Appendices

Appendix Figure 1. Flow Diagram

Survey link sent (n= 5244)

Analysed survey (n= 384)
 Excluded from analysis (no question answered) (n= 69)

Full survey completion (n=319)

Participants (n=453)

Opened survey link (n= 934)

Appendix 1 Survey questionnaire

**PART 1 DEMOGRAPHICS
1. You received this survey by: (drop down menu)**

**2. I am**

1. 20-29 years-old
2. 30-39 years-old
3. 40-49 years-old
4. 50-59 years-old
5. 60-69 years-old
6. 70-79 years-old
7. 80 years-old and more

**3. How many** ​**years**​ **have you been in** ​**practice**​**?**

a) 0-5 years
b) 6-10 years
c) 11-15 years
d) 16-20 years
e) 21-25 years
f ) 26-30 years
g) > 30 years

**4. What is your health care related** ​**profession**​**?**

a)  Physician
b)  Medical Fellow
c)  Medical Resident
d)  Pharmacist
e)  Pharmacy Resident
f)  Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**5. What is your primary** ​**specialty**​**?**

a)  Anesthesiology
b)  Emergency medicine
c)  Internal medicine
d)  Critical care
e)  Family medicine
f)  Other (if not on the list or if > 1): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**6. Do you have any added** ​**expertise**​**?**

a)  Clinical pharmacology
b)  Clinical/medical toxicology
c)  Epidemiology
d)  Substance abuse/addiction medicine
e)  Other:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**7. I am ...**

a) Full time practice
b) Part time practice (less than or equal to 2 days a week) c) Retired and not in practice
d) Other:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

If you are actively practicing, please provide your location and the kind of health institute you work for (choose all that apply):

**Location**

Drop down menu for all countries

**Health institute**

a)  Hospital (tertiary center)
b)  Hospital (secondary center)
c)  Private Practice
d)  Rural clinic / Dispensary
e)  Nursing Home
f)  Poison control center
g)  Drug information service
h)  Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**7. How often do you treat ethanol withdrawal syndrome (EWS)?**

a) At least once a day
b) At least once a week
c) At least once a month
d) At least once a year

**8. Which type of benzodiazepine do you use as your most common first choice to treat EWS?**

a) Lorazepam
b) Diazepam
c) Chlordiazepoxide
d) Oxazepam
e) Other:\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**PART 2: DEFINITION OF RESISTANT ETHANOL WITHDRAWAL**

 **9. Which score do you usually use to evaluate EWS severity in your patients?**​ **(with PDF version of the score related)**

a) RASS
b) CIWA-Ar
c) Modified CIWA-Ar
d) Other:\_\_\_\_\_\_\_\_\_\_

**10. According to your clinical experience and, what constitutes YOUR definition of benzodiazepine-resistance in a patient with EWS?**

1) A high score on ​**the evaluation tool I used Specify score**

Specify tool:

2) High benzodiazepine dosage (ex 40 mg in 2h):

Specify dosage:
Specify time interval:

3) Clinical symptoms

Seizures
Persistent tachycardia
Other:

**Other page in the survey**

**11. Order the following definitions from 1 to 3 according to their accuracy in defining “refractory to benzodiazepine” (1 being the most accurate).**

\_\_\_: R.E.B.E.L. MD

**“However, some patients are** ​***refractory to benzodiazepines*, defined as > 10 mg lorazepam equivalents in 1 hour or > 40 mg lorazepam equivalents in 4 hours”**

\_\_\_: NCT01652326

**-  a requirement of either 200 mg of diazepam (or diazepam equivalents) in 4 hrs;**

**-  > 40mg of diazepam (or diazepam equivalents) in 1 hr; or**

**-  an individual dose of 40 mg or greater of intravenous diazepam for control of agitation**

​\_\_\_: «Resistant Alcohol Withdrawal: Does an Unexpectedly Large Sedative Requirement Identify These Patients Early » Hack and al 2006.

**Diazepam intravenous more than 200 mg of cumulative dose at 3 hours combined to abnormal vital signs**

**12. Do you consider all these definitions equivalent?**​ Yes / No

**Appendix 2**

**Collaborating associations:**

Canadian Association of Emergency Physicians (CAEP);

European Association of Poison Centres and Clinical Toxicologists (EAPCCT);

American Academy of Clinical Toxicologists (ACCT);

Asian Pacific Association of Medical Toxicologist (APAMT);

American College of Medical Toxicology (ACMT);

“Association des Pharmaciens d’Établissements de Santé” of Quebec (APES).

**Appendix Table 1. Respondents Characteristics**

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **N** | **%** |
| **Age Group**  |  |
| 20-29 years | 18 | 4.7 |
| 30-39 years | 132 | 34.4 |
| 40-49 years | 127 | 33.1 |
| 50-59 years | 67 | 17.4 |
| 60-69 years | 34 | 8.9 |
| 70-79 years | 6 | 1.6 |
| **Organization** |  |
| Canadian Association of Emergency Physicians (CAEP) | 178 | 46.4 |
| American Academy of Clinical Toxicology (AACT) | 54 | 14.1 |
| Association des Pharmaciens Hospitaliers du Quebec (APES) | 57 | 14.8 |
| American College of Medical Toxicology (ACMT) | 39 | 10.2 |
| European Association of Poison Centres and Clinical Toxicologists (EAPCCT) | 18 | 4.7 |
| Other  | 38 | 9.9 |
| **Health Care Profession** |  |
| Attending physician | 302 | 78.6 |
| Pharmacist | 71 | 18.5 |
| Medical Fellow | 5 | 1.3 |
| Other  | 6 | 1.6 |
| **Job Description** |  |
| Full-time | 344 | 89.6 |
| Part-time | 32 | 8.3 |
| Other  | 8 | 2.1 |
| **Years in Practice** |  |
| 0-5 years | 86 | 22.4 |
| 6-10 years | 66 | 17.2 |
| 11-15 years | 62 | 16.1 |
| 16-20 years | 69 | 18.0 |
| 21-25 years | 21 | 5.5 |
| 26-30 years | 34 | 8.9 |
| >30 years | 46 | 12.0 |
| **Specialty** |  |
| Emergency Medicine | 270 | 70.3 |
| Family Medicine | 36 | 9.4 |
| Internal Medicine | 20 | 5.2 |
| Critical Care | 19 | 5.0 |
| Other  | 39 | 10.2 |
| **Health Institution\*** |  |
| Tertiary Care Centre | 238 | 62.0 |
| Secondary Care Center | 86 | 22.4 |
| Primary Care Center | 72 | 18.2 |
| Poison Control Center | 58 | 15.1 |
| Other  | 35 | 9.1 |
| **Country/Region** |  |
| Canada | 247 | 64.3 |
| United States | 101 | 26.3 |
| Europe | 11 | 3.0 |
| Australia | 8 | 2.1 |
| Asia | 14 | 3.7 |
| Other  | 3 | 0.8 |
| **Frequency of AWS treatment** |  |
| At least once a day | 48 | 12.5 |
| At least once a week | 175 | 45.6 |
| At least once a month | 123 | 32.0 |
| At least once a year | 35 | 9.1 |
| Not applicable (Does not treat EWS) | 3 | 0.8 |

\*Category not mutually exclusive

**Appendix 3**

**Consent Form**

**Principal investigator:** ​Sophie Gosselin, M.D., ​CSPQ, FRCPC(EM), FAACT **Co-investigator coordinating:** ​Hugo Langlois, Pharm. D. Candidate **Co-investigators:** ​Éric Villeneuve, B.Pharm., M.Sc., Pharm. D., BCPS

Robert S. Hoffman, MD, FAACT, FACMT, FRCP Edin, FEAPCCT ​Saif Al-Ghafri, M.D.
Monique J. Cormier, Research Assistant

**Survey: Controversies regarding Ethanol withdrawal management : How should it be defined?**

Benzodiazepine​**s** (BZD) are the treatment of choice in patients with the ethanol withdrawal syndrome ​(EWS) and a modified-CIWA above 7 for many years. However, in some cases, BZD resistance is observed, with one operational definition proposed by Hack and al. in 2006. These authors stated that patients were at higher risk of resistance if a combination of abnormal vital signs and a total dose of diazepam (or equivalent) >200mg over 3 hours was present. Subsequently, articles discussing treatment of BZD resistance in patients with the EWS often have cited this paper to justify their choice of action based on BZD resistance. R.E.B.E.L MD suggested that >10mg of Lorazepam in an hour or > 40mg in four hours would define BZD resistance. Another clinical, defined BZD resistance on three different criteria: 1. >200 mg of diazepam in 4 hours 2. >40mg of diazepam in 1 hour 3. An individual dose of >40 mg of diazepam to control agitation. In regard of the low evidence available on that subject, ​researchers designed this survey to understand your definition of BZD resistance in EWS (if any) and/or that one of your local EWS management guidelines, with the goal of and possibly adjusting the actual definition to the realities of medical practice in 2017.We also included in that survey some questions regarding the place of phenobarbital in EWS resistant to BZD and adjuvant therapy posologies to determine different dosage used by physicians.

**What will you be asked?**
This is a 25 questions survey using an agreement-type questionnaire. The approximate time to complete the survey is less than ten minutes. If you already filled out that survey as a member of another association, please do not continue.

**Participation**
Your participation is completely voluntary. You can decide to stop answering at any time during the survey. Conclusions from the survey could be published and/or presented in a poster conference.

**Anonymity**
All your answers will be anonymous, and you will never be asked to provide an information that could allow your identification.

**Contact and Questions**
All questions and comments regarding this survey may be sent to: Principal investigator supervisor: Dr. Sophie Gosselin.

E-mail: sophie.gosselin@mcgill.ca
Phone number: +1(514) 934-1934 extension 34277

**Statement and Acknowledgement:**

I have read the above information and I am satisfied with my understanding of the study to make an informed decision about my involvement. Completion of the following survey certifies my agreement to participate in this study. I understand that no individual identifiers are to be collected and that only aggregate results will be used in upcoming publications.

􏰍Yes
􏰍No