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Research Article

Overdose in the Intensive Care Unit: Severity and Barriers to Care

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Abstract

Objective: Whilst drug Overdose (OD) is increasingly prevalent in critical care, the burden of care of those patients admitted to the ICU has been minimally described. We aim to explore three domains in this cohort: the historical and demographical features on presentation, their supportive care requirements and duration of admission within the ICU, and the factors surrounding psychiatric assessment.

Design: A retrospective study of data from the Canberra Health Service (CHS) Digital Health Record system (MetaVision) of those admitted with a drug overdose.

Setting: A single-centre study within a tertiary ICU for the Australian Capital Territory (ACT).

Participants: All patients admitted to the ICU with a primary diagnosis of drug overdose from 2018 to the conclusion of 2021.

Main Outcome measures: The Primary outcome measure was ICU length of stay. A composite outcome measure (≥ 2 ICU therapies required) was used to quantify an eventful admission for risk assessment.

Results: 419 admissions occurred during the study period, representing 4.73% of all ICU admissions during this period. The majority were polypharmacy overdoses (63%), with most having a known psychiatric diagnosis (73%). The median ICU length of stay was found to be 37.70 hours (IQR, 20.90-62.35), lower when compared with a median of all admissions (48.8 hours, 25.2-94.4). Most patients required multiple therapies (50.12%); however, a proportion were identified as non-required admissions (20.76%) with overall low illness severity amongst admissions (ANZROD 0.63). Psychiatric review was requested with 68.74% of presentations, but only 72% were reviewed during their ICU stay. Those either living in a regional location (OR 3.30; $p < 0.005$) or transferred from a regional hospital (OR 2.65; $p = <0.005$) were at greater risk of an eventful admission.

Conclusion: Drug overdose accounts for a notable proportion of ICU admissions and is associated with multiple ICU therapies with a high psychiatric workload, despite low mortality and illness severity. Further exploration is required for various at-risk groups.

Introduction

Drug Overdose (OD) is increasingly prevalent within the critical care environment in regards to Emergency Department (ED) presentations [1-3], as well as admissions to intensive care units (ICUs) within Australia [4,5]. This is reflected in similar developed health care systems around the world [6,7]. In Australia, these presentations represent a total of over 150,000 hospital admissions alone in 2020-2021 [8] - a significant strain on our health care system [9]. Furthermore, these presentations are leading to an increasingly significant amount of morbidity and mortality throughout the developed world [10-12]. There are well-established increasing usage trends with both opioid [10] and benzodiazepine OD [13,14], in particular accidental OD [11]. There is also a trend towards increased mortality with subsequent overdoses in these populations. An increasing prevalence of both sedating antipsychotic and stimulant overdose is noted within Australia [15-17], despite an

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unclear effect on morbidity and mortality. In Australia, this is further complicated by the disproportionate number of patients admitted with OD, both from an indigenous background and regional areas [18]. The recent COVID-19 pandemic has also led to periods of isolation and increased psychosocial stress amongst our most vulnerable populations, which increases the risk of overdose and drug-related harm [19].

Despite the awareness of the impact of overdoses within Australian Intensive Care Departments, several knowledge gaps remain. Whilst it is recognised that repeated presentations are burdensome on the critical care system [20], it is unknown what stress these admissions have on the ICU in regard to severity of illness and supportive care requirements. Furthermore, patients may be admitted to the ICU and not require any supportive care therapies, or require psychiatric evaluation before discharge, contributing to logistical burden via increased bed pressure. Attempting to quantify this burden of care, along with other historical and clinical predictors of a more resource-intensive admission, would be beneficial.

We aim to explore these factors that may impact OD patients presenting to a tertiary ICU within Australia from 2018 to the conclusion of 2021. We focused on three main domains: the presenting historical features and demographical data surrounding this population; the supportive care requirements (or lack thereof) needed during their admission; and factors associated with psychiatric assessment, such as psychiatric review compliance. In addition, we also focused on their total length of stay within the ICU and time awaiting ward transfer.

Methods

A retrospective study was performed on the data from The Canberra Hospital (TCH) MetaVision database for all ICU admissions from January 1st, 2018, until December 31st, 2021. This included a review of scanned written documentation before their ICU admission, such as within the ward and ED environments, along with their electronic medical record of their ICU admission. The ACT Health Human Research Ethics Committee (Canberra, ACT) approved this study for low-risk research. Population data was gained from the Australian Bureau of Statistics, along with selected reports from the Australian Institute of Health and Welfare (AIHW) [8,18].

All patients admitted to the TCH ICU over the age of 18 with the primary diagnosis of Drug Overdose were included, irrespective of intentionality. Each instance was reviewed to ensure it confirmed to an actual case of overdose, defined as an intentional or unintentional consumption of a substance/s (either legally obtained or illicit) in toxic amounts that results in harm. This was confirmed by the presence of a history of consumption (either on presentation or later in admission) or via serum and urine drug levels. Patients were excluded from the study if they were admitted for another severe, concomitant condition (e.g., severe trauma due to drug overdose) or were deceased less than 4 hours after ICU admission.

- Those included were analysed according to the following outcomes:Data associated with their initial care of their overdose: This included time until presentation; frequency and location of toxicology advice being sought (via the Toxicology Hotline); admission or transfer location before ICU arrival; prior presentation during study period; monopharmacy or polypharmacy overdose.

- Markers describing length of stay within ICU: Total ICU and hospital length of stay (LoS); LoS within ICU once medically cleared for discharge.

- Psychiatric descriptors and markers: rates of referral for psychiatric assessment (initiated when deemed appropriate for review); compliance of psychiatric review within the ICU; rates of Acute Mental Health Unit (AMHU) admission resulting from OD.

- Demographical characteristics: These included age, comorbidities (divided into nil, 1-3, or > 3), Aboriginal and Torres Strait Islander (ATSI) status, rurality, known mental health history, and presence of polypharmacy

A further component of analysis was the requirement for advanced supportive therapies within the ICU. We stratified patients as having either requiring multiple therapies (both 2-3 and ≥ 4), a single therapy (1), or no therapies (0). Those needing ≥ 2 therapies were further classified as having an eventful admission for further risk analysis. These interventions are outlined in Table 1 and were thought to represent the major reasons for admission to the ICU in this cohort of patients. In particular, this included intubation and the requirement of Invasive Mechanical Ventilation (IMV), the commencement of vasopressors, and more than 1.5L of IVF resuscitation within the ICU. This aligns with similar trials for severity in progress currently within Europe [21], where two interventions were thought to reflect a critically complex and unwell patient.

Data was shown as frequencies, with provided percentages and medians with interquartile ranges (IQRs) as required. To account for groups at significant risk of eventful admission to the ICU (due to requiring multiple therapies), Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were used to express the risk of these previously identified groups. STATA software, version 14 (StataCorp), was used for statistical analysis of the above-described methods.

Results

Of the 8,861 patients admitted to the TCH ICU within the defined study period, a total of 424 instances were identified. On review, 1 was excluded due to having an incorrect primary APACE III diagnosis, with a further 4 excluded for being less than 18 years of age, resulting in a total of 419 instances for further analysis (4.73% of total admissions). This equated to a total of 364 individual patients, as a number of patients were admitted multiple times during the study period. The baseline characteristics and outcomes for this cohort are demonstrated in Table 2. Most patients were female (57.52%) with a median age of 40.38 years (IQR, 28.62-51.75). The majority originated from metropolitan areas (86.16%) and were likely to have a known psychiatric diagnosis documented on presentation

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Table 1: Characteristics of care within the Intensive Care Unit (Per Instance).

Admission Characteristic	Data	Severity Characteristics	Data
Mortality, n (%)	4 (0.95%)	FiO_2 > 40%, n (%)	58 (13.84%)
Severity scoring on Admission (Median)		IMV, n (%)	233 (55.61%)
APACHE III score on admission (IQR)	43 (29-62)	Vasopressors, n (%)	117 (27.92%)
APACHE III Risk of Death (%, IQR)	1.29 (0.52-3.69)	RRT, n (%)	21 (5.01%)
ANZROD score on admission (%, IQR)	0.63 (0.30-1.33)	CPR, n (%)	8 (1.91%)
ICU Therapy Requirement (≥ 1 criteria), n (%)	332 (79.24%)	Antidote, n (%)	95 (22.67%)
1 Therapy required, n (%)	122 (29.12%)	TTM, n (%)	13 (3.10%)
2-3 Therapies required, n (%)	148 (35.32%)	IVF Resus > 1.5L, n (%)	133 (31.74%)
≥4 Therapies required, n (%)	62 (14.80%)	Sedation, n (%)	94 (22.43%)
ICU LoS			
Median admission length, hours, (IQR)	37.20 (20.90-62.35)		
Median LoS once cleared, hours (IQR)	6 (3.00-11.00)		
Median Hospital LoS, hours (IQR)	87.47 (44.26-156.42)		
Psychiatric Input and outcomes			
Referred to Psychiatry, n (%)	288 (68.74%)		
Reviewed if referred, n (%)	207 (71.88%)		
AMHU admissions from ICU, n (%)	42 (10.02%)		
ICU involvement post-discharge			
MET 48hrs of discharge, n (%)	9 (2.15%)		
ICU readmission in 48hrs, n (%)	1 (0.24%)		

APACHE III: Acute Physiology, Age and Chronic Health Evaluation III; ANZORD: Australia New Zealand Risk of Death); ICU: Intensive Care Unit; LoS: Length of Stay; AMHU: Adult Mental Health Unit; MET: Medical Emergency Team;
IMV: Invasive Mechanical Ventilation; RRT: Renal Replacement Therapy; CPR: Cardiopulmonary Resuscitation; TTM: Targeted Temperature Management; IVF: Intravenous Fluid

Table 2: Demographics of Those Presenting with Overdose (Per Individual).

Characteristic	Data
Median age, years (IQR)	40.38 (28.62-51.75)
Gender, n (%)	
Male	155 (44.80%)
Female	190 (54.91%)
Indeterminate	1 (0.29%)
Rurality (ASGS-RA rating), n (%)	
Major Cities of Australia	291 (84.10%)
Inner Regional Australia	36 (10.40%)
Outer Regional Australia	19 (5.49%)
Comorbidities before admission, n (%)	
Nil prior	124 (35.84%)
1-3 prior	149 (43.06%)
>3 prior	73 (21.10%)
ATSI Status, n (%)	
Yes	19 (5.49%)
No	305 (88.15%)
Unknown	22 (6.36%)
Prior Psychiatric Diagnosis on Admission, n (%)	253 (73.12%)
Polypharmacy (≥5 concurrent medications) prior, n (%)	190 (45.35%)

ASGS-RA: Australian Standard Geography Standard – Remoteness Area; ATSI: Aboriginal and Torres Strait Islander

(73.12%). This included mood disorders, personality disorders, and schizophrenia; however, data for each disorder were not obtained. Only a small proportion of admissions were identified as ATSI (5.49%); however, 6.36% were also recorded as having an unknown status. Analysis of the pre- and post-pandemic OD admission rates was performed (using the WHO declaration of a COVID-19 pandemic [22]). This was equivalent when comparing the pre-pandemic (n = 231 with a mean of 8.88 (SD, 3.47)) with post-pandemic admissions (n = 189, mean 8.59 per month (SD = 3.07)). A comparison of means yielded no significant difference between these two periods (p = 0.37).

The characteristics of those presenting with overdose are described in Table 3. The majority were polypharmacy overdoses (63.01%), with the time of consumption unknown in most cases (68.97%). If known, there was generally a median delay of 1.875 (IQR 1.00-3.19) hours until presentation. Toxicology advice was sought in 40.57% of cases at some point throughout their critical care admission, with the majority of discussions occurring within the pre-ICU environment (33.14%). Most admissions were referred through the TCH Emergency department (77.29%), with a proportion arising from regional centres (14.24%), as well as from the inpatient wards (6.44%). There were instances where patients were represented throughout the study period (33.31% of instances), which accounted for a total of 36 patients (10.40%). In particular, 8 patients (2.31% of the total patients involved) presented 4 or more times throughout the study period, accounting for a total of 49 (11.69%) instances of overdose.

The factors impacting care of this cohort were described in Table 1. The observed mortality within the ICU for the study population was 0.95%. This was reflected in the median APACHE III score on admission of 43 (IQR 29-62), as well as low APACHE III Risk of Death (1.29%, 0.51-3.69) and ANZORO scores (0.62%, 0.30-1.33). The majority of patients required multiple therapies (50.12%) – and hence were designated an eventful admission – with 14.8% requiring 4 or more therapies during their ICU admission. A proportion, however, did not meet any predefined ICU-level supports throughout their ICU admission (20.76%). It was unclear from our identified variables why these patients were admitted to the ICU in these cases, as there was not always a documented rationale for admission (i.e., for cardiac monitoring). When comparing individual interventions for severity, the most common ICU interventions were invasive mechanical ventilation (55.61%),

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additional IV fluid resuscitation (31.74%), and vasopressors (27.92%).

Overall, the median duration of ICU admission was 37.20 hours (IQR 20.90-62.35), with a median total hospital length of stay of 87.47 hours (IQR 44.26-156.42). This was shorter than the median ICU length of stay for all admissions during this period (48.8 hours, IQR 25.2-94.4). During this time, psychiatric input was sought in most patients (68.74%), with a proportion of these being reviewed whilst within the ICU (71.88%). Only a small proportion were subsequently admitted to AMHU (10.02%). On further analysis of total ICU admission length, a median of 6 hours was spent within the ICU whilst awaiting transfer to a ward after being cleared of ICU-level support. This was comparable to the ICU length of stay of all ICU admissions during the same period. This patient cohort also did not contribute to a significant burden on the ICU outreach service upon discharge, with minimal Medical Emergency Team (MET) calls or readmissions noted for those included in the study Table 4.

The likelihood of an eventful admission (due to ≥ 2 therapies) was explored in a variety of domains. Several factors were associated with a decreased likelihood, including living in a major metropolitan area (OR 0.30, $p < 0.005$) and being admitted from an inpatient ward within TCH (OR 0.31, $p = 0.0157$). There was also a borderline association in those who represented throughout the study period (OR 0.59, $p = 0.0456$) and those who represented during admission (OR 0.59, $p = 0.0456$). There was no significant association in those with a prior psychiatric diagnosis (OR 0.66, $p = 0.0749$). Of note was a trend towards increased eventful admissions in those from regional and rural areas, such as those residing in these locations (OR 3.30, $p < 0.005$) and being transferred from a regional or rural hospital (OR 2.65, $p < 0.005$). No association was found based on age cohorts or ATSI background.

Table 3: Presentation characteristics for those admitted for Overdose (Per Instance).

Characteristic	Data
Overdose Time	
Known, n (%)	130 (31.03%)
Median time to presentation, hours (IQR)	1.875 (1.00-3.19)
Type of Overdose	
Polypharmacy, n (%)	264 (63.01%)
Monopharmacy, n (%)	155 (36.99%)
Instances of prior overdose with ICU admission in the study period, n (%)	140 (33.31%)
Number of Persons presenting multiple times, n	36
Two (2) Presentations in Total, n (%)	23 (63.89%)
Three (3) Presentations in Total, n (%)	5 (13.89%)
Four or more (≥4) Presentations in Total, n (%)	8 (22.22%)
Toxicology Involvement with Care	
Pre-ICU, n (%)	140 (33.41%)
During ICU, n (%)	74 (17.66%)
Any point throughout admission (Pre +/- Intra ICU), n (%)	170 (40.57%)
Source of Admission to ICU	
Emergency Department, n (%)	228 (77.29%)
Inpatient ward, n (%)	19 (6.44%)
Other Metropolitan Hospital, n (%)	6 (2.03%)
Other Regional Hospital, n (%)	42 (14.24%)

ICU: Intensive Care Unit

Table 4: Odds ratios for Eventful Admission to ICU (Per Instance).

Variable	Odds ratio (95% CI)	*p*
Age group, years		
≤ 44 *vs.* >45	0.88 (0.58-1.30)	0.5108
45-64 *vs.* remainder	1.16 (0.76-1.76)	0.4926
65-84 *vs.* remainder	1.01 (0.45-2.27)	0.9827
> 85 *vs.* ≤84	0.93 (0.06-14.98)	0.9595
Rurality (ASGS-RA rating)		
Major Cities of Australia (1)	0.30 (0.16-0.57)	< 0.005
Inner Regional Australia (2)	2.05 (1.001-4.201)	0.0496
Outer Regional Australia (3)	9 (2.06-30.30)	0.0157
Metropolitan *vs.* Regional (1 *vs.* 2+3)	3.30 (1.75-6.24)	< 0.005
Admission location		
Emergency Department	0.69 (0.43-1.13)	0.1413
Inpatient ward	0.31 (0.12-0.80)	0.0157
Other Metropolitan Hospital	2.36 (0.45-12.30)	0.3084
Other Regional/Rural Hospital	2.65 (1.41-4.98)	< 0.005
Pre-existing Comorbidities		
Nil known prior	1.59 (1.05-2.41)	0.0279
1-3 known prior	0.95 (0.65-1.40)	0.7989
> 3 known prior	0.61 (0.39-0.96)	0.0337
Polypharmacy vs. Monopharmacy overdose	1.35 (0.91-2.01)	0.1399
Prior overdose during study period	0.59 (0.36-0.99)	0.0456
Patient identifies as ATSI	1.48 (0.63-3.50)	0.3726

ASGS-RA: Australian Standard Geography Standard – Remoteness Area; ATSI: Aboriginal and Torres Strait Islander

Discussion

Key findings

As expected, this population comprised a notable proportion of total ICU admissions throughout the study period - a total of 4.73%. This admission rate was greater than a similar evaluation of OD within Australian ICUs (2.04%) in 2013-2018 [4]. The reason behind this increased incidence in this heterogeneous population is likely multifactorial and beyond the scope of this study. This would at the very least indicate a burden on the limited resources of any critical care environment, in particular the ICU. It should be noted that the proportion of OD patients that comprise the ICU population varies significantly globally. This includes a disproportionate increase in admission rates amongst youths in North America [23] and an increase in illicit drug OD in Europe and the US [24-26]. Whilst our mortality within this study period was low, lower than comparable literature (1.7-2.1%), [4,12], this study would not be adequately powered or structured to assess this. This low mortality, however, would be supported by the concurrent low severity of illness of this population (as per the utilised risk-adjustment tools), as supported by low ANZROD (0.63; 95% CI 0.30-1.33) and APACHE III (1.29; 95% CI 0.52-3.69). The ANZROD score, in particular, is best representative of our population in Australia, due to better validation in this patient cohort. The overall length of stay within the ICU for this cohort was not unexpected, and the similarity of waiting times for ward discharge as compared to the normal ICU population was reassuring.

Whilst it was expected that most admissions would arise from the emergency department, several admissions occurred from the ward. Despite being associated with a lower risk of

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eventful ICU admission, this is concerning for iatrogenesis and overall patient safety. Also noted was an increased risk of an eventful admission in those from regional areas within our catchment. This could potentially be because, as a referral centre, we would only receive patients who can only be cared for at a Level 3 ICU, rather than their originating regional hospital. As a result, we would potentially only look after the most unwell regional patients. This does, however, raise the question about whether using a pre-defined cutoff of therapy requirement (i.e.,≥ 2 ICU therapies) could be used to identify those in need of transfer earlier, rather than assessing on a case-by-case basis (as is currently the practice). On the other hand, metropolitan patients were less likely to have an eventful admission. This likely reflects ease of access to tertiary centre assessment and management.

Impact of psychiatric illness and assessment

The psychiatric factors that were assessed were not found to be associated with an eventful admission. This was about either a known prior psychiatric diagnosis, presence or absence of psychiatric input, or in those who represented – and therefore thought to have failed their prior psychiatric evaluation. Only a small number of patients were admitted directly from the ICU to the Acute Mental Health Unit (AMHU); however, this did not reflect patients who may have been admitted after transfer to the ward. The only component of note was that of the patients referred for a psychiatric consult; 81 patients were not reviewed before ICU discharge (28%). This may reflect a number of factors, such as overall psychiatric workflow and resource limitations, and the potential for an inappropriate early referral of patients to the service for review. In addition, a feature of concern was the significant representation rate of participants throughout the study period (33.31%), with those with four or more presentations accounting for a disproportionate amount of admissions. This would appear to highlight a cohort of patients who have failed interventions to prevent recurrent overdoses, and would be worthy of future exploration. In particular, whether this would be due to gaps in psychiatric follow-up post-discharge, or gaps in community care of these individuals.

Implications of eventful admission

An important component of this retrospective analysis was the evaluation of factors that would be associated with an eventful admission (that is, having two or more ICU levels of support). A point of note was that a proportion of patients (20.76%) were admitted without any overt indication for ICU admission (i.e., no eventful admission criteria). Whilst this was not explored explicitly within our study, this may be due to other factors such as clinical concern and gestalt for the patient, toxicology advice for monitoring of both neurological (such as low GCS not requiring intubation, high potential for seizure) and cardiac (such as continuous ECG monitoring, invasive blood pressure monitoring) complications, or external bed pressures leading to incomplete resuscitation of the overdose patient. This may also reflect a lack of other admission locations for patients, requiring purely cardiac or neurological monitoring within our centre.

Strengths and limitations

This retrospective study has utilised a novel and wide-ranging approach to analysing such a heterogeneous population in a tertiary ICU within Australia. We have also had the ability to evaluate some of the common components of management important to the care and discharge of this patient cohort, including prevalence of common ICU-level interventions, psychiatric assessment, overall rates of resource-intensive admissions, and timing of ward transfer. The cutoffs for these ICU therapies and criteria for eventful admission are easily reproducible and clinically relevant to practice. This has also had the ability to highlight some potential at-risk populations for further analysis, such as patients with known polypharmacy, those from regional centres, and representatives.

A number of limitations need to be acknowledged in this study. This was a retrospective, single-centre study, and thus will be limited regarding the applicability of its findings. No information was gathered regarding specific overdose types (such as opioid versus benzodiazepine overdose) and the effect this would have on outcomes, nor accidental versus intentional overdose. A more detailed insight into patients admitted to the ICU but not requiring ICU-level interventions was also not performed, such as exploring admission rates for cardiac monitoring (such as continuous ECG monitoring) and neurology monitoring (such as risk of seizures). Further evaluation surrounding the clinical components of a patient's presentation, such as the prevalence of cardiac dysrhythmias, seizures, level of consciousness, and other toxidromes, was also not performed, and would be beneficial. Data collection on the ATSI population was expected to potentially be a larger contributor to admissions; however, a significant amount was deemed unknown. Thus, it is difficult to ascertain the prevalence of this vulnerable community, and may reflect a lack of awareness about indigenous status. Finally, further exploration of a patient's psychiatric illness would be beneficial. This could include an analysis of specific psychiatric diagnoses presenting with an overdose (such as mood disorder *vs.* personality disorder), the presence of markers suggesting a serious attempt at suicide (such as planning), and whether those presenting had community supports in place to prevent overdose.

Conclusion

This study has demonstrated that the majority of overdose admissions to an Australian ICU will be resource-intensive, with most requiring multiple therapies during their admission, along with psychiatric review. A number of areas have been identified that are associated with a greater risk of an eventful admission, such as the regional location of a patient and transfer from a regional facility. However, a portion of admissions required no ICU-level support, potentially due to monitoring requirements that could not be achieved elsewhere. The presence of psychiatric illness is high amongst this cohort, with some markers of failure of prior treatment (due to representation with OD), and only partial review of these patients within the ICU is notable.

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This study, whilst limited in scale, also offers the scope for reproducibility on a larger scale to identify potential populations at risk of increased morbidity and mortality. Further exploration of the prevalence of various mental health disorders in overdose, along with rates of intentional *vs.* unintentional overdose (i.e., drug misuse) would be beneficial. Further exploration of the severity of various types of overdoses could be performed in the future to further risk-stratify patients on presentation to the ICU. This study also opens avenues for further exploration for at-risk areas, such as earlier identification and retrieval for those presenting in a regional or rural area, repeat overdose presentations, and the impact this may have on the healthcare system. What is clear is that this patient population should not be ignored, especially in a society with evolving risks and stressors for future drug overdose, whether intentional or not.

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