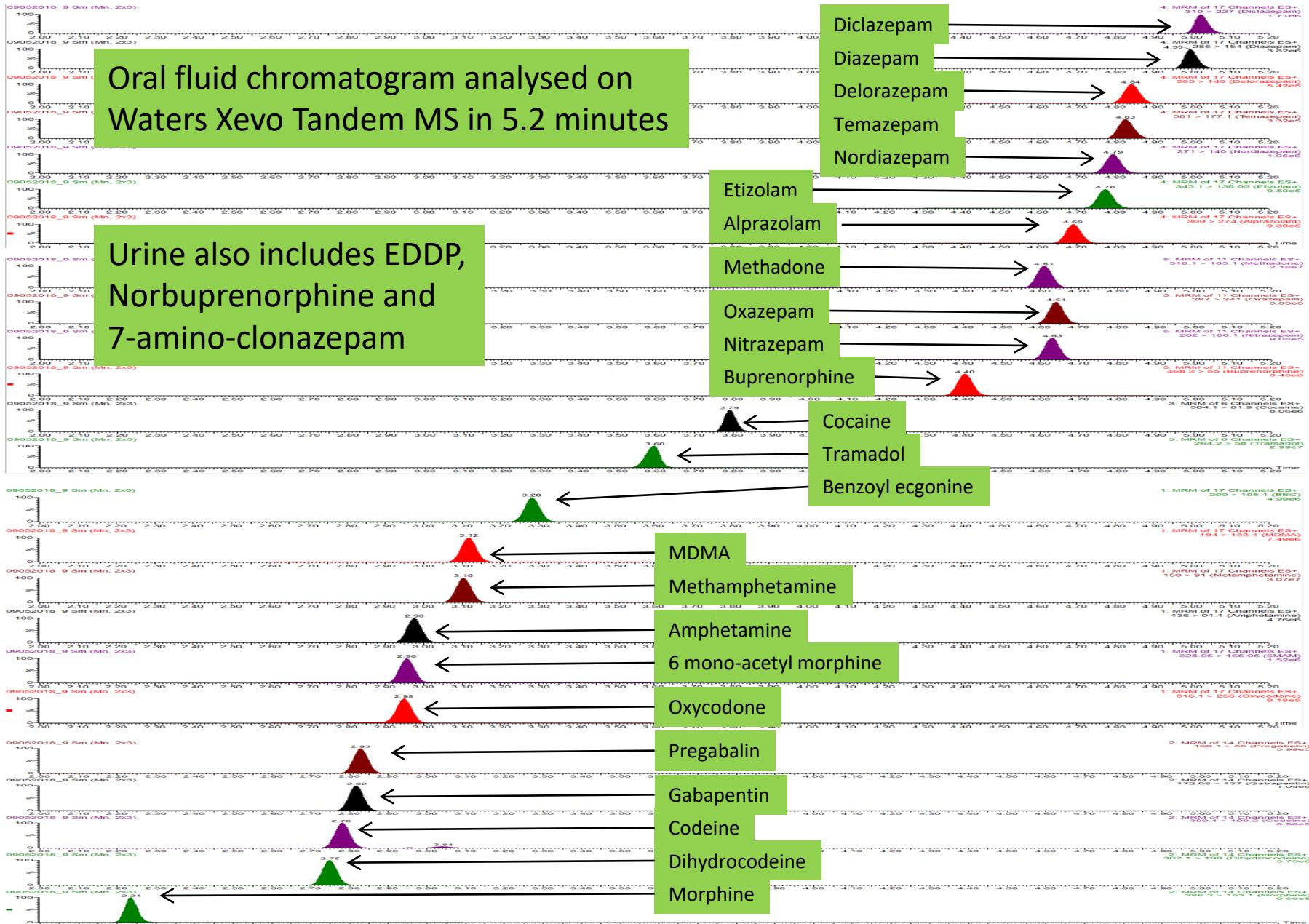
# TANDEM MS Detector

# Lothian have an established, cost effective Tandem MS method for drugs of abuse

- Lothian service covers both urine and oral fluid.
- 50µL sample              6 min. per sample
- ISO 15189 accredited proven method
- >40,000 urine; >40,000 oral fluid to date
- Electronic ordering and reporting
- Cannabis only available in urine by immunoassay screening

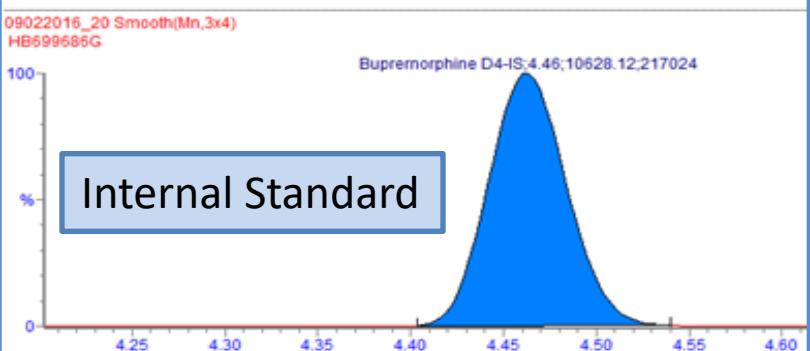
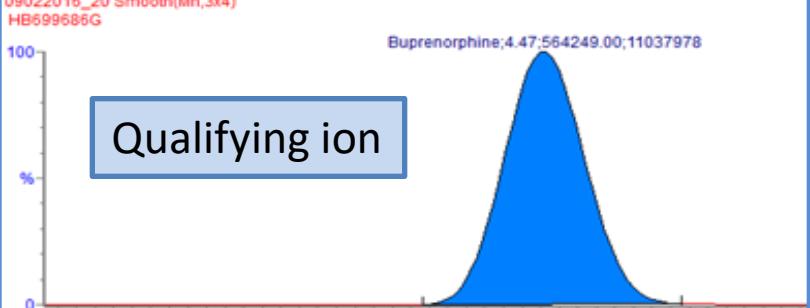
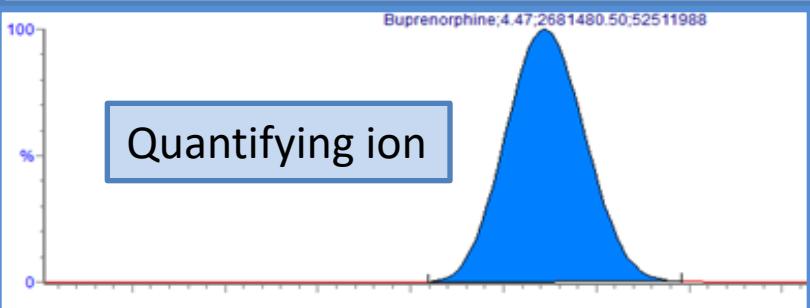


# Chromatogram of 24 drugs



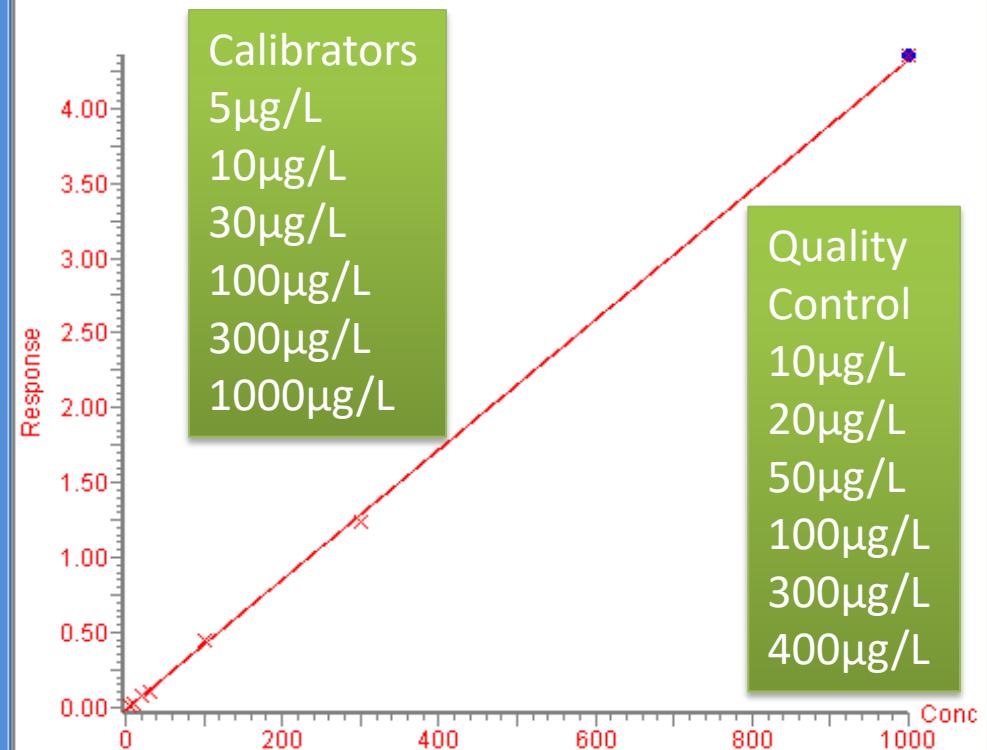
## Drug identification:

- 1) Retention times match Internal Standard
- 2) Peaks are same shape.
- 3) Ratio of quantifying : qualifying match calibrators.



## Calibration curve

Compound name: Nordiazepam  
Correlation coefficient:  $r = 0.999453$ ,  $r^2 = 0.998906$   
Calibration curve:  $0.00434045 * x + -0.0162782$   
Response type: Internal Std ( Ref 45 ), Area \* ( IS Conc. / IS Area )  
Curve type: Linear, Origin: Exclude, Weighting: 1/x, Axis trans: None



## Source of oral fluid drug thresholds

Drug	Threshold oral fluid	Threshold oral fluid	Threshold oral fluid	Threshold oral fluid
DRiving Under Influence of Drugs European Workplace Drug Testing	DRUID	EWDTs screen	EWDTs confirmation	RIE
<b>Morphine</b>	20	40	40	20
<b>Codeine</b>	20	40	40	20
<b>6MAM</b>	20	4	4	10
<b>DHC</b>	20	40	40	20
<b>AMP</b>	50	40	30	30
<b>Met AMP</b>	50	40	30	30
<b>MDMA</b>	50	40	30	30
<b>Cocaine</b>	10	30	8	10
<b>BEC</b>	10	30	8	10
<b>Methadone</b>	20	50	20	20
<b>EDDP</b>		50	20	NA
<b>Diazepam</b>	5	10	10	1
<b>Nordiazepam</b>	1	10	10	1
<b>Temazepam</b>	1	10	10	5
<b>Oxazepam</b>	1	10	10	5
<b>Nitrazepam</b>	1	10	10	5
<b>Clonazepam</b>	1	10	10	NA
<b>Gabapentin/Pregab</b>				40
<b>Tramadol</b>				40
<b>Buprenorphine</b>		5	5	1
<b>Norbuprenorphine</b>		5	5	NA

## Drug thresholds and duration of detectability

Drug	Threshold urine µg/L	Threshold Oral fl µg/L	Duration of detectability
Amphetamine MDMA Methamphetamine	300	30	48 hrs urine 24 hrs oral fluid
Diazepam Nordiazepam Other Benzodiazepines	5 5-20	1 1-5	long-acting 7+ day urine <7 days Oral fluid
Cannabinoids	50	N/A	2-28 days urine – varies with usage
Cocaine metabolite Cocaine	300 N/A	10 10	48 -72 hrs urine 1-5 days oral fluid
Methadone EDDP	300 100	20 N/A	7 days urine <7 days Oral fluid
Opiates 6-MAM	50 50	20 10	48 hrs urine 1-5 days oral fluid
Buprenorphine Norbuprenorphine	N/A 10	1 N/A	<12-48 hrs Oral fluid 4-6 days urine
Gabapentinoids Tramadol	300 300	40 40	48 hrs urine <48 hrs Oral fluid

## **Heroin (Diacetyl Morphine + Acetyl Codeine)**

- metabolised too quickly to detect in urine

**6-MonoAcetyl Morphine 327.4**

**Morphine 285.3**

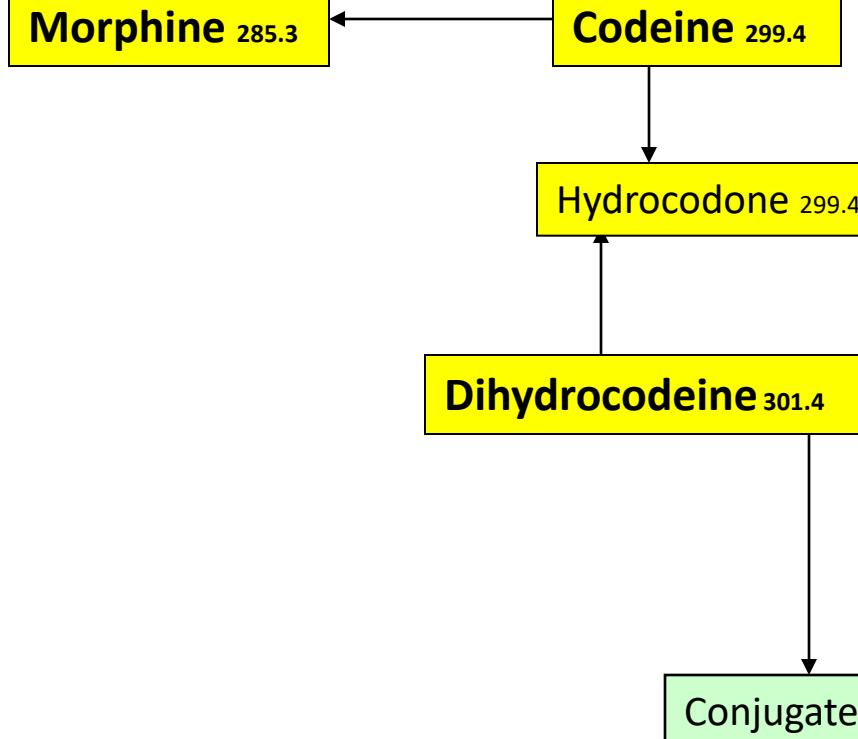
Conjugates

**Codeine 299.4**

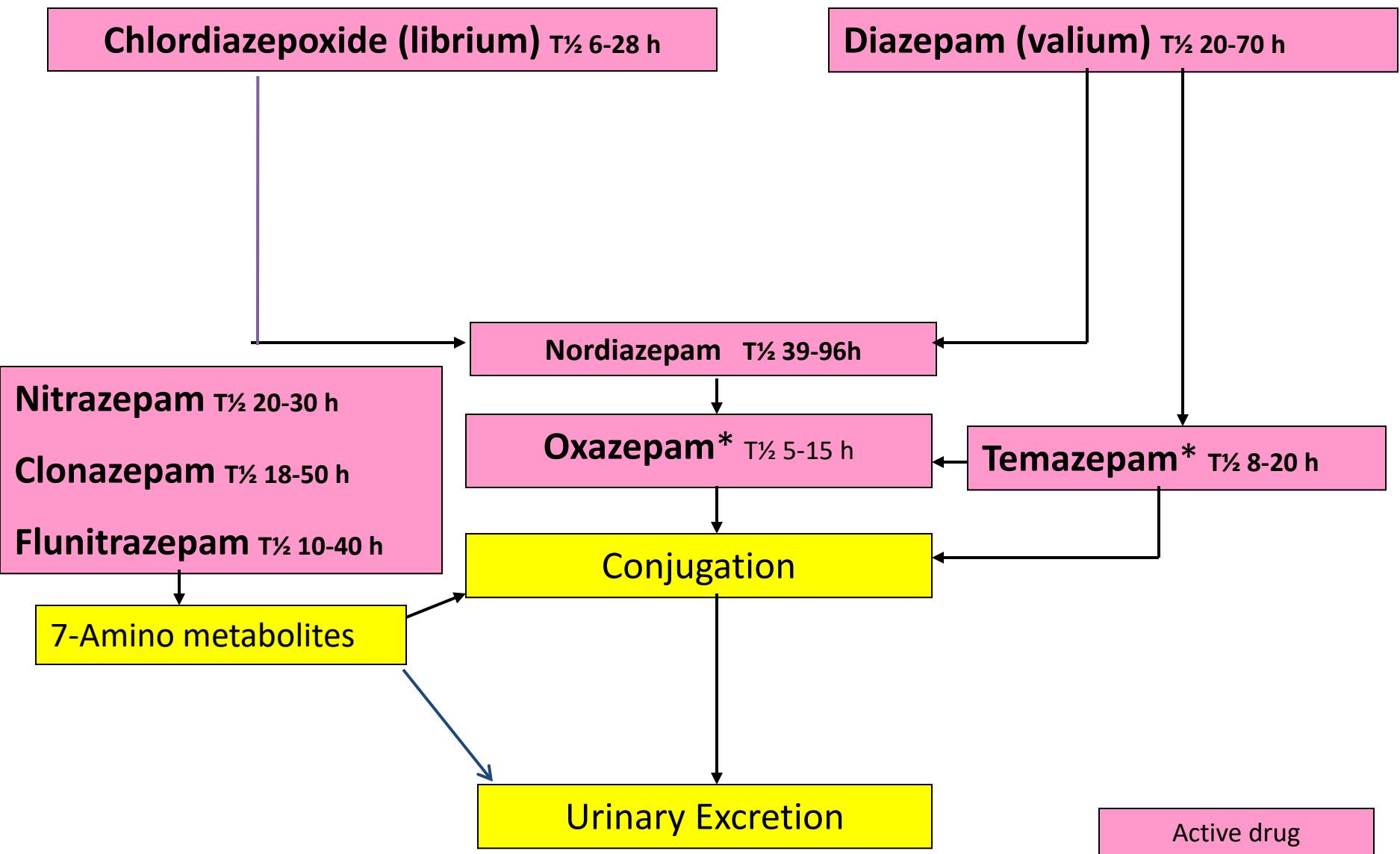
**Hydrocodone 299.4**

**Dihydrocodeine 301.4**

Conjugates

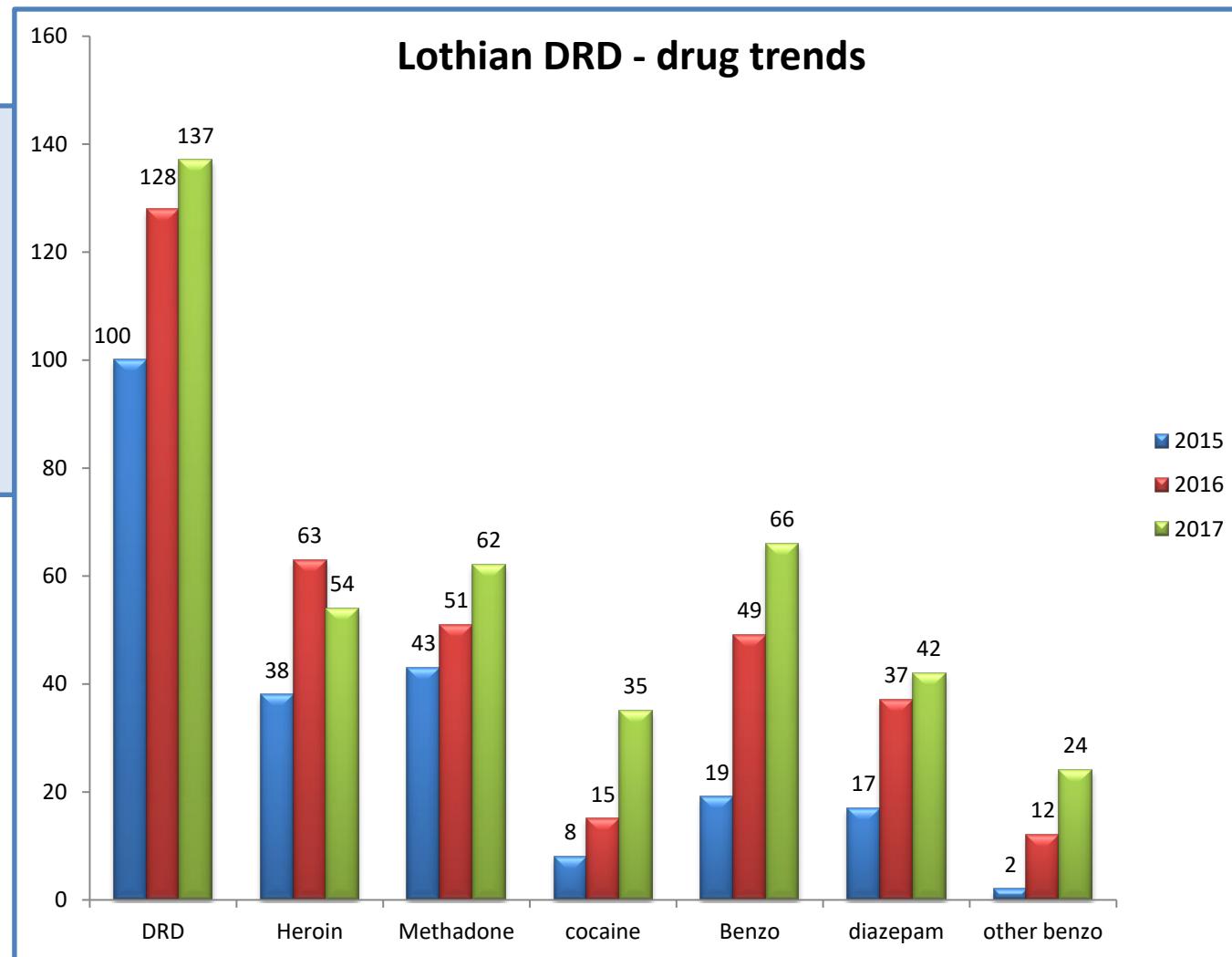


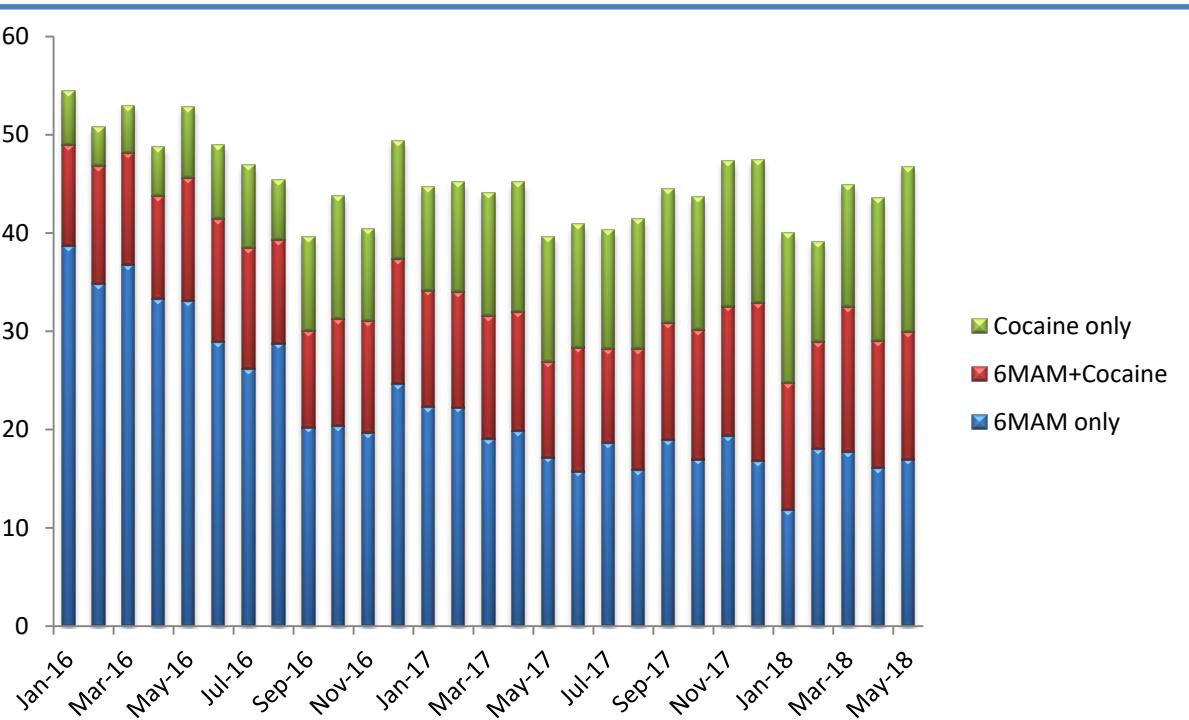
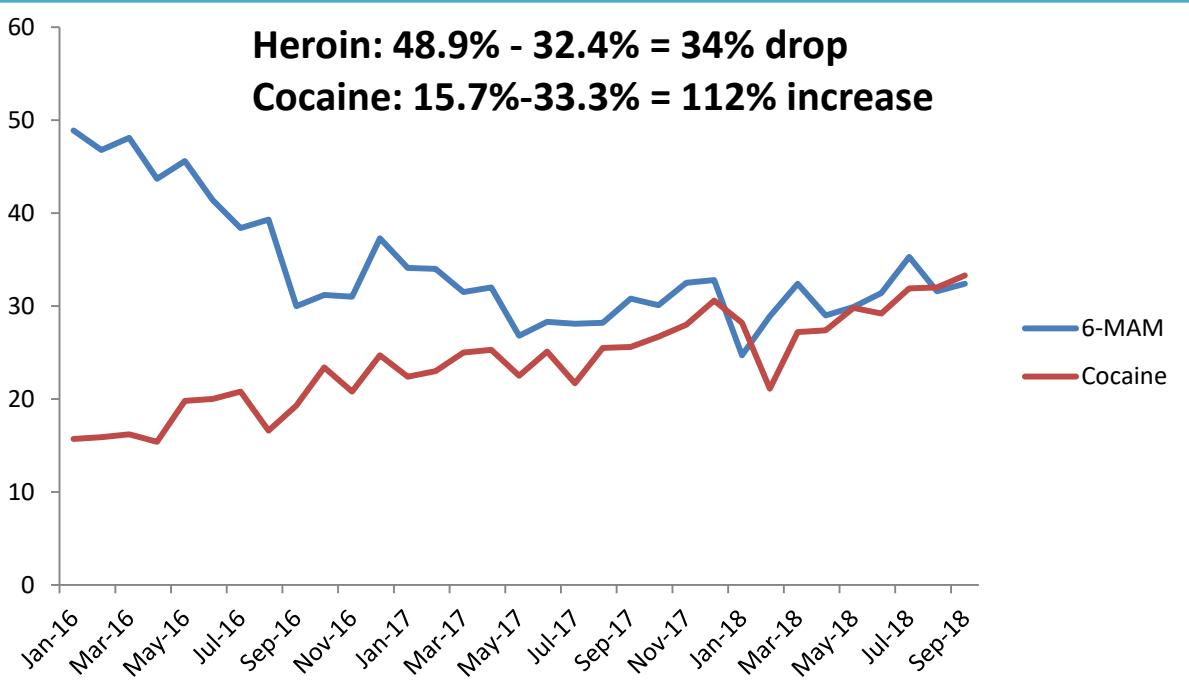
# Benzodiazepine metabolism



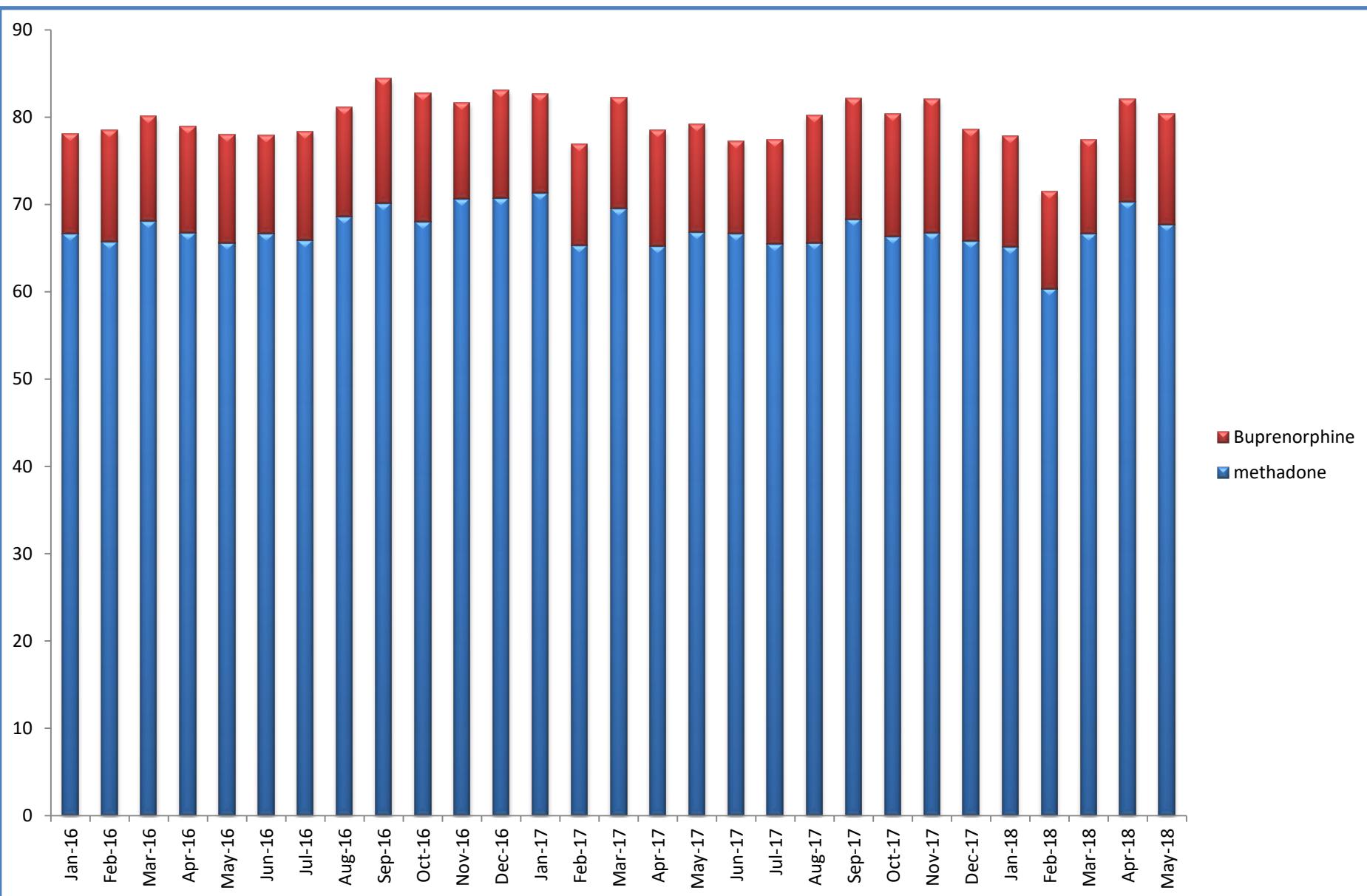
# Drugs implicated in Drug-related deaths in Lothian 2015-2017

- DRD continue to increase
- Heroin peaked in 2016
- Methadone increase
- Cocaine increase
- Benzos increase
- Diazepam increase
- Street benzos increase

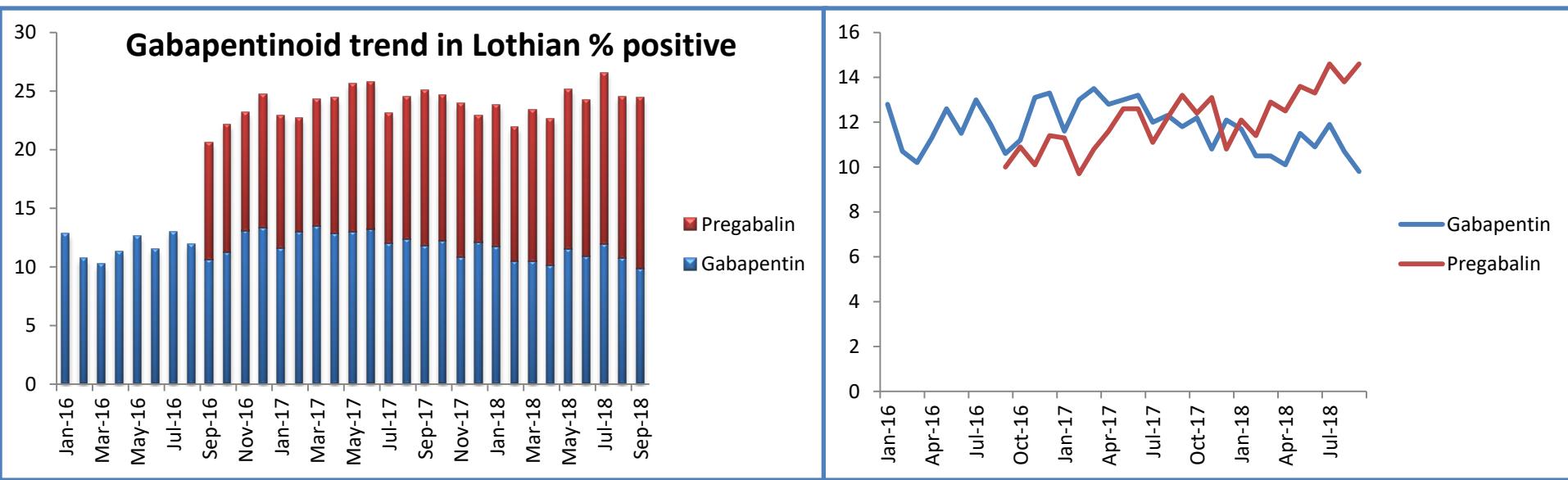




# Methadone and buprenorphine in oral fluid % positive



# Gabapentinoid trend analysis in Lothian Jan 2016 to Sep 2018

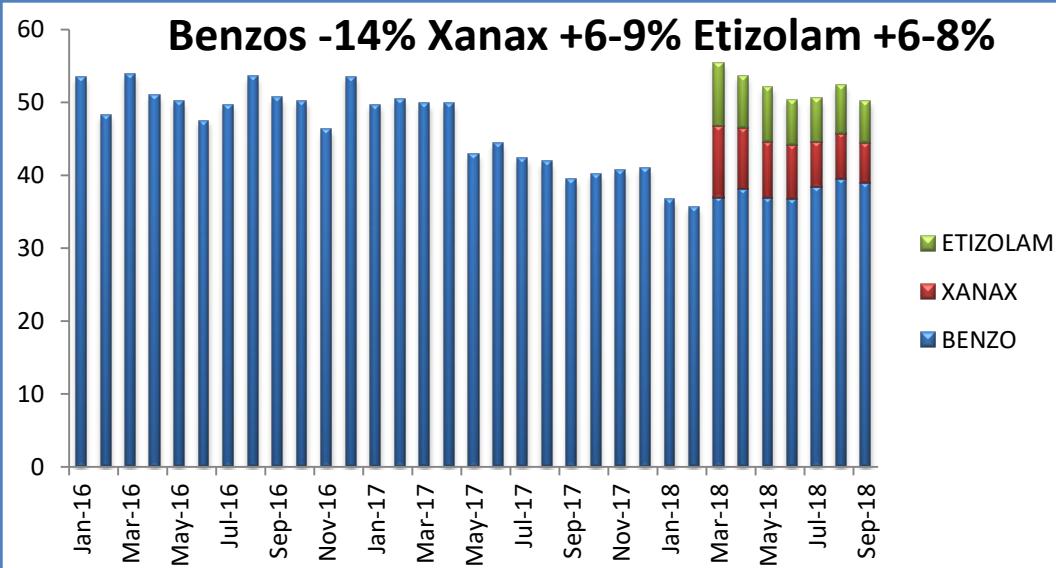


Gabapentin/pregabalin consistently present in 20-25% of all samples – almost always with opioid: 92% of these take methadone or buprenorphine. Pregabalin increasing, gabapentin falling.

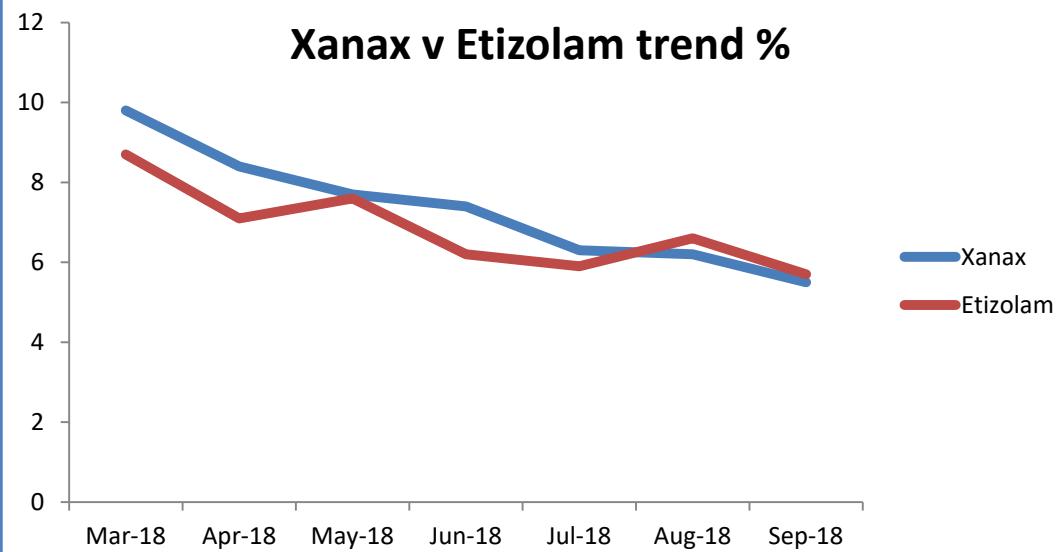
A survey of substance misusers in Lothian in 2012: 22% admitted abusing gabapentinoids to potentiate the high obtained from methadone and to increase the level of intoxication.

Ref: Baird CRW, Fox P, Colvin LA. Gabapentinoid abuse in order to potentiate the effects of methadone: a survey among substance misusers. Eur Addict Res; 2014; 20:115-118

Lothian trend in benzodiazepines:  
Diazepam; nordiazepam; temazepam;  
oxazepam and nitrazepam



Lothian trend in street benzos:  
March - Sept 2018  
Diclazepam 22/10925 = 0.20%  
Delorazepam 28/10925 = 0.26%



Glasgow urine samples for amphetamine confirmations:  
April – Sept 2018

Total	Etizolam	Diclazepam	Delorazepam	Alprazolam	Total
146	51	2	8	0	61
	34.9%	1.40%	5.50%		41.80%

## Novel “street” Benzodiazepines properties

### Etizolam (thienotrizolodiazepine):

- is rapidly absorbed and levels peak in 1-2 hours.
- Half-life is around 3-4 hours with duration of detectability around 48 hrs
- 10 times more potent than diazepam.

### Diclazepam:

- metabolises to delorazepam and then to lorazepam.
- is a longer acting benzo with a half life 42 hours and duration of detectability 7 days.

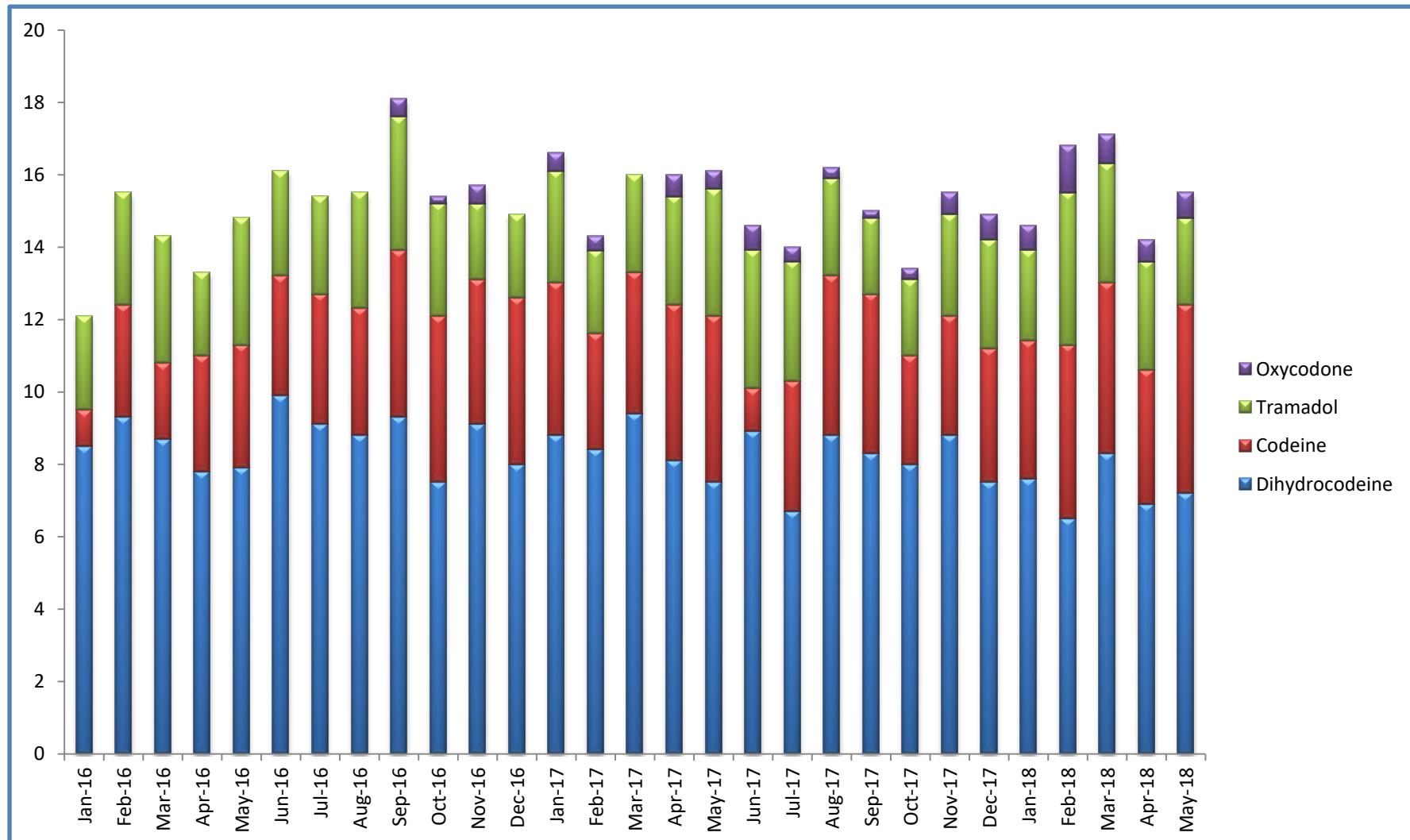
### Delorazepam:

- also an active metabolite of diclazepam, metabolised to lorazepam
- is rapidly absorbed and peak levels within 1-2 hours.
- half life of 80-115 hours and duration of detectability is around 7 days.
- like diclazepam is 10 times more potent than diazepam.

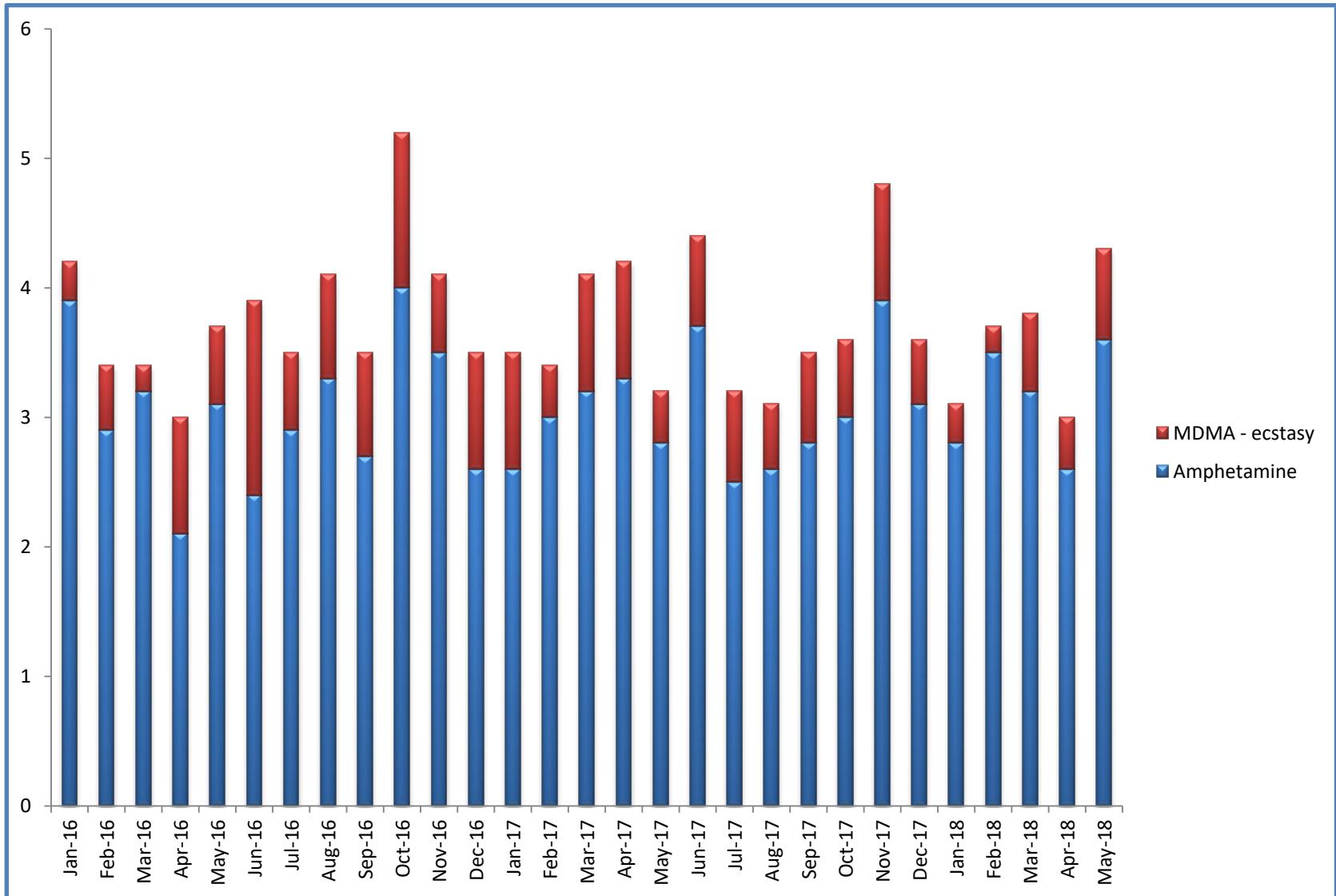
### Alprazolam (Xanax):

- Rarely prescribed in the UK – almost always due to street Xanax.
- Short-acting: rapidly absorbed and levels peak 1-2 hours the dose.
- Half-life is 6-27 hours and duration of detectability is 2-3 days.
- is around 6 times more potent than diazepam.

# Dihydrocodeine / codeine / oxycodone / tramadol in oral fluid % positive



## Amphetamines / MDMA in oral fluid % positive



Methamphetamine – 1 positive in 40,000 samples over 3 years  
Present in 14 samples (>30µg/L) as contaminant of street amphetamine

# Possible candidates for inclusion in drugs of abuse panel

								Not prescribed
	2011	2012	2013	2014	2015	2016	2017	% DRD 2015/16
Total number of DRDs	584	581	527	614	706	868	934	
Drug / substance name								
<b>ANTI-DEPRESSANTS</b>								38%
AMITRIPTYLINE	28	32	47	30	41	45	36	
FLUOXETINE	3	7	5	8	8	12	12	
MIRTAZAPINE	10	18	20	19	35	35	59	
SERTRALINE	3	4	4	8	8	12	12	
<b>ANTI-PSYCHOTICS</b>								50%
OLANZAPINE	5	12	3	3	10	8	9	
QUETIAPINE	6	7	4	6	12	5	11	
<b>BENZODIAZEPINES</b>								
FLUBROMAZEPAM	.	.	.	.	2	2	8	
LORAZEPAM	.	1	1	.	6	11	8	
PHENAZEPAM	13	19	34	6	6	6	30	
<b>OTHER DRUGS</b>								
CITALOPRAM	11	10	7	9	12	7	5	
FENTANYL	4	7	4	4	3	7	15	
PROMETHAZINE	1	2	3	7	5	2	6	
ZOPICLONE	4	9	15	9	20	22	29	82%

# Current service in rest of Scotland

- Other HB offer only urine testing by immunoassay
- Confirmation testing by Gas Chromatography Mass Spectrometry:- slow, labour intensive and expensive – not available for benzos
- Oral fluid by commercial company using immunoassay - unconfirmed drug results.
- Identification of gabapentinoids or street benzodiazepines not available

# Business case for NHS oral fluid service by tandem MS for Scotland

- Outline business case approved by Diagnostic Steering Group – to proceed to full business case
- National v Regional options
- Reduce costs?
- Improve service
- Need for accurate workload
- Clinical Buy-in?

# Predicted drug workload - Scotland

Health Board	Population	Drug users	OF tests predicted	Urine	Total
Scotland	5,348,600	61,500 (100%)	110,000		
Grampian	584,220	4,600 (7%)	8,300	??	
Highland	320,730	2,000 (3%)	3,600	??	
Orkney	21,580	30	50	0	50
Shetland	23,220	340	600	0	600
Tayside	413,800	4,600 (7%)	8,300	??	
Western isles	27,250	110	200	0	200
<b>NORTH</b>	<b>1,390,800 (25%)</b>	<b>11,680 (19%)</b>	<b>21,050 (90/day)</b>		
Borders	114,000	710 (1%)	1,300	800	2,100
Fife	367,250	2,900 (5%)	5,200	2,900	8,100
Lothian	858,120	9,800 (16%)	<b>17,500 (1.8 tests/yr/user)</b>	4,500	22,000
<b>EAST</b>	<b>1,339,370 (25%)</b>	<b>13,410 (22%)</b>	<b>24,000 (100/day)</b>	<b>8,200</b>	<b>32,200</b>
Ayrshire & Arran	371,140	4,100 (7%)	7,400	??	
Dumfries & Galloway	148,900	1,300 (2%)	2,300	??	
Forth Valley	300,400	3,100 (5%)	5,600	0	5,600
Lanarkshire	653,300	6,900 (11%)	12,400	??	
Glasgow & Clyde	1,142,390	20,900 (34%)	37,600	20,000	57,600
<b>WEST</b>	<b>2,616,390 (49%)</b>	<b>36,300 (59%)</b>	<b>65,300 (270/day)</b>		