Distinguishing the relevant features of frequent suicide attempters.

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Introduction

The World Health Organization (WHO) estimates that every three seconds there is a suicide attempt (SA), amounting to 10-20 million attempts and one million completed suicides every year (World Health Organization (WHO), 1999). Similar figures have been reported in Europe, where a recent study calculates that SAs are 10 to 40 times more frequent than completed suicides (Platt *et al.*, 1992). Suicide attempters in EU and worldwide are well-known consumers of psychiatric resources (Rissmiller *et al.*, 1994). The estimated cost for SAs that resulted in hospitalization is $9,127 for medical costs and $11,146 for work-loss cost (American Foundation for Suicide Prevention, 2009). Most importantly, self-harm behaviours (Appleby et al., 1999a; Cooper et al., 2005) and SAs (Christiansen & Jensen, 2007; Isometsa & Lonnqvist, 1998) have been consistently shown to be the best predictors of subsequent SAs and with increased risk of a fatal outcome (Beck *et al.*, 1975). A systematic review showed that the estimated rates of nonfatal repetition among suicide attempters were about 16% at 1 year, 23% at 4+ years (Owens *et al.*, 2002) and 40% after 3 to 8 years of follow up (Brauns & Berzewski, 1988; Johnsson Fridell et al., 1996; Rygnestad, 1988).

Risk reduction and preventive strategies usually target high-risk individuals in the aftermath of a SA. Despite the recurrence of SAs and the special care required by suicide attempters, to date there are no universally accepted guidelines for managing suicide attempters to prevent further attempts after discharge (Baca-Garcia et al., 2004; Baca-Garcia et al., 2006; Mann et al., 2005). This may be in part because there is no clear understanding of the hierarchy or relationship between a variety of factors that predict repeat attempts. These include sociodemographic factors such as age (Christiansen & Jensen, 2007; Corcoran et al., 2004), unemployment (Tejedor *et al.*, 1999), not being married (Kreitman & Foster, 1991) or low educational level

(Christiansen & Jensen, 2007) which have been associated with repetition of suicidal behaviour (Osvath *et al.*, 2003). Clinical factors include lethality of the index attempt (Gibb *et al.*, 2005), poor physical health (Colman *et al.*, 2004), and mental illness or psychiatric comorbidity, which has been noted to be a risk factor for repetition in studies on parasuicides (Colman et al., 2004; Osvath et al., 2003), non-fatal suicidal behaviours (Kapur *et al.*, 2006) and SAs among inpatients (Spiessl *et al.*, 2002).

At the same time, risk evaluation is frequently inaccurate (Appleby *et al.*, 1999b) because available predictive models are imprecise, hampering our ability to identify potential re-attempters (Bille-Brahe et al., 1997; Oquendo et al., 2006). To date, most studies addressing the prediction of suicide re-attempts have used no measures of predictive accuracy (Bille-Brahe et al., 1997; Cedereke & Ojehagen, 2005; Colman et al., 2004; Morton, 1993; Sidley et al., 1999), limiting the clinical utility of their findings (Galfalvy *et al.*, 2008). However, when the precision of the prediction is measured, the results are disappointing, finding roughly 39% sensitivity and 86% specificity in a study of sociodemographic risk factors of parasuicide (Kreitman & Foster, 1991), 28% sensitivity and 99% specificity in a sample of children after deliberate self-harm (Chitsabesan *et al.*, 2003), or 85-94% sensitivity and 26-38% specificity when assessing self-harm in emergency settings (Cooper *et al.*, 2007). Thus, the weak predictive value of risk factors leads to large numbers of false-positives or false-negatives (Maris, 2002).

Suicide attempters are widely recognized as a high-risk group. Accurate identification of high-risk suicide attempters is crucial to the development and implementation of targeted interventions to be provided according to the potential for re-attempt and the available resources (Carter *et al.*, 2005). In this study, we used a variable selection technique, Causal Discovery (CD), which is useful for both interpretation and prediction of relationships between variables (Pearl, 2000; Spirtes et

al., 2000). CD searches algorithms that match the data displayed in probabilistic graphical models (Bayesian networks) to investigate the structure of causal processes. Using this technique, we aimed to build a pathway of frequent SAs based on a large, well-characterized sample. Such a model could help to develop efficient triage of patients to graded levels of follow up care following discharge.

Method

Subjects and Experimental Design

Suicide attempters (n = 1,349) over 18 years of age were recruited from consecutive admissions to the Emergency Department (ED) of two university hospitals – Ramon y Cajal University Hospital in Madrid and Lapeyronie University Hospital in Montpellier– between 1994 and 2006. The two hospitals are part of the Spanish and French National Health Systems respectively and provide medical coverage for all emergencies in a catchment area covering a population around 500,000 people in Madrid and 400,000 people in Montpellier. After complete description of the study to the subjects, written informed consent was obtained. The study was approved by the local research ethics committees in Madrid (Spain) and Montpellier (France) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Protocols and assessment procedures in both centres are based on the Columbia Suicide History Form (Mann *et al.*, 1999). Though some differences might be expected in the sampling procedure, key demographics of both samples are similar (Table 1) and regular meetings between the centres were held to enhance inter-rater reliability.

SAs were identified in the charts by experienced psychiatrists according to the definition adopted by the National Institute of Mental Health: "self-inflicted, potentially

injurious behaviour with a nonfatal outcome for which there is evidence (either explicit or implicit) of intent to die" (O'Carroll *et al.*, 1996). During the study period, the subject's visit to the ED for management of a SA was labelled the "Index Episode." Subjects were assessed close to the time of discharge after a significant improvement of the suicidal crisis, in most cases at least 24 hours after the attempt. Participants with a history of at least 3 attempts at index evaluation (including the index attempt) were considered recurrent or frequent attempters in agreement with the Beck Scale for Suicide Ideation (BSSI), which identifies the presence of at least three attempts as a marker of repetitive suicidal behaviour (Beck *et al.*, 1991).

Assessment instruments

Trained psychiatrists or psychologists interviewed all patients. The French or Spanish version of the Diagnostic Interview for Genetics Studies (DIGS) or the Mini International Neuropsychiatric Interview (MINI) (Nurnberger & Blehar, 1994; Preisig et al., 1999; Sheehan et al., 1998) was used to obtain Axis I DSM-IV diagnoses. Suicide attempters were classified as violent or non-violent according to Asberg et al.'s (Asberg *et al.*, 1976) criteria: Hanging, use of firearms or knives, throwing oneself under a train and jumping from heights were all considered to be violent attempts; drug overdose and superficial wrist cutting were considered to be non-violent SA. Age at first SA was defined as the age at which the patient first made a SA. Age at first SA was assessed by the interviewer and then blindly rated by an independent psychiatrist according to medical case notes and interviews. Lifetime diagnosis was determined using a best-estimate procedure. The psychiatrist in charge of the patient's care assigned the diagnosis based on DIGS or MINI interviews, medical records and, when available, information from relatives.

The Suicide Intent Scale (SIS) (Beck *et al.*, 1974) is a semi-structured 15-item rating scale yielding a global score that indicates the severity of suicidal intent. The Risk-Rescue Rating Scale (Weissman & Worden, 1974) is a 10-item interviewer administered scale designed to assess the lethality and intent of a suicide attempt measuring the life risk derived from it and the likelihood of a rescue intervention at the time of attempt.

Socio-demographic variables included age (defined as the age at the index episode), sex, profession, current working status, marital status, number of children (if any) and educational level. Family history of suicidal behaviour, age at the first suicide attempt and violence of the suicide attempt were also measured. Psychiatric diagnoses were classified in the following categories: mood disorder, specifying depression or bipolar disorder, anxiety disorders, obsessive-compulsive disorder, alcohol or drug misuse, psychotic disorders, eating disorders, somatoform disorders, and adjustment disorders. Items from the Risk-Rescue Rating (Weissman & Worden, 1974) and the Beck Suicide Intent Scale (Beck *et al.*, 1974) provided the rest of variables included. Frequent suicide attempt was the variable of interest.

Data analysis

Our objective was to study the causal structure of the data, using only the registered variables and avoiding *a priori* assumptions. Our approach is based on Bayesian networks: an inferential exploration of the relationships among variables and the description of these relationships upon discovery. The observed data served to compute probabilistic graphs formed by nodes (random variables) and edges (direct relationships between the variables). Causal influence is represented as an edge between the parent and the descendant nodes. Variables at the parent level are conditionally independent; therefore a probability distribution can be calculated for the target variable for each

parent node regardless of the others. The definition of causality we use is based exclusively on the manipulation criterion: "if we had a way of setting just the values of A and then measuring B, the causal influence of A on B will be reflected as a change in the conditional distribution of B" (Mani *et al.*, 2007).

In the first step, we searched for the Markov Blanket (MB) of the variable of interest: frequent SA. The MB encompasses all statistically relevant information about the target variable (Guyon *et al.,* 2007). When searching for the MB, the aim is to identify the minimal set of variables that will make the target statistically independent of the remaining variables. This task was executed with the Incremental Association Markov Blanket (IAMB) algorithm (Tsamardinos *et al.*, 2003). IAMB identifies the variables of the MB by incrementally maximizing the mutual information connecting the variables and the target given a tentative MB. Patients with more than 10% of unknown variable values were excluded in a pre-processing step. For those remaining patients with missing data, the algorithm introduces a new state to take into account the uncertainty in the variable. A Support Vector Machine (SVM) was used to automatically classify the number of suicide attempts in a binary fashion: history of 1 or 2 SA [value=0] versus history of > 2 attempts [value=1], following the variables in the MB. Data was divided into one training and one test set. The SVM was trained with the training set, using a 10-fold cross validation. Once the SVM generated a classifying algorithm, the test set was employed to measure the performance of the classifier.

In the second step, following identification of relevant features, a Max-Min Hill-Climbing (MMHC) algorithm was used with these variables to build a probabilistic graph for the variable "frequent SA." The software for CD can be publicly obtained (www.dsl-lab.org) (Aliferis *et al.*). To maintain independence assumptions, the "marital status" variable was excluded from the analysis due to its high cardinality. After

building a pathway for the variable "Frequent SA," we explored the risk associated with its parent and descendant nodes. The *a priori* probabilities represent the knowledge about a variable before any data have been observed and were calculated using a bootstrap approach. Finally, the ROC curve of the classifier was also computed. Further details on the methods can be found in the supplementary material.

Results

General characteristics of the population

A detailed description can be seen in Table 1. Two thirds of the subjects were females. The mean age of the participants was 38.5 years (SD 19.8). 732 subjects had a history of 1 or 2 SAs (36.8% males and 63.2% females), while 617 had a history of > 2 attempts (27.6% males and 72.4% females). Violent attempts comprised approximately 10% of the sample. 41% of the sample was single and another 33% married. Almost half of the suicide attempters (45.2%) had completed secondary education, and another 29.8% had university studies. Most of the attempters were employed (57%) and one third of the sample was unemployed at the time of index SA (28%). The most common diagnoses in the sample were mood disorders, followed by anxiety disorders (87.2% and 52.5% respectively).

First Step – Markov Blanket

The Markov Blanket for frequent SA contained the following variables. Age at the time of the index attempt, divided in three categories (before 35 years; 35 - 64 years; after 65 years), was the variable obtaining the highest precision (75.8%) and specificity (97.1%) and the lowest sensitivity (51.4%) in this task. Presence or absence of a concomitant anxiety disorder was the variable with the lowest precision (67.6%) and specificity

(67.9%) but, together with alcohol and drug use diagnosis, had the highest sensitivity (67.1%) among variables selected by the model. The selected variables, together with the precision, sensitivity and specificity values attained by each of them, are listed in Table 2. The area under a Receiver Operating Curve (ROC) of the classifier illustrates these results (Figure 2).

Second Step - Probabilistic graph

The parent variables of "Frequent SA" found by the model were "anxiety disorder", "age" (at the index episode), and "age at first SA" (1= < 35 years; 2= 35-64 years; 3= ≥ 65 years). The descendant variables of "Frequent SA" were "alcohol and drug use diagnosis", and "treatment required" (Risk factor for Weissman and Worden's scale: First aid, ER; Medical admission; Intensive care Unit). "Age at first SA" was also a parent of "treatment required". The full pathway for the variable "Frequent SA" is shown in Figure 1 and detailed results are shown in Table 3.

The *a priori* probability found in the sample for having more than 2 SA ("Frequent SA") was 45.7% (95% CI = 43.0-48.3); and for having 1 or 2 SA was 54.3% (95% CI = 51.7-56.9).

Compared to subjects who were younger at index SA, the risk of having frequent SAs was increased among the middle-aged (OR=1.59; 95% CI=1.28-1.99), but decreased among the older subjects (OR=0.52; 95% CI=0.33-0.81). The risk of frequent SAs decreased as age at first attempt advanced from younger to middle-aged (OR=0.67; 95% CI=0.54-0.84) and older subjects (OR=0.10; 95% CI=0.06-0.17).

The risk of frequent SAs was significantly increased in patients with anxiety disorders (OR=4.06; 95% CI=3.19-5.16), in particular among elderly patients (age>65) (OR =

19.51; 95% CI = 4.70-80.75), followed by the younger ones (age<35) (OR = 5.46; 95% CI = 3.83-7.79) and the middle-aged group (age 35-65) (OR = 2.91; 95% CI = 2.13-3.98). Among patients without anxiety disorders, the risk of frequent SAs was increased among the middle-aged group (OR = 2.34; 95% CI = 1.66-3.31) compared to the younger group.

Frequent attempters showed a higher risk of intensive care unit hospitalization when compared both to first aid/ER attention (OR = 2.25; 95% CI = 1.66-3.05) and inpatient admission to a different hospital department (medical admission; OR = 3.28; 95% CI = 2.31-4.67). However, frequent attempters had a higher risk of requiring first aid/ER attention than medical admission (OR = 1.46; 95% CI = 1.08-1.96).

Finally, frequent SA was associated with an increased risk of alcohol or substance use disorder when no concomitant anxiety disorder was present (OR=3.21; 95% CI=2.19-4.69).

Discussion

Pathway of frequent suicide attempts

In the present study, bioinformatics techniques were used on a large dataset of suicide attempters to investigate the relationships between variables associated with frequent SA. The direction and strength of these associations was calculated from probability estimates. The frequent SA variable presented parent (anxiety disorder, age at index evaluation, and age at the time of first SA) and descendant variables (diagnoses of alcohol and substance use disorders and intensity of the medical treatment required.)

In agreement with previous studies (Christiansen & Jensen, 2007; Corcoran et al., 2004), subjects older than 35 at their first attempt became frequent attempters more

rarely. This trend was especially noticeable among those in the older group. Two reasons can explain this finding: i) suicide attempts are more common in the young (Kessler *et al.*, 1999a); and ii) there is a higher risk of completed suicide among the elderly (Maris, 2002). The association of young age at first SA and anxiety disorders is also consistent with earlier investigations (Slama *et al.*, 2009). Yet, frequent SAs in the older group, particularly among women, might increase the risk for suicide completion (Bradvik & Berglund, 2009).

A second finding of clinical relevance is that the risk of frequent SAs increases when an anxiety disorder is present, particularly among young (under 35) and old (over 65) patients. The effect of anxiety on the risk of suicidal behaviours is presently under debate; even anxiety symptoms with no diagnosed anxiety disorder may increase suicidality (Diefenbach *et al.*, 2009). However, findings are inconsistent when the suicidality associated with anxiety disorders is adjusted for comorbid mental disorders (Diefenbach et al., 2009; Placidi et al., 2000). Our results suggest that age might modulate the association of anxiety with frequent SAs, independently of any other comorbid mental disorder. This view is supported by the surprising absence of bipolar disorder (BD) or depression (MD) diagnoses in the model in spite of the well-known association of BD and MD with higher risk of SAs (Chen & Dilsaver, 1996; Kessler et al., 1999b). In fact, mood disorders are the most frequent mental disorders underlying suicide behaviours. Several reasons might explain this discrepancy: firstly, the specificity of the target population (frequent attempters) may increase the relevance of other factors like anxiety disorder and perhaps personality traits (Black *et al.*, 2004); secondly, no measure on the severity of the depression or the number of lifetime episodes was included in the analysis; finally, BD is associated with more severe

attempts (Guillaume *et al.*, 2009) and may lead to complete suicide more often than repeated SAs.

An increased risk for diagnoses of alcohol and substance use disorders was found in the model among frequent attempters. In agreement with these results, frequent attempters have been shown to be more likely to receive substance abuse diagnoses than attempters without multiple attempts (Forman *et al.*, 2004). Similarly, it has been reported that suicide ideation among adolescents increases the risk of future substance use disorders (Reinherz *et al.*, 1995). Frequent SA might be a marker of distress, eventually leading to substance use disorders. This interpretation is supported in our model by the finding that anxiety is a common cause for both frequent SA and substance abuse. However, the coping strategies of suicide attempters may lead to substance use and/or frequent SA, as part of the same (sedative effects for obtaining a relief of the "psychache") or distinct processes (substance use enhanced disinhibition leads to repeated SA.)

Likewise, the risk of an increased intensity of the medical treatment required (intensive care compared to ER/medical admission) among frequent attempters would be explained if repetition escalates the severity of subsequent SAs (Haw *et al.*, 2007). Repeated deliberate self-harm (Zahl & Hawton, 2004) or SA(Christiansen & Jensen, 2007; Nordentoft, 2007) has been frequently associated with a higher risk of suicide death. Epidemiological data also supports that the severity of the SA increases with repeat attempts, possibly explaining the increased risk for subsequent completed suicide (Carter et al., 2005; Malone et al., 1995).

Frequent suicide attempt prediction

The main result of this study is that frequent SA prediction may be improved through the consideration of current age, age at onset of SA and anxiety disorders. In all age

groups, and particularly among older frequent attempters (≥65 years), there is a high risk of repetition when an anxiety disorder is present. Anxiety disorders increase the risk of presenting frequent SAs as the age of the patient advances. However, among patients without anxiety diagnoses, the risk is higher among the middle-aged. Considering only the parent variables of frequent SA (age, age at first attempt, anxiety and educational level), the results show a sensitivity of 69.3% and a specificity of 70.1% (Figure 2). These findings might be compared with a recent report that predicted the risk of a SA in the two years after a major depressive episode with above 70% sensitivity and specificity (Galfalvy *et al.*, 2008). However, the study considered a small number of predictor variables and did not include subjects with substance abuse (Galfalvy *et al.*, 2008).

The statistical correlations found in this model imply a pathway that can be used to drive future hypotheses for prospective studies. The methodology we have used in this study is commonly used in other fields to generate pathways and predict the outcome of future interventions using the existing data (Fenton & Neil, 2007). The model introduces new hypotheses on the determinants of frequent SA, namely the effect of age and anxiety disorders, and a new methodology to evaluate interventions in mental health.

Strengths and limitations

The findings of this study should be interpreted considering several limitations. First, it is a naturalistic cross sectional study. Moreover, it cannot be ruled out that the temporal proximity between assessment and attempt could have affected the recollection of data. Secondly, causal claims are beyond the scope of the study, which was intended to suggest future hypothesis testing. Finally, some relevant variables were insufficiently

considered in our model. Borderline personality disorder (BPD) diagnosis was not included due to the absence of a personality assessment of the sample. We also lacked a measure of severity of the depressive episodes. Both (BPD and MD) are leading causes of non-lethal SAs (Black et al., 2004; Chen & Dilsaver, 1996).

On the other hand, the study examines a large and representative sample of treatment-seeking suicide attempters. As an example of its representativeness, sex distribution in our sample matched the commonly described 2-3 fold more frequent non-fatal suicidal behaviour among women (Kessler et al., 1999a; Weissman et al., 1999). By developing a sensitive predictive tool based on a few, easily obtainable clinical parameters, our study provides a new angle on the prediction of frequent SA. The strengths of our study also include: (i) the assessment of the same large panel of clinical variables in a large sample; (ii) the broad inclusion criteria used, making our results generalizable to other treatment-seeking populations; (iii) the use of an innovative method to analyse a large number of variables. The use of data mining techniques allowed for selection of the most relevant parameters among those investigated, and also permitted us to design a model based exclusively on mathematical results, thus avoiding any handling biases. In the future, the predictive value of this clinical tool composed of 7 variables should be tested in prospective studies.

Conclusion & perspectives

A WHO community survey found that in most places worldwide less than half of suicide attempters received medical attention (Bertolote *et al.*, 2005). However, a majority of the attempters reattempt (Bille-Brahe & Jessen, 1994). An intervention directed to all attempters after self-harm or suicidal behaviours has been suggested to be the only method for achieving a reduction of suicide risk (Owens *et al.*, 2002). The

prediction model applied in our study provides preliminary data that may eventually be used to guide studies that identify patients at risk of frequent SA. In turn, this may improve the triaging of clinical care in psychiatric facilities. Moreover, the results of this model give rise to hypotheses to be confirmed in future longitudinal prospective studies: i) suicide attempters may be more prone to develop substance abuse, starting a form of kindling for new SAs; ii) the age at first SA may determine, at least partially, the severity of the subsequent attempts; and iii) the effect of anxiety disorders on the risk for frequent SAs might be modulated by age. At a procedural level, the methods employed in this study may provide a new avenue to identify risk factors and plausible causal relationships in the prediction of other psychiatric illnesses.

References

Aliferis, C, Tsamardinos, I, & Statnikov, A. Discovery Systems Laboratory.

American Foundation for Suicide Prevention. (2009). Suicide Prevention Priorities for Health Reform.

Appleby, L, Dennehy, JA, Thomas, CS, Faragher, EB, & Lewis, G. Aftercare and clinical characteristics of people with mental illness who commit suicide: a case-control study. *Lancet* 1999a; **353,** 1397-1400.

Appleby, L, Shaw, J, Amos, T, McDonnell, R, Harris, C, McCann, K, Kiernan, K, Davies, S, Bickley, H, & Parsons, R. Suicide within 12 months of contact with mental health services: national clinical survey. *BMJ* 1999b; **318,** 1235-1239.

Asberg, M, Traskman, L, & Thoren, P. 5-HIAA in the cerebrospinal fluid. A biochemical suicide predictor? *Arch Gen Psychiatry* 1976; **33,** 1193-1197.

Baca-Garcia, E, Diaz-Sastre, C, Resa, EG, Blasco, H, Conesa, DB, Saiz-Ruiz, J, & de Leon, J. Variables Associated With Hospitalization Decisions by Emergency Psychiatrists After a Patient's Suicide Attempt. *Psychiatr Serv* 2004; **55,** 792-797.

Baca-Garcia, E, Perez-Rodriguez, MM, Basurte-Villamor, I, Saiz-Ruiz, J, Leiva-Murillo, JM, Prado-Cumplido, M, Santiago-Mozos, R, Artes-Rodriguez, A, & De Leon, J. Using data mining to explore complex clinical decisions: A study of hospitalization after a suicide attempt. *Journal of Clinical Psychiatry* 2006; **67,** 1124-1132.

Beck, AT, Beck, R, & Kovacs, M. Classification of suicidal behaviors: I. Quantifying intent and medical lethality. *American Journal of Psychiatry* 1975; **132,** 285-287.

Beck, AT, Resnik, HLP, & Lettieri, DJ. *The prediction of suicide*: Charles Press Plublishers, 1974.

Beck, AT, Steer, RA, Sanderson, WC, & Skeie, TM. Panic disorder and suicidal ideation and behavior: discrepant findings in psychiatric outpatients. *Am J Psychiatry* 1991; **148,** 1195-9.

Bertolote, JM, Fleischmann, A, De Leo, D, Bolhari, J, Botega, N, De Silva, D, Tran Thi Thanh, H, Phillips, M, Schlebusch, L, Varnik, A, Vijayakumar, L, & Wasserman, D. Suicide attempts, plans, and ideation in culturally diverse sites: the WHO SUPRE-MISS community survey. *Psychol Med* 2005; **35,** 1457-65.

Bille-Brahe, U, & Jessen, G. Repeated suicidal behavior: a two-year follow-up. *Crisis* 1994; **15,** 77-82.

Bille-Brahe, U, Kerkhof, A, De Leo, D, Schmidtke, A, Crepet, P, Lonnqvist, J, Michel, K, Salander-Renberg, E, Stiles, TC, Wasserman, D, Aagaard, B, Egebo, H, & Jensen, B. A repetition-prediction study of European parasuicide populations: a summary of the first report from part II of the WHO/EURO Multicentre Study on Parasuicide in co-operation with the EC concerted action on attempted suicide. *Acta Psychiatr Scand* 1997; **95,** 81-6.

Black, DW, Blum, N, Pfohl, B, & Hale, N. Suicidal behavior in borderline personality disorder: prevalence, risk factors, prediction, and prevention. *J Pers Disord* 2004; **18,** 226-39.

Bradvik, L, & Berglund, M. Repetition and severity of suicide attempts across the life cycle: a comparison by age group between suicide victims and controls with severe depression. *BMC Psychiatry* 2009; **9,** 62.

Brauns, ML, & Berzewski, H. Follow-up study of patients with attempted suicide. *Int J Soc Psychiatry* 1988; **34,** 285-291.
Carter, G, Reith, DM, Whyte, IM, & McPherson, M. Repeated self-poisoning: increasing severity of self-harm as a predictor of subsequent suicide. *Br J Psychiatry* 2005; **186,** 253-7.
Cedereke, M, & Ojehagen, A. Prediction of repeated parasuicide after 1-12 months. *Eur Psychiatry* 2005; **20,** 101-9.
Chen, YW, & Dilsaver, SC. Lifetime rates of suicide attempts among subjects with bipolar and unipolar disorders relative to subjects with other Axis I disorders. *Biol Psychiatry* 1996; **39,** 896-9.
Chitsabesan, P, Harrington, R, Harrington, V, & Tomenson, B. Predicting repeat self-harm in children--how accurate can we expect to be? *Eur Child Adolesc Psychiatry* 2003; **12,** 23-9.
Christiansen, E, & Jensen, BF. Risk of repetition of suicide attempt, suicide or all deaths after an episode of attempted suicide: a register-based survival analysis. *Aust N Z J Psychiatry* 2007; **41,** 257-65.
Colman, I, Newman, SC, Schopflocher, D, Bland, RC, & Dyck, RJ. A multivariate study of predictors of repeat parasuicide. *Acta Psychiatr Scand* 2004; **109,** 306-12.
Cooper, J, Kapur, N, & Mackway-Jones, K. A comparison between clinicians' assessment and the Manchester Self-Harm Rule: a cohort study. *Emerg Med J* 2007; **24,** 720-1.
Cooper, J, Kapur, N, Webb, R, Lawlor, M, Guthrie, E, Mackway-Jones, K, & Appleby, L. Suicide after deliberate self-harm: a 4-year cohort study. *Am J Psychiatry* 2005; **162,** 297-303.
Corcoran, P, Keeley, HS, O'Sullivan, M, & Perry, IJ. The incidence and repetition of attempted suicide in Ireland. *Eur J Public Health* 2004; **14,** 19-23.
Diefenbach, GJ, Woolley, SB, & Goethe, JW. The association between self-reported anxiety symptoms and suicidality. *J Nerv Ment Dis* 2009; **197,** 92-7.
Fenton, N, & Neil, ME. (2007). Managing Risk in the Modern World: Applications of Bayesian Networks. A Knowledge Transfer Report from the London Mathematical Society and the Knowledge Transfer Network for Industrial Mathematics. London: London Mathematical Society.
Forman, EM, Berk, MS, Henriques, GR, Brown, GK, & Beck, AT. History of multiple suicide attempts as a behavioral marker of severe psychopathology. *Am J Psychiatry* 2004; **161,** 437-43.
Galfalvy, HC, Oquendo, MA, & Mann, JJ. Evaluation of clinical prognostic models for suicide attempts after a major depressive episode. *Acta Psychiatr Scand* 2008; **117,** 244-52.
Gibb, SJ, Beautrais, AL, & Fergusson, DM. Mortality and further suicidal behaviour after an index suicide attempt: a 10-year study. *Aust N Z J Psychiatry* 2005; **39,** 95-100.
Guillaume, S, Jaussent, I, Jollant, F, Rihmer, Z, Malafosse, A, & Courtet, P. Suicide attempt characteristics may orientate toward a bipolar disorder in attempters with recurrent depression. *J Affect Disord* 2009.
Guyon, I, Aliferis, C, & Elisseeff, A. Causal Feature Selection, *Huan Liu and Hiroshi Motoda. Computational Methods for Feature Selection*: Chapman Hall/CRC Press, 2007.
Haw, C, Bergen, H, Casey, D, & Hawton, K. Repetition of deliberate self-harm: a study of the characteristics and subsequent deaths in patients presenting to a general

hospital according to extent of repetition. *Suicide Life Threat Behav* 2007; **37,** 379-96.
Isometsa, ET, & Lonnqvist, JK. Suicide attempts preceding completed suicide. *Br J Psychiatry* 1998; **173,** 531-535.
Johnsson Fridell, E, Ojehagen, A, & Traskman-Bendz, L. A 5-year follow-up study of suicide attempts. *Acta Psychiatr Scand* 1996; **93,** 151-7.
Kapur, N, Cooper, J, King-Hele, S, Webb, R, Lawlor, M, Rodway, C, & Appleby, L. The repetition of suicidal behavior: a multicenter cohort study. *J Clin Psychiatry* 2006; **67,** 1599-609.
Kessler, RC, Borges, G, & Walters, EE. Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. *Arch Gen Psychiatry* 1999a; **56,** 617-626.
Kessler, RC, Borges, G, & Walters, EE. Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. *Arch Gen Psychiatry* 1999b; **56,** 617-26.
Kreitman, N, & Foster, J. The construction and selection of predictive scales, with special reference to parasuicide. *Br J Psychiatry* 1991; **159,** 185-92.
Malone, KM, Haas, GL, Sweeney, JA, & Mann, JJ. Major depression and the risk of attempted suicide. *J Affect Disord* 1995; **34,** 173-185.
Mani, S, Aliferis, C, Krishnaswami, S, & Kotchen, T. Learning causal and predictive clinical practice guidelines from data. *Stud Health Technol Inform* 2007; **129,** 850-4.
Mann, JJ, Apter, A, Bertolote, J, Beautrais, A, Currier, D, Haas, A, Hegerl, U, Lonnqvist, J, Malone, K, Marusic, A, Mehlum, L, Patton, G, Phillips, M, Rutz, W, Rihmer, Z, Schmidtke, A, Shaffer, D, Silverman, M, Takahashi, Y, Varnik, A, Wasserman, D, Yip, P, & Hendin, H. Suicide prevention strategies: a systematic review. *JAMA* 2005; **294,** 2064-2074.
Mann, JJ, Waternaux, C, Haas, GL, & Malone, KM. Toward a clinical model of suicidal behavior in psychiatric patients. *American Journal of Psychiatry* 1999; **156,** 181-189.
Maris, RW. Suicide. *Lancet* 2002; **360,** 319-26.
Morton, MJ. Prediction of repetition of parasuicide: with special reference to unemployment. *Int J Soc Psychiatry* 1993; **39,** 87-99.
Nordentoft, M. Prevention of suicide and attempted suicide in Denmark. Epidemiological studies of suicide and intervention studies in selected risk groups. *Dan Med Bull* 2007; **54,** 306-69.
Nurnberger, JI, & Blehar, MC. Diagnostic interview for genetic studies: rationale, unique features and training. *Arch Gen Psychiatry* 1994; **51,** 849-859.
O'Carroll, PW, Berman, AL, Maris, RW, Moscicki, EK, Tanney, BL, & Silverman, M. Beyond the Tower of Babel: a nomenclature for suicidology. *Suicide Life Threat Behav* 1996; **26,** 237-235.
Oquendo, MA, Currier, D, & Mann, JJ. Prospective studies of suicidal behavior in major depressive and bipolar disorders: what is the evidence for predictive risk factors? *Acta Psychiatr Scand* 2006; **114,** 151-8.
Osvath, P, Kelemen, G, Erdos, MB, Voros, V, & Fekete, S. The main factors of repetition: review of some results of the Pecs Center in the WHO/EURO Multicentre Study on Suicidal Behaviour. *Crisis* 2003; **24,** 151-4.
Owens, D, Horrocks, J, & House, A. Fatal and non-fatal repetition of self-harm. Systematic review. *Br J Psychiatry* 2002; **181,** 193-9.

Pearl, J. *Causality models, reasoning, and inference*. Cambridge, New York: Cambridge University Press, 2000.

Placidi, GP, Oquendo, MA, Malone, KM, Brodsky, B, Ellis, SP, & Mann, JJ. Anxiety in major depression: relationship to suicide attempts. *Am J Psychiatry* 2000; **157,** 1614-8.

Platt, S, Bille, BU, Kerkhof, A, Schmidtke, A, Bjerke, T, Crepet, P, De, LD, Haring, C, Lonnqvist, J, & et, a. Parasuicide in Europe: the WHO/EURO multicentre study on parasuicide. I. Introduction and preliminary analysis for 1989. *Acta Psychiatr Scand* 1992; **85,** 97-104.

Preisig, M, Fenton, BT, Matthey, ML, Berney, A, & Ferrero, F. Diagnostic interview for genetic studies (DIGS): inter-rater and test-retest reliability of the French version. *Eur Arch Psychiatry Clin Neurosci* 1999; **249,** 174-9.

Reinherz, HZ, Giaconia, RM, Silverman, AB, Friedman, A, Pakiz, B, Frost, AK, & Cohen, E. Early psychosocial risks for adolescent suicidal ideation and attempts. *J Am Acad Child Adolesc Psychiatry* 1995; **34,** 599-611.

Rissmiller, DJ, Steer, R, Ranieri, WF, Rissmiller, F, & Hogate, P. Factors complicating cost containment in the treatment of suicidal patients. *Hosp Community Psychiatry* 1994; **45,** 782-8.

Rygnestad, T. A prospective 5-year follow-up study of self-poisoned patients. *Acta Psychiatr Scand* 1988; **77,** 328-331.

Sheehan, DV, Lecrubier, Y, Sheehan, KH, Amorim, P, Janavs, J, Weiller, E, Hergueta, T, Baker, R, & Dunbar, GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998; **59 Suppl 20,** 22-33.

Sidley, GL, Calam, R, Wells, A, Hughes, T, & Whitaker, K. The prediction of parasuicide repetition in a high-risk group. *Br J Clin Psychol* 1999; **38 (Pt 4),** 375-86.

Slama, F, Courtet, P, Golmard, JL, Mathieu, F, Guillaume, S, Yon, L, Jollant, F, Misson, H, Jaussent, I, Leboyer, M, & Bellivier, F. Admixture analysis of age at first suicide attempt. *J Psychiatr Res* 2009; **43,** 895-900.

Spiessl, H, Hubner-Liebermann, B, & Cording, C. Suicidal behaviour of psychiatric in-patients. *Acta Psychiatr Scand* 2002; **106,** 134-8.

Spirtes, P, Glymour, C, & Scheines, R. *Causation, Prediction, and Search* (2nd ed.). Cambridge, MA: MIT Press, 2000.

Tejedor, MC, Diaz, A, Castillon, JJ, & Pericay, JM. Attempted suicide: repetition and survival--findings of a follow-up study. *Acta Psychiatr.Scand.* 1999; **100,** 205-211.

Tsamardinos, I, Aliferis, C, & Statnikov, A. (2003). Algorithms for Large Scale Markov Blanket Discovery, *The 16th International FLAIRS Conference*. St. Augustine, Florida, USA.

Weissman, A, & Worden, J. Risk-Rescue Rating in suicide assessment. In R. H. Beck AT, Lettieri DJ (Ed.), *The Prediction of Suicide*. Philadelphia, Pa: Charles Press, 1974.

Weissman, MM, Bland, RC, Canino, GJ, Greenwald, S, Hwu, HG, Joyce, PR, Karam, EG, Lee, CK, Lellouch, J, Lepine, JP, Newman, SC, Rubio-Stipec, M, Wells, JE, Wickramaratne, PJ, Wittchen, HU, & Yeh, EK. Prevalence of suicide ideation and suicide attempts in nine countries. *Psychol Med* 1999; **29,** 9-17.

World Health Organization (WHO). (1999). Figures and Facts about Suicide. Geneva.

Zahl, DL, & Hawton, K. Repetition of deliberate self-harm and subsequent suicide risk: long-term follow-up study of 11,583 patients. *Br J Psychiatry* 2004; **185,** 70-5.

Table 1. General characteristics of the population

		Montpellier	Madrid	Total
Suicide attempters		737	612	1349
Male		209 (28.4%)	215 (35.1%)	424 (31.4%)
Female		528 (71.6%)	397 (64.9%)	925 (68.6%)
Age	Mean	40.2	36.6	38.5
	Standard deviation	13.5	14.5	19.8
Marital status	Single	214 (29.0%)	286 (46.7%)	500 (37.0%)
	Married	201 (27.2%)	210 (34.3%)	411 (30.4%)
	Separated-Divorced	166 (22.5%)	92 (15.0%)	258 (19.1%)
	Widowed	20 (2.7%)	23 (3.7%)	43 (3.2%)
	Missing data	136 (18.4%)	1 (0.2%)	137 (10.1%)
Children	No	197 (26.7%)	226 (36.9%)	423 (31.3%)
	Yes	348(47.2%)	234 (38.2%)	582 (43.1%)
	Missing data	192 (26.0%)	152 (24.8%)	344 (25.5%)
Educational level	Illiterate	0 (0.0%)	15 (2.4%)	15 (1.1%)
	Primary school	62 (8.4%)	225 (36.7%)	287 (21.3%)
	High school/ Professional training	313 (42.4%)	235 (38.4%)	548 (40.6%)
	University	232 (31.5%)	129 (21.0%)	361 (26.7%)
	Missing data	130 (17.7%)	8 (1.3%)	138 (10.2%)
Current working status	Employed	373 (50.6%)	319 (52.1%)	692 (51.3%)
	Unemployed	178 (24.1%)	166 (27.1%)	344 (25.5%)
	Permanent disability	43 (5.8%)	44 (7.2%)	87 (6.4%)
	Transient disability	0 (0.0%)	49 (8.0%)	49 (3.6%)
	Retired	2 (0.3%)	34 (5.6%)	36 (2.6%)
	Missing data	141 (19.1%)	0 (0.0%)	141 (10.4%)
Family history of suicidal behavior	No	420 (56.9%)	385 (62.9%)	805 (59.6%)
	Yes	169 (22.9%)	86 (14.0%)	255 (18.9%)
	Missing data	148 (20.0%)	141 (23.0%)	289 (21.4%)
Agent Used	Overdose. cut. stabbing	635 (86.2%)	529 (86.4%)	1164 (86.3%)
	Suffocating. drowning. hanging/strangulation	42 (5.7%)	14 (2.3%)	56 (4.1%)
	Jumping. shooting	50 (6.8%)	24 (3.9%)	74 (5.4%)
	Missing data	10 (1.3%)	45 (7.3%)	55 (4.0%)
DSM-IV diagnoses	Anxiety disorders	428 (60.5%)	141 (37.5%)	569 (52.5%)
	Mood disorders	707 (97.1%)	257 (68.2%)	964 (87.2%)
	Alcohol or substances misuse disorders	213 (29.5%)	113 (29.8%)	326 (29.6%)
	Psychotic disorders	15 (2.1%)	21 (5.6%)	36 (3.3%)
	Major depressive disorders	553 (76.0%)	244 (64.7%)	797 (72.1%)
	Bipolar disorders	154 (21.2%)	13 (3.4%)	167 (15.1%)
	Eating disorders	66 (11.1%)	48 (12.8%)	114 (11.7%)
	Obsessive-compulsive disorder	42 (6.0%)	7 (1.9%)	49 (4.6%)

Table 2. Markov Blanket for frequent suicide attempts according to the IAMB algorithm.

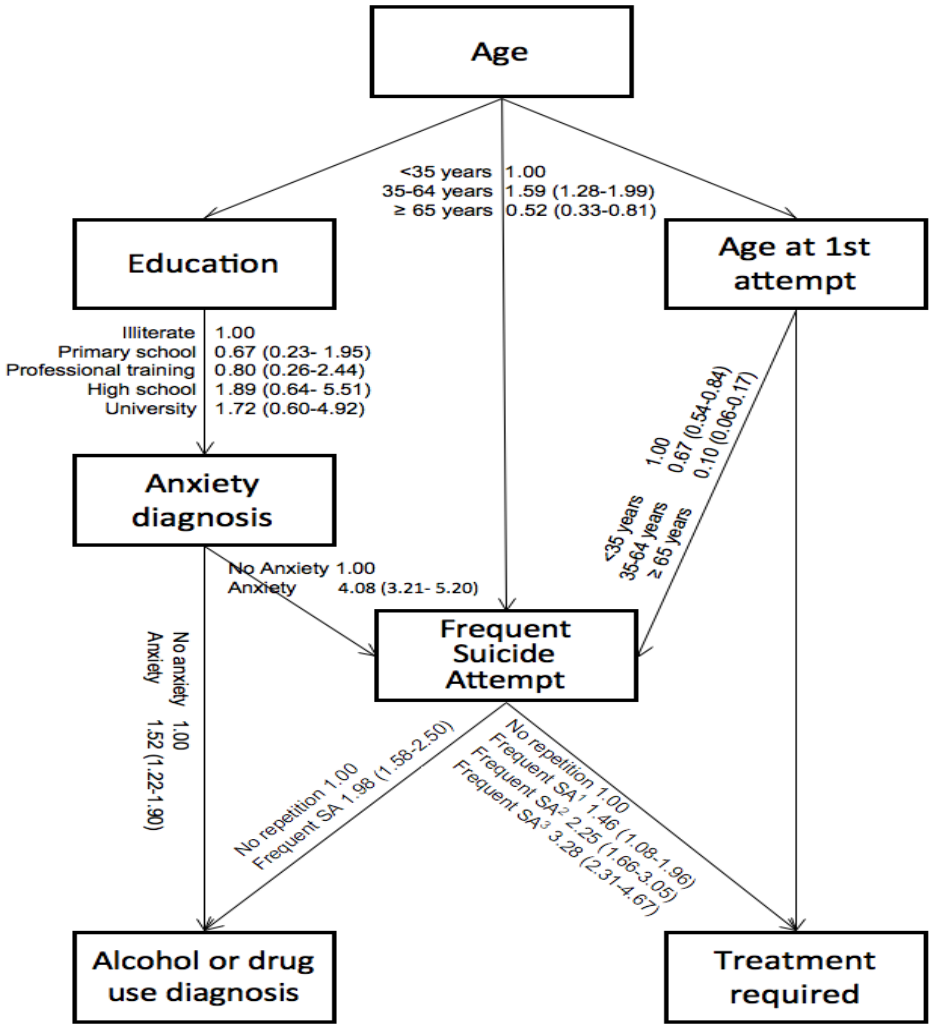
	Precision (%)	Sensitivity (%)	Specificity (%)
Anxiety disorder	67.6	67.1	67.9
Marital status	70.0	65.2	74.2
Alcohol and substance use disorder	70.7	67.1	73.8
Degree of premeditation of the attempt	72.2	55.2	87.1
Age at the first attempt	70.2	64.3	75.4
Accessibility to rescue	72.4	63.3	80.4
Level of Education	72.4	63.3	80.4
Treatment Required after the SA	72.9	60.0	84.2
Expectations about the lethality of the attempt	74.9	65.7	82.9
Age	75.8	51.4	97.1

Table 3. Risk associated with the main variables in the Markov Blanket

Main variable	Class	OR	95% CI		Contrast variable
			Left	Right	
Age	1 (< 35)	1	-	-	Frequent SA
	2 (35-64)	1.59	1.28	1.99	
	3 (≥ 65)	0.52	0.33	0.81	
Age (Anxiety disorder absent)	1 (< 35)	1	-	-	Frequent SA
	2 (35-64)	2.34	1.66	3.31	
	3 (≥ 65)	0.37*	0.12	1.07	
Age (Anxiety disorder present)	1 (< 35)	1	-	-	Frequent SA
	2 (35-64)	1.25*	0.90	1.72	
	3 (≥ 65)	1.32*	0.48	3.60	
Age at first attempt	1 (< 35)	1	-	-	Frequent SA
	2 (35-64)	0.67	0.54	0.84	
	3 (≥ 65)	0.10	0.06	0.17	
Education	1 (Illiterate)	1	-	-	Anxiety disorder
	2 (Primary school)	0.67*	0.23	1.95	
	3 (Professional training)	0.80*	0.26	2.44	
	4 (High school)	1.89*	0.64	5.51	
	5 (University)	1.72*	0.60	4.92	
Anxiety disorder	0 (No)	1	-	-	Frequent SA
	1 (Yes)	4.06	3.19	5.16	
Anxiety disorder (age < 35)	0 (No)	1	-	-	Frequent SA
	1 (Yes)	5.46	3.83	7.79	
Anxiety disorder (age 35-64)	0 (No)	1	-	-	Frequent SA
	1 (Yes)	2.91	2.13	3.98	
Anxiety disorder (age ≥ 65)	0 (No)	1	-	-	Frequent SA
	1 (Yes)	19.51	4.70	80.75	
Frequent SA	0 (1-2 SA)	1	-	-	Alcohol and substance use disorder
	1 (>2 SA)	1.96	1.50	2.56	
Frequent SA (Anxiety disorder absent)	0 (1-2 SA)	1	-	-	Alcohol and substance use disorder
	1 (>2 SA)	3.21	2.19	4.69	
Frequent SA (Anxiety disorder present)	0 (1-2 SA)	1	-	-	Alcohol and substance use disorder
	1 (>2 SA)	1.10*	0.77	1.58	
Frequent SA	0 (1-2 SA)	1	-	-	Treatment Required (First aid/ER; Medical admission)
	1 (>2 SA)	1.46	1.08	1.96	
Frequent SA	0 (1-2 SA)	1	-	-	Treatment Required (Intensive care Unit; First aid/ER)
	1 (>2 SA)	2.25	1.66	3.05	
Frequent SA	0 (1-2 SA)	1	-	-	Treatment Required (Intensive care Unit; Medical admission)
	1 (>2 SA)	3.28	2.31	4.67	

* Non significant.

Figure 1. Pathway of Frequent SA*



∗ Odds ratios are indicated including CI in brackets near the edges. Odds ratios were calculated only when at least one of the variables was binary.

1 Risk estimate comparing First aid/ER with Medical admission

2 Risk estimate comparing Intensive care Unit with First aid/ER

3 Risk estimate comparing Intensive care Unit with Medical admission

Figure 2. The Receiver Operating Curve (ROC) shows the classification of suicide attempt repetition using our model. Average area under the curve (AUC): 71.67